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Revealing the Electrophilicity of N-Ac Indoles with $FeCl_3$: a mechanistic study

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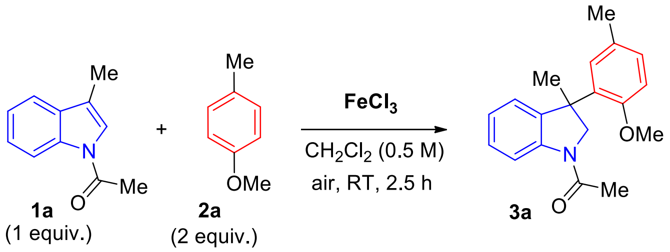

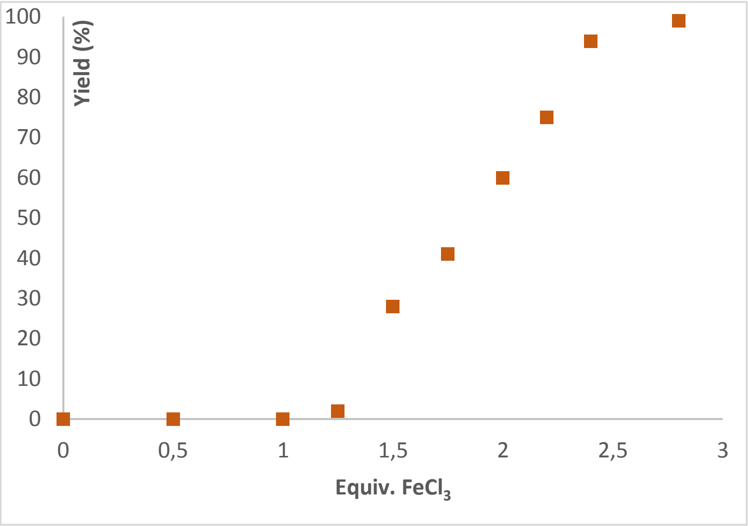

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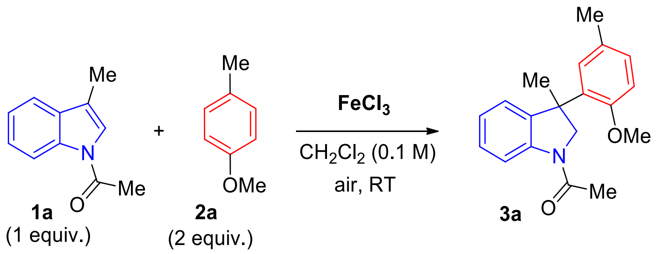
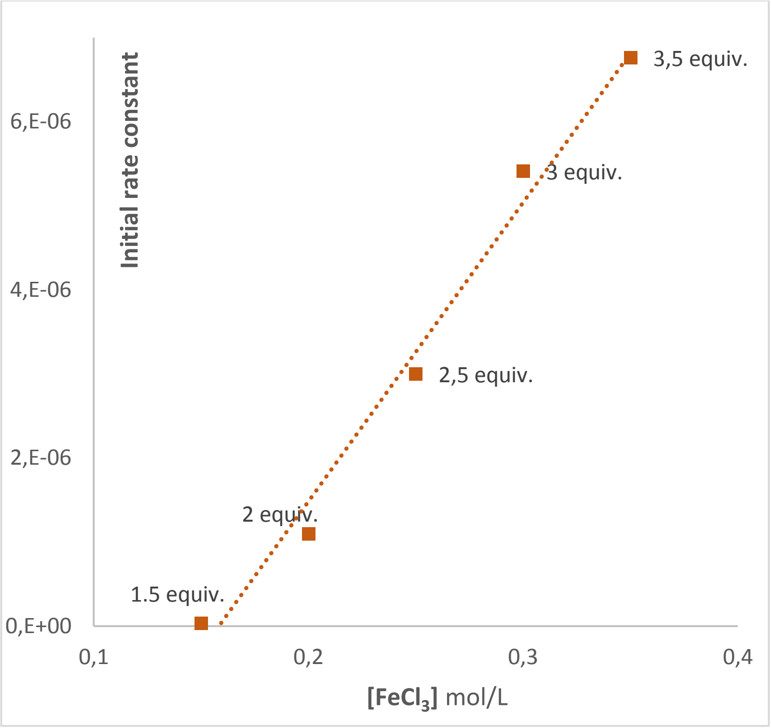
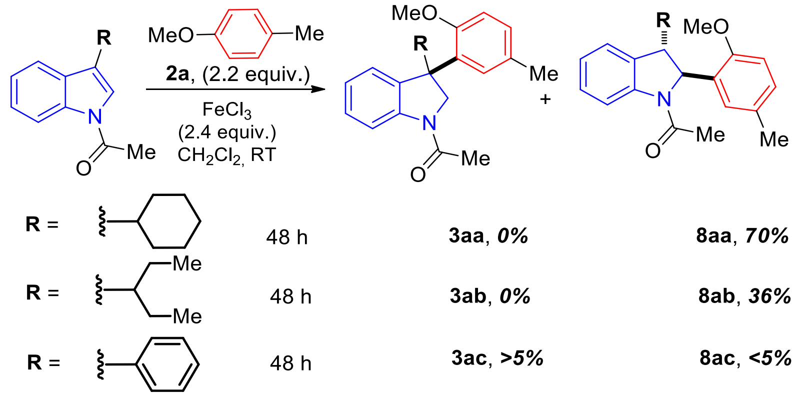
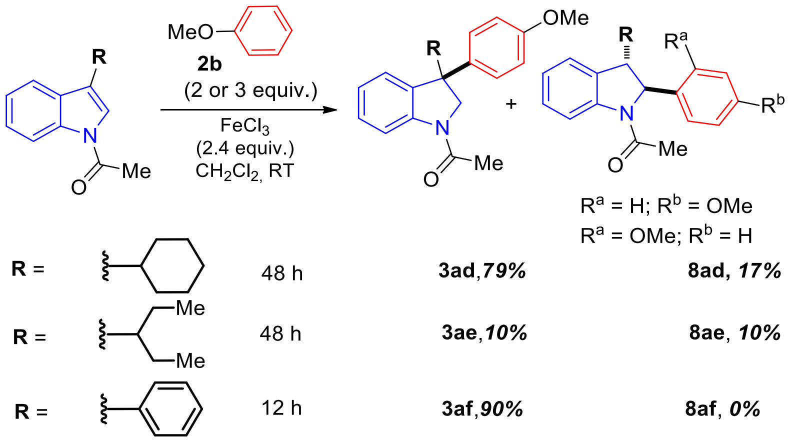




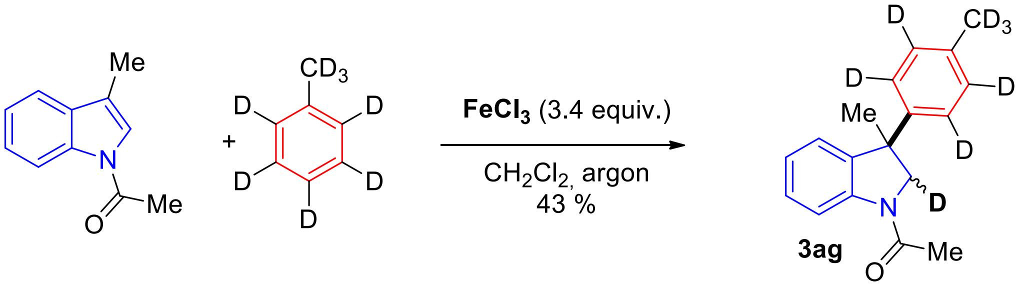
I.3 Influence of the C3-substituent on the hydroarylation.

Influence of the nature of the 3-substituent on the reactivity and regioselectivity





I.4 Hydroarylation with d8-toluene



I.5 X-ray crystallography and electron density topology

X-ray Data Collection. The crystallographic data of N-Ac skatole and its iron complex were collected at 100.0(1) K on a Kappa CCD APEX II diffractometer using graphite monochromated MoKα X-radiation (λ = 0.71073 Å). The data spots were recorded as ω–scans (Δω = 1.0°) in order to reconstruct accurate three dimensional diffracted intensity peak profiles. 12927 (N-Ac skatole) and 30319 (iron complex) unique reflections were collected up to a resolution of $\sin\theta_{\max}/\lambda = H/2 = 1.2$ Å^{-1}, where H is the Bragg vector modulus. An empirical absorption correction was applied using SADABS[1] computer program for the two data sets. SORTAV[2] program was used for sorting and averaging data revealing the excellent quality of the measurements (internal R_{int} = 0.0379 (N-Ac skatole **1a**) and 0.0486 (iron complex **6a**) with average data redundancy equal to 6.6 (N-Ac skatole **1a**) and 4.5 (iron complex **6a**)). Details of the X-ray diffraction experiment conditions and the crystallographic data for the two compounds are given below.

Data Collection and Refinement Details.

	N-Ac skatole **1a**	Iron complex **6a**
Empirical formula	$C_{11}ONH_{11}$	$FeCl_3C_{22}O_2N_2H_{22}$
Formula weight	173.2	508.6
Temperature (K)	100.0(1)	100.0(1)
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
Unit cell dimensions	a = 7.1804(2) Å	a = 7.2974(3) Å
	b = 15.7374(5) Å	b = 19.7534(8) Å
	c = 8.4332(3) Å	c = 15.4873(6) Å
	α = 90.00°	α = 90.00°
	β = 110.775(1)°	β = 101.063(2)°
	γ = 90.00°	γ = 90.00°
Volume	891.00(4)	2190.98(9) Å^3
Z	4	4
Density (calculated) (Mg/m^3)	1.290	1.540
Absorption coefficient (mm^{-1})	0.083	1.076
$[(\sin\theta)/\lambda]_{\max}$ (Å^{-1})	1.23	1.20
# Collected reflections	85100	135523
# Independent reflections	12927 [R_{int} = 0.0379]	30319 [R_{int} = 0.0486]
Spherical Refinement		
R_1, wR_2, gof [I>2sigma(I)]	0.0418, 0.1409, 1.023	0.0353, 0.0917, 1.015
Multipole Refinement		
R_1(F), wR_2(F), gof [I>3sigma(I)]	0.0268, 0.0223, 1.048	0.0226, 0.0232, 0.997

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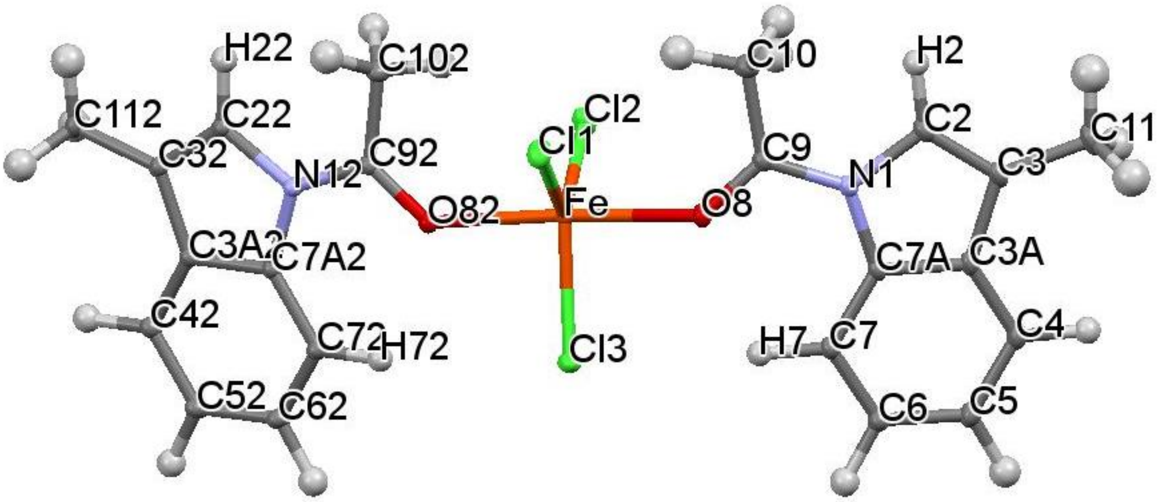
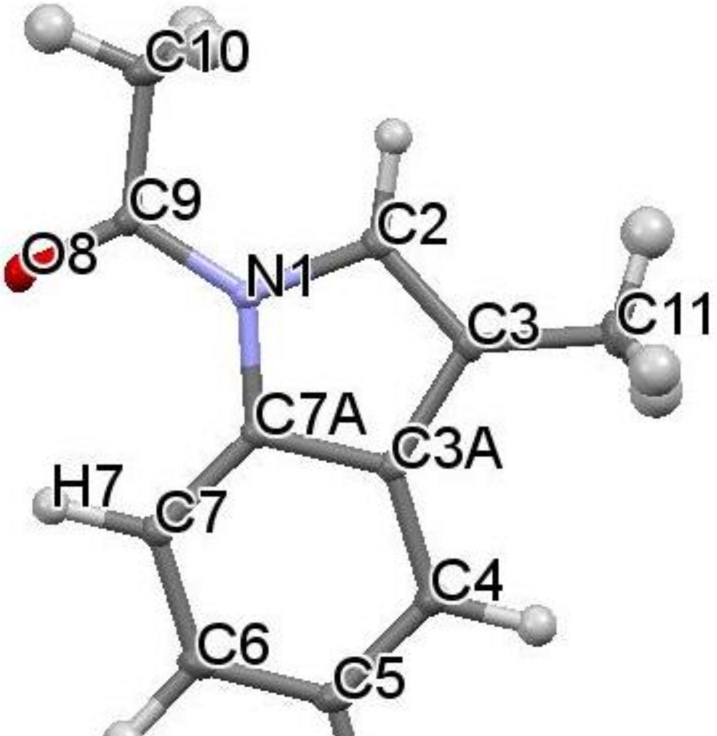
[1] S*ADABS* (Version 2.10). George Sheldrick, University of Göttingen, 2003

[2] Blessing, R. H. *J. Appl. Crystallogr.* **1997**, *30*, 421.

X-ray crystal structure of iron complex 6a with the numbering scheme.



X-ray crystal structure of N-Ac skatole 1a with the numbering scheme.



Spherical and Electron Density Refinements. The crystal structures of the two compounds were solved using SIR94 program[3] and refined using SHELX97[4] implemented in WinGX[5] package. For the electron density refinements, the Hansen-Coppens model[6] was used. The frozen core and normalized valence spherical densities are obtained from the Hartree-Fock wave functions of the free atoms or ions.[7] The aspherical part of the pseudo-atom electron density is described by real normalized harmonics $y_{lm\pm}$ basis set (l = 0 (monopole) to 4 (hexadecapole)) and modulated by a Slater-type radial function $R_{nl}(r) = Nr^{n_l}\exp(-\xi_l r)$, where N is a normalization factor. The exponents ξ_l (in bohr^{-1}) of the radial functions are chosen equal to 3.176, 4.466, 3.839, 4.259, 7.450, for C (n_l = 2, 2, 3 up to octupoles (l = 3)), O (n_l = 2, 2, 3 up to octupoles (l = 3)), N (n_l = 2, 2, 3 up to octupoles (l = 3)), Cl (n_l = 4, 4, 6 up to octupoles (l = 3)) and Fe (n_l = 4, 4, 4 up to hexadecapoles (l = 4)) atoms, respectively; ξ_l = 2.00 bohr^{-1} and n_l = 1 (dipole level, l = 1) for the hydrogen atoms. MOPRO program[8] was used for the electron density refinements against all the structure factors F with no statistical standard deviations based cut-off ($I > 0$). Indeed, this program combines both conventional and conjugated gradient least-square procedures and requires all observed diffraction intensities. To obtain accurate atomic positions and atomic displacement parameters (ADP's) for non-H atoms, a high-order refinement was carried out using data with $\sin\theta_{\max}/\lambda > 0.8$ Å^{-1}; corresponding parameters for hydrogen atoms were refined against all data. In the first cycles of the refinements, chemical constraints on the multipole parameters were imposed for equivalent atoms of the two compounds.

Electron Density Topology, Atomic Charges and Experimental Electrostatic Potential. Topological features of the total electron density $\rho(\mathbf{r})$ were revealed using the AIM (Atoms In Molecules) theory of Bader.[9] This analysis allows a quantitative description of the bonds and the electronic structure of atoms in molecules through the gradient and the Laplacian $\nabla^2\rho$ of the total electron density. The gradient of the electron density $\nabla\rho(\underline{\mathbf{r}}_{CP})$ vanishes at the critical points (CP) corresponding to the extrema and saddle points of $\rho(\mathbf{r})$. Each CP is therefore characterized by two numbers: the number of the eigenvalues (for non-degenerating cases) and the signature of the eigenvalues triplet (λ_1, λ_2, λ_3). The ellipticity defined by $\varepsilon = (\lambda_1/\lambda_2 - 1)$ is an index of the type of the chemical bonds (σ or π). Atomic charges were obtained after the multipole refinement of the electron density. These charges correspond to the integration of the total electron density over the atomic basins defined in the theory of Bader.[14] The electrostatic potential is based on the Hansen-Coppens electron density model.[11, 13] This important property exhibits the nucleophilic (negative potential) and electrophilic (positive potential) regions of the molecule and is a good indicator of the chemical reactivity. Topological features of the electron density, atomic charges and experimental electrostatic potential were obtained using VMOPRO program.[13]

Crystal Structures. The same atomic labels were used for the N-Ac skatole and its iron complex. The main geometrical features of the two compounds are listed below. The bond distances for the two iron-linked

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[3] Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A. *J. Appl. Crystallogr.* **1993**, *26*, 343.

[4] Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112.

[5] Farrugia, L. J. *WinGX* (Version 1.80.03). *J. Appl. Crystallogr.* **1999**, *32*, 837.

[6] Hansen, N. K.; Coppens, P. *Acta Crystallogr.* **1978**, *A34*, 909.

[7] (a) Clementi, E.; Roetti, C. Atomic data and Nuclear data tables. Academic press, New York, USA, 1974, 14, 177; (b) Clementi, E.; Raimondi, D.L. *J. Chem. Phys.* **1963**, *41*, 2686.

[8] (a) Guillot, B.; Viry, L.; Guillot, R.; Lecomte, C.; Jelsch, C. *J. Appl. Crystallogr.* **2000**, *34*, 214; (b) Jelsch, C.; Guillot, B.; Lagoutte, A.; Lecomte, C. *J. Appl. Crystallogr.* **2005**, *38*, 38.

[9] Bader, R. F. W. *Atoms in Molecules – A Quantum Theory*; Clarendon Press: Oxford, 1990.

molecules are very comparable. When we compare the N-Ac skatole molecule **1a** and its iron complex **6a**, the main differences are found for C9=O8, C9-N1, C2=C3, C2-N1 bonds. The C9=O8 double bond distances of the carbonyl groups of the iron complex **6a** (1.2435 and 1.2437 Å) are longer than the corresponding one in N-Ac skatole **1a** (1.2203 Å). In contrast, the C9-N1 bond distance is shorter for the complex **6a** (1.3534 or 1.3551 Å) than those in the free molecule **1a** (1.3857 Å). It is diagnostic of the more important delocalization of the nitrogen lone pair in the C9=O8 carbonyl for the iron complex **6a** compared to N-Ac skatole **1a**. In addition, the C2=C3 double bond distances are slightly shorter for the complex **6a** (1.3498 and 1.3517 Å) than the one in the isolated molecule **1a** (1.3572 Å), while the C2-N1 bond distance are slightly longer for the complex **6a** (1.4154 and 1.4163) than the one in **1a** (1.4077 Å). It indicates that in the case of the iron complex **6a**, the nitrogen lone pair is indeed less delocalized in the N1-C2=C3 enamide system in comparison to N-Ac skatole **1a**. In the iron complex, we can notice that the Fe-O bond distance (2.09 Å in average) is short compared to the Fe-Cl one (2.21 Å in average). Also, the O-Fe-O and Cl-Fe-Cl bond angle values reveal a slight distortion of the metal coordination polyhedron (bottom).

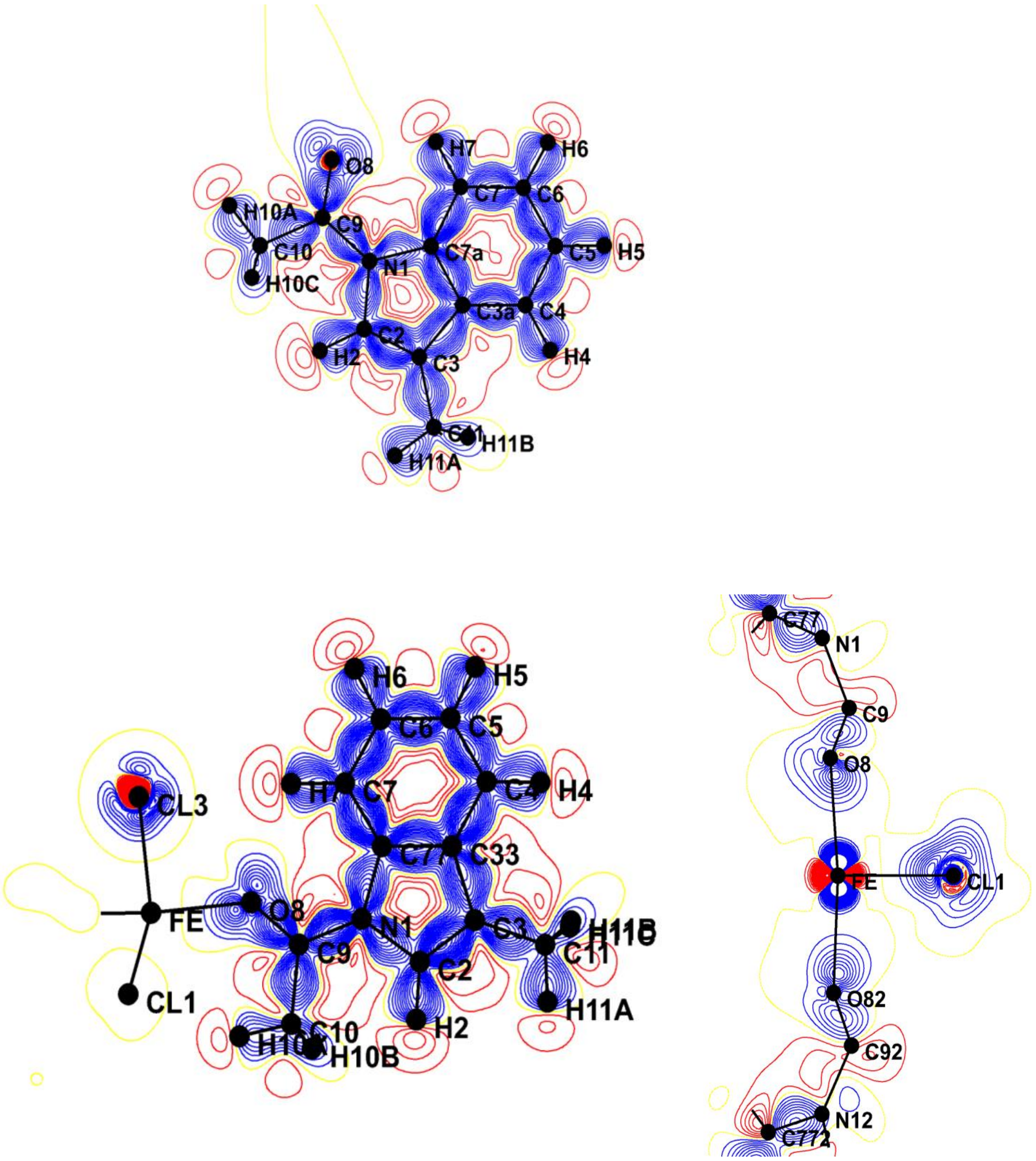
Selected bond lengths (Å) and angles (°). The particular features are indicated in bold.
Standard deviations are given in parentheses.

N-Ac skatole **1a**		Iron complex **6a**			
C9 - O8	**1.2203(1)**	**C9 - O8**	**1.2435(2)**	**C92 - O82**	**1.2437(2)**
C9 - N1	**1.3857(1)**	**C9 - N1**	**1.3534(2)**	**C92 - N12**	**1.3551(2)**
C9 - C10	1.5033(1)	C9 - C10	1.4912(2)	C92 - C102	1.4948(2)
C2 - N1	1.4077(1)	C2 - N1	1.4154(2)	C22 - N12	1.4163(2)
C2 - C3	**1.3572(1)**	**C2 - C3**	**1.3498(2)**	**C22 - C32**	**1.3517(2)**
C3 - C3a	1.4459(1)	C3 - C3a	1.4521(2)	C32 - C3a2	1.4520(2)
C3 - C11	1.4883(1)	C3 - C11	1.4857(2)	C32 - C112	1.4859(2)
C3a - C7a	1.4096(1)	C3a - C7a	1.4053(2)	C3a2 - C7a2	1.4059(2)
C3a - C4	1.3961(1)	C3a - C4	1.3935(2)	C3a2 - C42	1.3941(2)
C4 - C5	1.3904(1)	C4 - C5	1.3901(2)	C42 - C52	1.3906(2)
C5 - C6	1.4040(1)	C5 - C6	1.3991(2)	C52 - C62	1.3977(2)
C6 - C7	1.3943(1)	C6 - C7	1.3941(2)	C62 - C72	1.3951(2)
C7 - C7a	1.3938(1)	C7 - C7a	1.3916(2)	C72 - C7a2	1.3902(2)
C7a - N1	1.4030(1)	C7a - N1	1.4126(2)	C7a2 - N12	1.4128(2)
				O8 - Fe	2.0988(1)
				O82 – Fe	2.0867(1)
				Cl1 – Fe	2.2143(1)
				Cl2 – Fe	2.2166(1)
				Cl3 – Fe	2.2180(1)
				O8 - Fe - O82	**173.75(1)**
				Cl1 - Fe - Cl3	**120.674(8)**
				Cl1 - Fe - Cl2	**116.369(7)**
				Cl2 - Fe - Cl3	**122.953(7)**

<u>*Static Electron Densities and Topological Features.*</u> Below are displayed the static electron deformation densities of the two compounds. The atomic bond covalent character of the organic part of the two compounds is clearly shown. As expected, the electron concentration in the C2=C3 double and the C=O bonds is slightly higher than for the other C-C, C-H and C-N bonds. Furthermore, for the two compounds the electron density oxygen lone pairs are clearly depicted. In the iron complex, these lone pairs are polarized toward the metal atom for both O8

and O82 as shown. The chlorine electron density is also polarized toward the Fe ion which displays electron concentration lobes in the direction of the oxygen atoms and electron depletion ones toward the chlorine atoms.

Static electron deformation density for the N-Ac skatole 1a (top) and the iron complex 6a (bottom).
Contours are ± 0.05 eÅ^{-3}, negative contours are in red.



As described in the previous section, the total electron density was analyzed using the AIM theory.[14] The topological properties of the atomic bonds are listed in below. In the Bader's theory, negative Laplacian values at the bond critical point (CP) indicate shared-shell (or covalent) interactions. In contrast, positive Laplacian values correspond to closed-shell (or ionic) interactions. Such interactions are observed in the vicinity of the iron ion. As shown in next table, both O-Fe and Cl-Fe exhibit the same properties ($\rho = 0.47$ eÅ^{-3}, $\nabla^2\rho = 7.34$ eÅ^{-5} and ε close to 0.0). All the bonds in the organic parts are characterized by negative Laplacian of the electron density. It is worthy to note that, during the metal complexation, the sensitive parts of the N-Ac skatole are the C9-O8 and C9-

N1 bonds. Both the electron density and the Laplacian values at the bond critical point are higher for the C9-N1 bond ($\rho = 2.099$ eÅ^{-3}, $\nabla^2\rho = -21.03$ eÅ^{-5} in N-Ac skatole compared to the iron complex ($\rho = 2.360$ and 2.297 eÅ^{-3}, $\nabla^2\rho = -26.27$ and -22.24 eÅ^{-5}). For the C9-O8 bond, the isolated molecule exhibit a significant higher electron density peak ($\rho = 2.951$ eÅ^{-3} compared to 2.795 and 2.757 eÅ^{-3} for the complex); the Laplacian, however, is slightly lower ($\nabla^2\rho = -27.46$ compared to -29.82 and -27.93 eÅ^{-5} for the complex). For the other bonds in the organic parts, we found the highest values of both ρ and $\nabla^2\rho$ in the aromatic rings. Among these bonds, C2-C3 one displays large values of ρ and $\nabla^2\rho$ (2.314 eÅ^{-3} and –21.38 eÅ^{-5} in N-Ac skatole; 2.387, 2.371 eÅ^{-3} and -23.56, -22.43 eÅ^{-5} for the complex). For this last bond, we can notice that both ρ and $\nabla^2\rho$ are enhanced in the iron complex. Moreover, for the studied compounds, all the bonds having high peaks of electron density also exhibit high values of ellipticities ε corresponding to the π-character. The highest values were found for C2-C3 bond ($\varepsilon = 0.28$ (N-Ac skatole), $\varepsilon = 0.30$ and 0.32 (iron complex)). The lowest values (close to 0.0) were found for both C-H in the organic part, Fe-O and Fe-Cl bonds.

Topological properties of N-Ac skatole 1a and the Iron complex 6a.

$\rho(\underline{r}_{CP})$ (in eÅ^{-3}) and $\nabla^2\rho(\underline{r}_{CP})$ (in eÅ^{-5}) are the electron density and the Laplacian values at the critical points (CP); ε is the ellipticity of the bond. High values of ρ and $\nabla^2\rho$ are given in bold.

N-Ac skatole **1a**				Iron complex **6a**							
Bond	$\rho(\underline{r}_{CP})$	$\nabla^2\rho(\underline{r}_{CP})$	ε	Bond	$\rho(\underline{r}_{CP})$	$\nabla^2\rho(\underline{r}_{CP})$	ε	Bond	$\rho(\underline{r}_{CP})$	$\nabla^2\rho(\underline{r}_{CP})$	ε
C9 - C10	1.769	-13.04	0.09	C9 - C10	1.811	-14.06	0.06	C92 - C102	1.790	-13.16	0.09
C9 - N1	**2.099**	**-21.03**	**0.15**	**C9 - N1**	**2.360**	**-26.27**	**0.20**	**C92 - N12**	**2.297**	**-22.24**	**0.10**
C9 - O8	**2.951**	**-27.46**	**0.10**	**C9 - O8**	**2.795**	**-29.82**	**0.09**	**C92 - O82**	**2.757**	**-27.93**	**0.06**
C10 - H10A	1.700	-14.90	0.07	C10 - H10A	1.715	-16.01	0.09	C102 - H102A	1.716	-18.32	0.10
C10 - H10B	1.766	-15.43	0.08	C10 - H10B	1.713	-16.91	0.07	C102 - H102B	1.691	-16.33	0.09
C10 - H10C	1.700	-15.25	0.05	C10 - H10C	1.770	-16.71	0.07	C102 - H102C	1.709	-15.71	0.08
C2 - H2	1.775	-19.44	0.07	C2 - H2	1.776	-19.42	0.00	C22 - H22	1.862	-22.12	0.06
C2 - C3	**2.314**	**-21.38**	**0.28**	**C2 - C3**	**2.387**	**-23.56**	**0.30**	**C22 - C32**	**2.371**	**-22.43**	**0.32**
C2 - N1	1.985	-15.40	0.17	C2 - N1	1.957	-14.84	0.11	C22 - N12	1.965	-14.62	0.22
C3 - C3a	1.941	-14.17	0.15	C3 - C3a	1.944	-14.70	0.11	C32 - C3a2	1.939	-14.56	0.09
C3 - C11	1.786	-12.80	0.08	C3 - C11	1.783	-13.39	0.11	C32 - C112	1.775	-12.48	0.06
C3a - C4	**2.115**	**-18.68**	**0.20**	**C3a - C4**	**2.142**	**-18.75**	**0.22**	**C3a2 - C42**	**2.166**	**-19.47**	**0.26**
C3a - C7a	**2.114**	**-17.76**	**0.20**	**C3a - C7a**	**2.146**	**-17.67**	**0.21**	**C3a2 - C7a2**	**2.165**	**-17.75**	**0.15**
C4 - H4	1.778	-17.66	0.04	C4 - H4	1.739	-16.95	0.05	C42 - H42	1.816	-18.18	0.05
C4 - C5	**2.172**	**-19.83**	**0.19**	**C4 - C5**	**2.119**	**-18.69**	**0.19**	**C42 - C52**	**2.193**	**-20.41**	**0.22**
C5 - H5	1.765	-17.16	0.06	C5 - H5	1.830	-18.86	0.06	C52- H52	1.777	-17.87	0.08
C5 - C6	**2.151**	**-18.89**	**0.18**	**C5 - C6**	**2.176**	**-19.83**	**0.18**	**C52 - C62**	**2.122**	**-18.17**	**0.20**
C6 - H6	1.763	-17.80	0.05	C6 - H6	1.840	-20.08	0.06	C62 - H62	1.802	-18.18	0.03
C6 - C7	**2.129**	**-18.51**	**0.18**	**C6 - C7**	**2.214**	**-21.74**	**0.14**	**C62 - C72**	**2.126**	**-18.25**	**0.19**
C7 - H7	1.792	-18.18	0.04	C7 - H7	1.781	-18.29	0.07	C72 - H72	1.814	-18.56	0.07
C7 - C7a	**2.167**	**-19.06**	**0.23**	**C7 - C7a**	**2.195**	**-20.47**	**0.23**	**C72 - C7a2**	**2.168**	**-19.53**	**0.20**
C7a - N1	1.995	-15.42	0.13	C7a - N1	1.997	-16.02	0.09	C7a2 - N12	2.004	-15.32	0.08
C11 - H11A	1.727	-14.16	0.12	C11 - H11A	1.720	-15.45	0.08	C112 - H112A	1.730	-16.24	0.08
C11 - H11B	1.658	-14.04	0.11	C11 - H11B	1.689	-16.22	0.07	C112 - H112B	1.720	-15.60	0.08
C11 - H11C	1.636	-14.21	0.10	C11 - H11C	1.643	-14.83	0.08	C112 - H112C	1.687	-16.72	0.11

Bond	$\rho(\underline{r}_{CP})$	$\nabla^2\rho(\underline{r}_{CP})$	ε
O8 - Fe	0.430	7.53	0.03
O82 - Fe	0.466	7.79	0.02
Cl1 - Fe	0.490	7.13	0.01
Cl2 - Fe	0.491	7.13	0.00
Cl3 - Fe	0.488	7.12	0.00

Atomic Charges. The integrated atomic charges for the two compounds are listed below. The highest negative charges are carried by respectively N1 (-0.99 e in N-Ac skatole increasing to -1.05 e in the iron complex), O8 (-1.14 e in N-Ac skatole which decreases to -1.27 e in the iron complex), and chlorine atoms (-0.6 e in average). The highest positive charge is found obviously for iron ion (+0.94 e). No particular features were observed for the other atoms in the organic parts of the two compounds. It is worthy to note, however, that C2 and C3 which are involved in the strong double bond are close to be neutral.

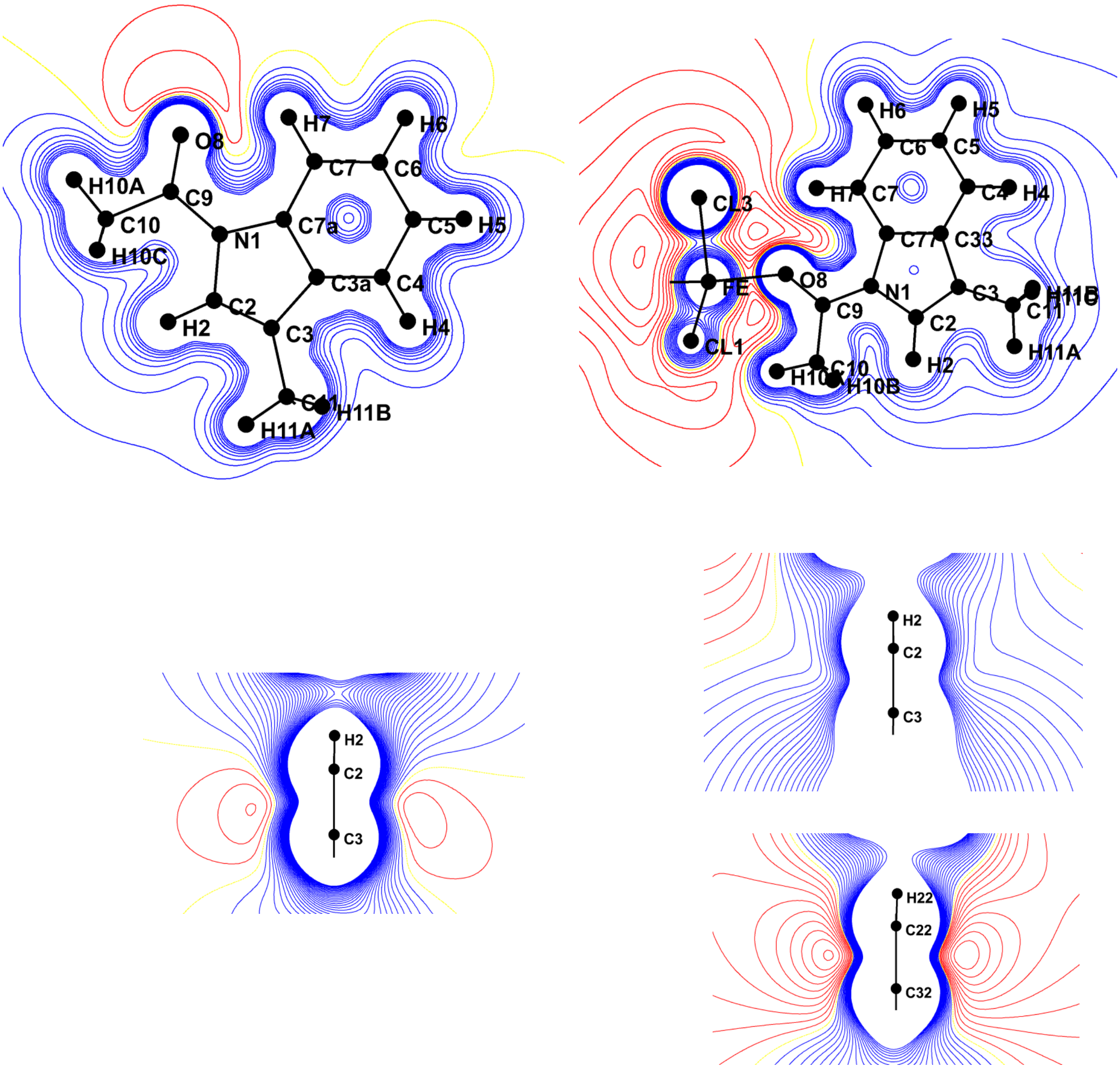
Atomic charges (in e) of 1a and 6a.

N-Ac skatole **1a**		Iron complex **6a**			
C9	1.293	C9	1.212	C92	1.244
C10	-0.242	C10	-0.255	C102	-0.372
H10A	0.168	H10A	0.227	H102A	0.267
H10B	0.054	H10B	0.231	H102B	0.259
H10C	0.202	H10C	0.177	H102C	0.231
C2	**0.088**	**C2**	**-0.005**	**C22**	**0.004**
H2	0.296	H2	0.332	H22	0.338
C3	**-0.057**	**C3**	**0.121**	**C32**	**-0.110**
C3a	-0.013	C3a	-0.089	C3a2	-0.066
C4	-0.093	C4	-0.051	C42	-0.180
H4	0.144	H4	0.267	H42	0.226
C5	-0.209	C5	-0.127	C52	-0.228
H5	0.161	H5	0.169	H52	0.200
C6	-0.243	C6	-0.162	C62	-0.018
H6	0.177	H6	0.231	H62	0.158
C7	-0.110	C7	-0.049	C72	-0.112
H7	0.213	H7	0.309	H72	0.257
C7a	0.220	C7a	0.140	C7a2	0.107
C11	-0.330	C11	-0.365	C112	-0.414
H11A	0.074	H11A	0.203	H112A	0.240
H11B	0.150	H11B	0.228	H112B	0.197
H11C	0.192	H11C	0.279	H112C	0.236
N1	-0.993	N1	-1.074	N12	-1.034
O8	-1.140	O8	-1.266	O82	-1.267
				Cl1	-0.581
				Cl2	-0.622
				Cl3	-0.575
				Fe	0.938

Electrostatic Potential. Next figure depicts the electrostatic potential features obtained after the multipole refinement of the electron density. For the N-Ac skatole, the minimum of the electrostatic potential (-0.109 eÅ^{-1}) is found in the vicinity of the O8 oxygen atom. All other parts of the molecule is surrounded by a positive electrostatic potential. For the iron complex, the positive charge (+0.938 e) of the iron ion is screened by the negative ones carried by the three chlorine and the two oxygen atoms (-0.6 e in average). This gives rise to deep negative potential between O and Cl atoms reaching -0.352 eÅ^{-1}. The other maps show the electrostatic potential in the plane perpendicular to the C2=C3 double bond. A weak negative potential is found in either side of the bond (-0.03 eÅ^{-1}) in the N-Ac skatole molecule. For the iron complex, however, C2=C3 and C22=C32 bonds exhibit different features, the last bond presenting a deeper electrostatic potential (-0.1 eÅ^{-1}). This implies that the two molecules should not be equivalent in the chemical reactivity or in the hydroarylation reaction.

Electrostatic potential maps for N-Ac skatole 1a (left column) and for the iron complex 6a (right column). Maps in the bottom part correspond to the electrostatic potential in the perpendicular plane to the C2-C3 and C22-C32 bonds.

Contours are ± 0.05 eÅ^{-1} for N-Ac skatole and for the iron complex and ± 0.01 eÅ^{-1} for the C2-C3 and C22-C32 bonds. Negative contours are in red and positive ones are in blue.

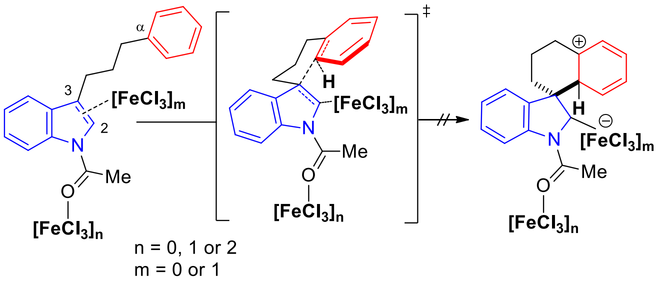


I.6 DFT study

Computations details: All the calculations were performed using the GAUSSIAN 09 software package.[10] The structures were optimized and characterized to be energy minima or transition states at the unrestricted B3PW91, B3LYP,[11] BP86,[12] M06, and M06-2X[13] levels. A spin of 6 was used for compounds with one iron atom, and of 11 for compounds with two iron atoms. The effective-core potential of Hay and Wadt with a double-ξ valence basis set (LANL2DZ) was used to describe Fe.[14] The other atoms were described by the 6-31G(d,p) basis set. Thermal corrections to Gibbs free energies were carried out at 298.15 K under 1 atm using the harmonic frequencies. Solvation energy in CH_2Cl_2 was obtained using the PCM model. Natural charges were obtained using the NBO 3.1 program implemented in Gaussian 09.

Reaction pathways: We considered the activation of **1** (R = $(CH_2)_3Ph$) towards hydroarylation by either one or two $FeCl_3$ molecules coordinated to the oxygen atom (n = 1 or 2, m = 0). Relaxed scans were performed showing that bringing C3 and Cα closer together until 1.5 Å resulted in a continuous rise of the energy of the system. Consistently, no transition state could be found. The same was true after coordination of the C2=C3 bond by $FeCl_3$ (m = 1), with or without complexation of the oxygen atom.

Unfavorable pathways studied by DFT computations: *no activation or activation of the C2=C3 bond by* $FeCl_3$.



We then reasoned that the use of an excess or $FeCl_3$ might give rise to protons if traces of water were present. Various combinations of $FeCl_3$ and H^+ were tested at both coordination sites, among which only two allowed to

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[10] Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

[11] (a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648-5652. (b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B*, **1988**, *37*, 785-789. (c) S. H. Vosko, L. Wilk, M. Nusair, *Can. J. Phys.* **1980**, *58*, 1200-1211. (d) P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623-11627.

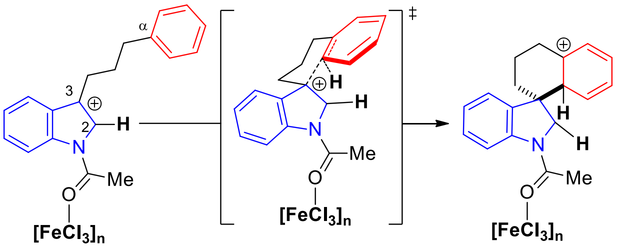
[12] (a) A. D. Becke, *Phys. Rev. A*, **1988**, *38*, 3098-3100. (b) J. P. Perdew, *Phys. Rev. B*, **1986**, *33*, 8822-8824.

[13] Y. Zhao, D. G. Truhlar, The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements. *Theor. Chem. Acc*. **2008**, *120*, 215-241.

[14] P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299-310.

locate hydroarylation transition states: one $FeCl_3$ at O and H^+ at C2=C3 (see **A1** to **B1**), and two $FeCl_3$ at O and H^+ at C2=C3 (see **A2** to **B2**).

Favorable activation of the acetyl by $FeCl_3$ and of the C2=C3 bond by a proton studied by DFT computations.



A1 (n = 1)
A2 (n = 2)

TS$_{A1B1}$ (n = 1)
TS$_{A2B2}$ (n = 2)

B1 (n = 1)
B2 (n = 2)

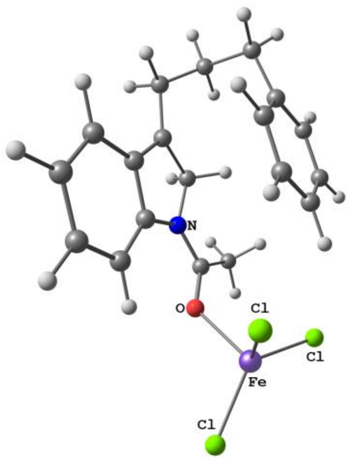
Computed Gibbs free energies (kcal/mol) relatively to A1 or B1.

	TS$_{A1B1}$		**B1**		**TS$_{A2B2}$**		**B2**	
	ΔG_{298}	ΔG_{solv}	ΔG_{298}	ΔG_{solv}	ΔG_{298}	ΔG_{solv}	ΔG_{298}	ΔG_{solv}
B3PW91	10.1	5.2	8.5	-11.2	6.4	-0.6	2.9	-12.2
B3LYP	13.1	6.4	12.4	-9.6	8.3	1.9	6.3	-9.3
BP86	9.8	2.4	9.6	-8.3	6.3	-2.9	4.6	-7.6
M06	7.1	3.5	4.4	-10.1	-	-	-	-
M06-2X	5.3	2.8	3.3	-10.2	3.0	0.4	0.6	-13.9

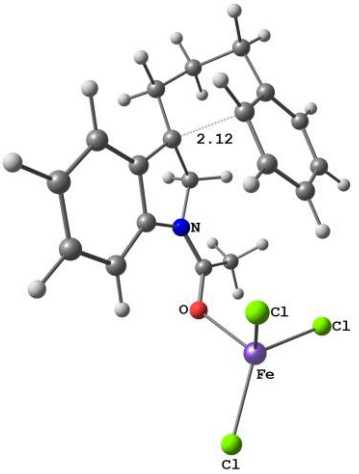
The Gibbs free energies were obtained using the various functionals for the iron complexes. In the absence of solvent correction, with one $FeCl_3$, the Gibbs free energies of activation greatly vary (ΔG_{298} 5.3-10.1 kcal/mol for **TS$_{A1B1}$**) but all barriers are accessible under the experimental conditions used. The formation of the Wheland intermediates **B1** is endergonic (ΔG_{298} 3.3 to 12.4 kcal/mol). With solvent correction, the activation energies are significantly reduced (ΔG_{solv} 2.8 to 6.4 kcal/mol for **TS$_{A1B1}$**) and the Wheland intermediates **B1** greatly stabilized so that the reaction becomes exergonic (ΔG_{solv} -8.3 to -11.2 kcal/mol). The electron depletion along the C2=C3 bond promoted by the coordination of a second $FeCl_3$ molecule to O reduces markedly all Gibbs free of activation, with or without solvent correction. At the B3PW91 and BP86 levels, the transition states are more stable than the starting compounds, which is a computational artefact. At the M06 level, **TS$_{A2B2}$** did not converge.

The geometries of the computed M06-2X iron complexes are displayed below. The effect of the double coordination of the oxygen atom materializes in the forming C3-Cα bond which is longer in **TS$_{A2B2}$** than in **TS$_{A1B1}$** (2.22 vs 2.12 Å), hence the lower activation energy. In the same vein, it should be mentioned that the natural charge at C3 significantly increases from one to two $FeCl_3$ in the starting compounds, from 0.275 to 0.293.

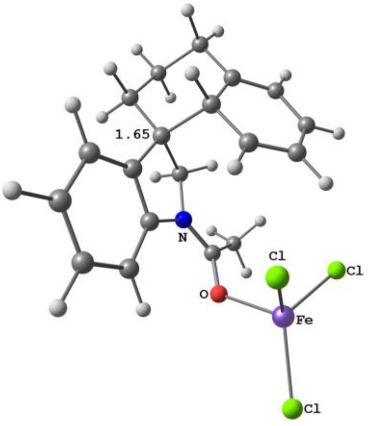
M06-2X Geometries of the iron complexes (selected distances in Å)



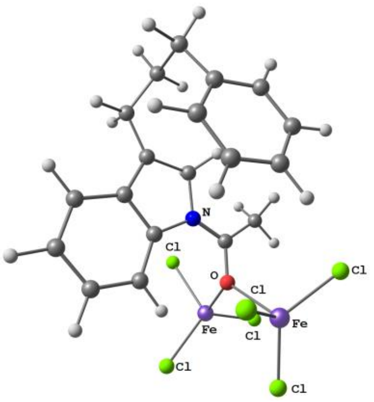
A1



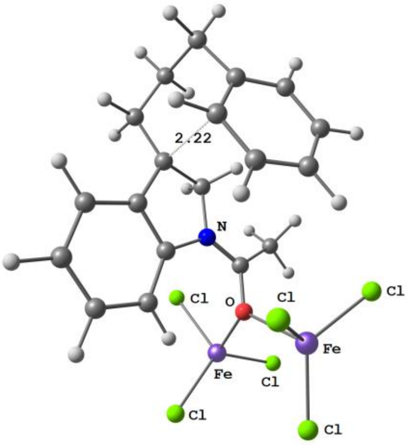
TS$_{A1B1}$



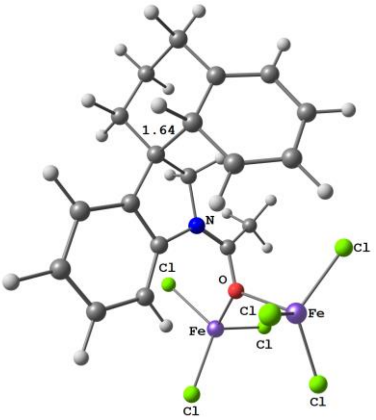
B1



A2



TS$_{A2B2}$



B2

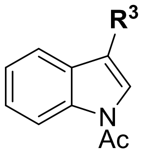
II. Experimental details

II.1 General Informations

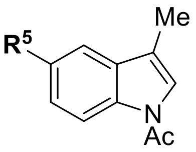
Unless otherwise stated, all reactions were carried out under air atmosphere. Dichloromethane was distilled under argon over CaH_2. Tetrahydrofuran was distilled under argon over sodium-benzophenone. Unless otherwise noted, all reagent-grade chemicals and other solvents were obtained from commercial suppliers and were used as received. Reactions were monitored with analytical thin-layer chromatography (TLC) on silica gel 60 F254 plates and visualized under UV (254 nm) and/or by staining with vanillin (1%) + sulfuric acid (5%) in EtOH or $KMnO_4$ solution followed by heating. Flash chromatography were performed on silica gel (Chromagel Si60ACC [70-200 µm]) as stationary phase. ^{1}H NMR spectra were recorded on Bruker AC250 (250 MHz), Bruker DRX300 (300 MHz), Bruker AM360 (360 MHz) and Bruker 400 (400 MHz) instruments; chemical shifts (δ) are given in parts per million with respect to the residual protonated solvent (δ = 7.26 ppm for $CDCl_3$), which served as an internal standard. ^{13}C NMR spectra were recorded on Bruker AC250 (62 MHz), DRX300 (75 MHz), AM360 (90 MHz) and; chemical shifts are expressed with respect to the deuterated solvent (δ = 77.23 ppm for $CDCl_3$). Coupling constant(s) in hertz (Hz) were measured from one-dimensional spectra and multiplicities were abbreviated as following: br (broad), s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet). Infrared spectra were recorded as neat on a Bruker Vertex 70 with ATR-GE spectrometer. High resolution mass spectra (HRMS) were recorded using Electrospray Ionization (ESI) method with a Bruker Daltonics MicrOTOF-Q instrument. HPLC analyses were conducted on Dionex instrument (Ultimate 3000) in our laboratory. This instrument is principally composed of gradient pump, Peltier effect column oven and Diodes array detector.

II.2 Preparation of N-Ac indoles

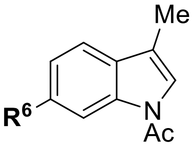
Most of the N-Ac indoles were described in previous reports from us: **(1a**, **1d-e**, **1l-o**, **1r, 1t)**[15] and (**1b-c**, **1k**, **1q)**.[16]



1a, R^3 = Me
1b, R^3 = Et
1c, R^3 = Bu
1d, R^3 = Bn
1e, R^3 = Ph
1f, R^3 = Cyclohexyl
1j, R^3 = 3-Pentyl

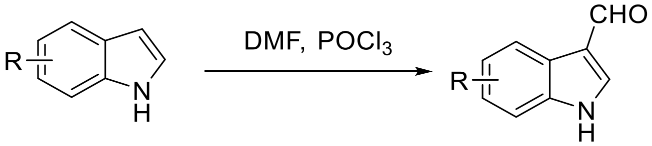


1k, R^5 = Me
1l , R^5 = Br
1m , R^5 = CO_2Et
1n, R^5 = CN
1o, R^5 = NO_2



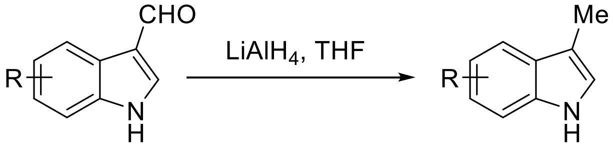
1p, R^6 = Me
1q, R^6 = F
1r, R^6 = Cl
1s, R^6 = Br
1t, R^6 = NO_2

1f, **1j, 1p, 1s** were synthesized using the following protocols.



General Procedure A

Phosphorus oxychloride (1.2 equivalents) was added dropwise to DMF (0.3 mL/mmol indole) with ice-bath. The mixture was stirred for 5 minutes then added dropwise to a solution of indole (1 equivalent) in DMF (0.3 mL/mmol indole) at 0 °C. The mixture was then to warm to room temperature and stirred for 30 minutes. The reaction became a heavy suspension that required vigorous stirring. 5.0 M aqueous potassium hydroxide was added until pH > 9 and the mixture was heated at 100 °C for 2 hours. The resulting suspension was cooled down to 0 °C, the precipitate was filtered off, washed with water then dried under vacuum overnight and used in the next step without further purification.



General procedure B

To a suspension of $LiAlH_4$ (2.5 equivalents) in THF (10 mL/mmol of indole) at 0 °C under argon atmosphere was added 3-formylindole (1 equivalent) over spatula. The suspension was then stirred at 70 °C for 4 hours. The reaction was cooled down to 0 °C, distillated water (100 μL/mmol of 3-formylindole) was added dropwise followed by 10% aqueous solution of NaOH (100 μL/mmol of 3-formylindole) and again H_2O (300 μL/mmol of 3-formylindole). The resulting slurry was stirred vigorously for 30 minutes, diluted with Et_2O and anhydrous $MgSO_4$ was added. The white precipitate was filtered on Celite then washed with Et_2O. The solvent was removed under vacuum and the product was used in the next step without further purification.

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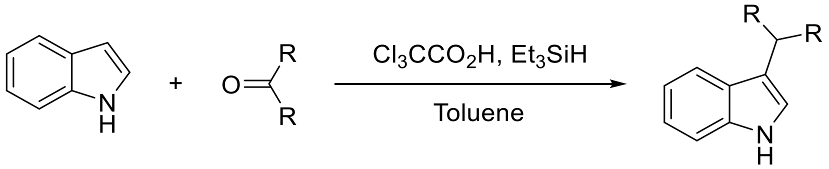
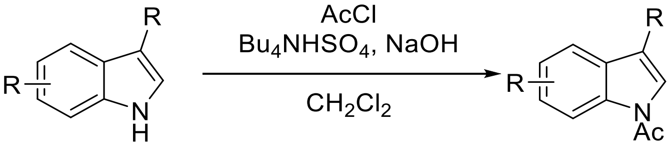
[15] Beaud, R.; Guillot, R.; Kouklovsky, C.; Vincent, G. *Chem. – Eur. J.* **2014**, *20*, 7492.

[16] Tomakinian, T.; Guillot, R.; Kouklovsky, C.; Vincent, G. *Angew. Chem. Int. Ed.* **2014**, *53*, 11881.



General procedure C

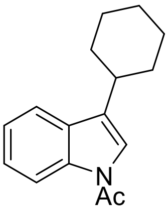
To a stirred solution of trichloroacetic acid (1.5 equivalents) in toluene (0.5 mL/mmol of indole) was added Et_3SiH (3 equivalents) and the resulting mixture was heated at 70 °C for 30 minutes. A solution of indole (1 equivalent) and 3-pentanone (1.1 equivalents) in toluene (0.5 mL/mmol of indole) was added and the reaction was heated at 70 °C for 3 hours. The resulting mixture was cooled down to 0 °C then quenched with sat. aq. Na_2CO_3 solution. The organic layer was diluted with EtOAc, separated and the aqueous layer was extracted twice with EtOAc. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated.



General procedure D

To a solution of a 3-substituted indole (1 equivalent) in dry dichloromethane (8 mL/mmol of indole) were successively added tetrabutylammonium hydrogen sulfate (0.1 equivalent) and freshly finely powdered sodium hydroxide (5 equivalents). The resulting solution was stirred for 15 minutes and acetyl chloride (3 equivalents) was added dropwise over 15 minutes. The resulting slurry was vigorously stirred for 2 hours and quenched by addition of water. The organic layer was separated and the aqueous layer was extracted twice with dichloromethane. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. Flash column chromatography purification using eluent as stated below led to 1-Acetyl-3-substituted indole.

1-Acetyl-3-cyclohexylindole (1f)

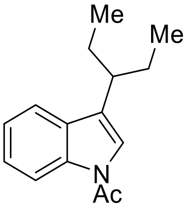


1f was prepared from indole (800 mg, 6.83 mmol) and cyclohexanone following ***General Procedure C*** then acetylated following ***General Procedure D***. Flash column chromatography purification (Cyclohexane/EtOAc : 95/5) led to **1f** as a green solid (950 mg, 3.93 mmol, 58% over 2 steps).

*Data for **1f***

R_f : 0.28 (Cyclohexane/EtOAc: 9/1); **^{1}H NMR (300 MHz, $CDCl_3$) *δ* (ppm):** 8.44 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.34 (ddd, *J* = 8.2, 7.2, 1.2 Hz, 1H), 7.27 (td, *J* = 7.2, 1.2 Hz, 1H), 7.13 (br s, 1H), 2.83 – 2.73 (m, 1H), 2.61 (s, 3H), 2.14 – 2.06 (m, 2H), 1.92 – 1.78 (m, 3H), 1.51 – 1.41 (m, 4H), 1.37 – 1.27 (m, 1H); **^{13}C NMR (75.5 MHz, $CDCl_3$) *δ* (ppm):** 168.6, 136.2, 130.3, 129.3, 125.1, 123.3, 120.2,119.4, 116.9, 35.2, 33.4 (2C), 26.8 (2C), 26.5, 24.2; **IR (NaCl), ν (cm^{-1}):** 3049, 2925, 2851, 1701, 1604, 1451, 1383, 1332, 1243, 1214, 933, 746; **HRMS (ESI$^+$)**: calculated: 264.1359 ([$C_{16}H_{19}NNaO$]$^+$;[M+Na]$^+$); found: 264.1355

1-Acetyl-3-(pentan-3-yl)indole (1j)

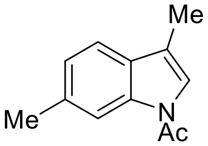


1j was prepared from indole (800 mg, 6.83 mmol) and 3-pentanone following ***General Procedure C*** then acetylated following ***General Procedure D***. Flash column chromatography purification (Cyclohexane/EtOAc: 95/5) led to **1j** as a colorless oil (460 mg, 2.00 mmol, 30% over 2 steps).

Data for ***1j***

R$_f$: 0.31 (Cyclohexane/EtOAc : 9/1); **^{1}H NMR (250 MHz, CDCl$_3$) *δ* (ppm) :** 8.45 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.55 (m, 1H), 7.34 (ddd, *J* = 8.2, 7.1, 1.3 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.14 (br s, 1H), 2.72 – 2.62 (m, 1H), 2.63 (s, 3H), 1.82 – 1.69 (m, 4H), 0.87 (t, *J* = 7.4 Hz, 6H); **^{13}C NMR (75.5 MHz, CDCl$_3$) *δ* (ppm):** 168.5, 136.4, 130.7, 126.6, 125.1, 123.3, 121.7, 119.7, 116.8, 40.2, 27.6 (2C), 24.3, 12.2 (2C); **IR (NaCl), ν (cm^{-1}):** 3050, 2961, 2929, 2872, 1702, 1604, 1450, 1387, 1329, 1215, 999, 747; **HRMS (ESI$^+$)**: calculated: 252.1359 ([$C_{15}H_{19}NNaO$]$^+$; [M+Na]$^+$); found: 252.1353

1-Acetyl-3,6-dimethylindole (1p)

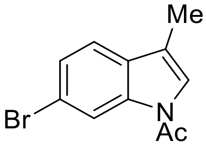


1p was prepared from commercially available 6-Methyl-*1H*-indole (1.08 g, 8.25 mmol) following ***General Procedure A*** for the formylation. The crude aldehyde was reduced following ***General Procedure B***. The crude indole was acetylated following ***General Procedure D***. Flash column chromatography purification (Cyclohexane/EtOAc: 95/5 to 9/1) led to **1p** as a black solid (940 mg, 5.02 mmol, 61% over 3 steps).

Data for ***1p***

R$_f$: 0.38 (Cyclohexane/EtOAc: 9/1); **^{1}H NMR (360 MHz, CDCl$_3$) *δ* (ppm)**: 8.26 (br s, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.14 (br s, 1H), 7.10 (m, 1H), 2.58 (s, 3H), 2.50 (s, 3H), 2.26 (d, *J* = 1.3 Hz, 3H); **^{13}C NMR (90.5 MHz, CDCl$_3$) *δ* (ppm)**: 168.4, 136.4, 135.4, 129.4, 124.9, 121.8, 118.5, 118.4, 117.0, 24.1, 22.0, 9.8; **IR (NaCl), *ν* (cm^{-1})**: 3107, 2916, 1694, 1429, 1394, 1346, 1262, 1223, 1208, 1027, 812, 666; **HRMS (ESI$^+$)**: calculated: 210.0889 ([$C_{12}H_{13}NNaO$]$^+$; [M+Na]$^+$); found: 210.0890

1-Acetyl-3-methyl-6-bromoindole (1s)



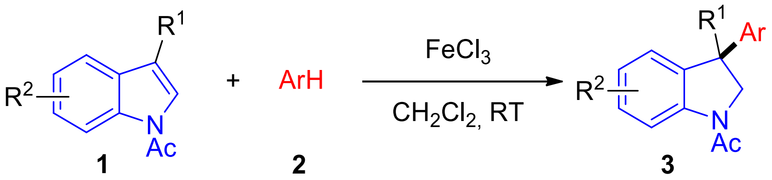
1s was prepared from commercially available 6-Bromo-*1H*-indole-3-carboxaldehyde (1.0 g, 4.46 mmol) following ***General Procedure B*** at room temperature instead of 70 °C. The crude indole was acetylated following ***General Procedure D*** using 5 equivalents of AcCl and 8.0 equivalents of NaOH. Flash column chromatography purification (Cyclohexane/EtOAc: 9/1) led to **1s** as an orange solid (227.4 mg, 0.902 mmol, 20% over 2 steps).

*Data for **1s***

R$_f$: 0.5 (Petroleum ether/EtOAc 8:2); **^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm)**: 8.61 (s, 1H), 7.41 – 7.28 (m, 2H), 7.12 (s, 1H), 2.57 (s, 3H), 2.25 (s, 3H); **^{13}C NMR (62.9 MHz, CDCl$_3$) δ (ppm)**: 168.2, 136.3, 130.2, 126.5, 122.7, 119.9, 119.6, 118.8, 118.1, 23.8, 9.6; **IR (neat) υ_{max} (cm^{-1})**: 1703, 1459, 1430, 1394, 874, 652; **HRMS (ESI$^+$)**: calculated: 273.9837, ([$C_{11}H_{10}BrNNaO$]$^+$; [M+Na]$^+$); found: 273.9838

II.3 Promotor loading and kinetic studies

Promotor loading: The yields of SI I.1 were obtained using ***general procedure E*** from **1a**, **2a** (2 equivalents) in 0.5M CH_2Cl_2 for 2.5 hours with various amounts of $FeCl_3$.



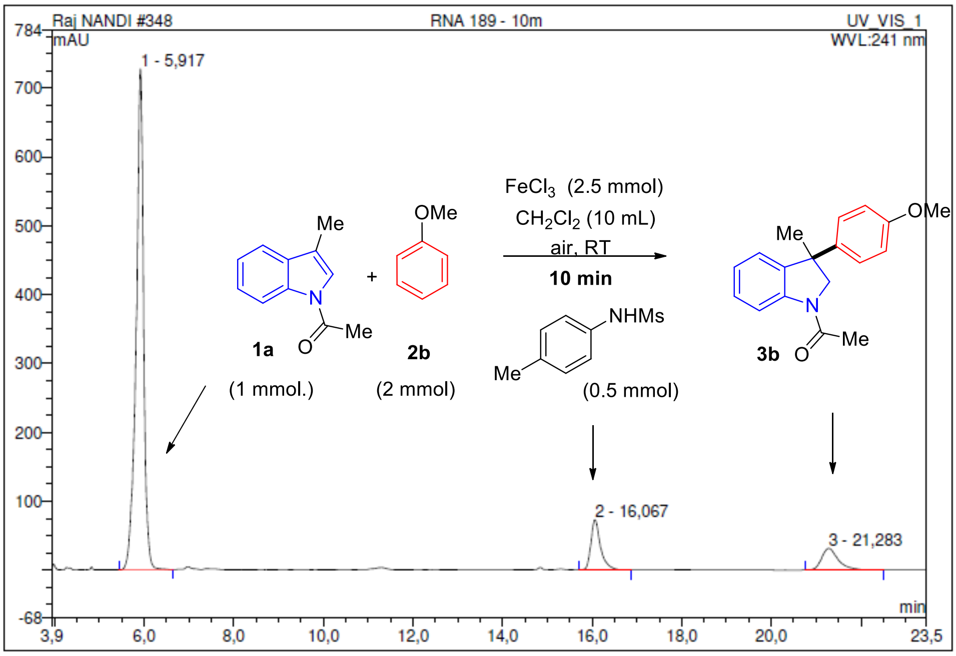
General Procedure E

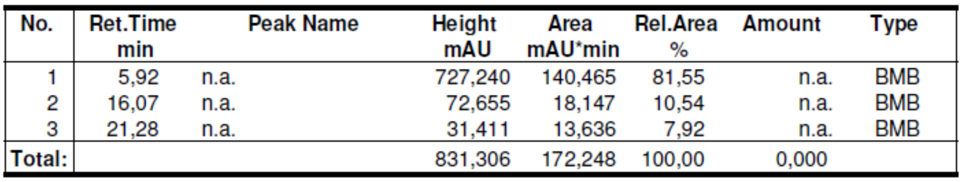
To a solution of the 3-substituted *N*-acetyl indole derivative **1** in CH_2Cl_2, was successively added electron-rich arene **2** and $FeCl_3$ in one portion. After completion of the reaction (checked by TLC) the reaction was quenched with a saturated NaCl aqueous solution and diluted with EtOAc. The phases were separated. The aqueous phase was then extracted twice with EtOAc. The combined organic phases were then dried over Na_2SO_4, filtered and concentrated under vacuum. The crude oil was then purified by flash column chromatography.

Kinetic study: The influence of the concentration of each component of the reaction on the reaction kinetic of SI I.2 were obtained as follow.

Typical procedure: To a solution of N-Ac skatole **1a** in 10 mL of CH_2Cl_2, was successively added anisole **2b,** *p*-methyl-N-Ms aniline (0.5 mmol) as internal standard and $FeCl_3$ in one portion. Aliquot of 100 µL were taken by syringe at regular times and filtered immediately through a short pad of silica gel with EtOAc. After evaporation, each aliquot were injected in HPLC (silica column, eluent: hexane/ EtOH: 98/2, 1 mL/min).

Representative chromatogram

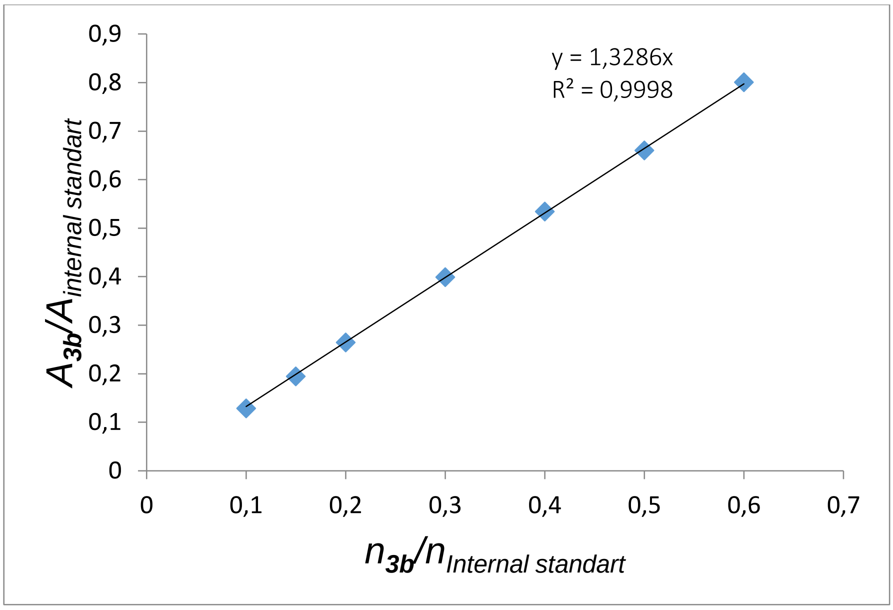




No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	5,92	n.a.	727,240	140,465	81,55	n.a.	BMB
2	16,07	n.a.	72,655	18,147	10,54	n.a.	BMB
3	21,28	n.a.	31,411	13,636	7,92	n.a.	BMB
Total:			831,306	172,248	100,00	0,000	

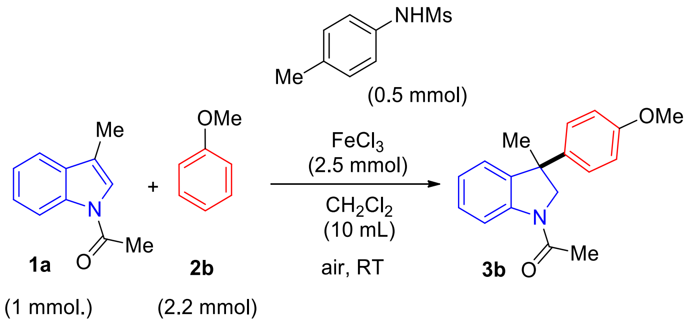
The calibration curve between **3b** and *p*-methyl-N-Ms aniline allowed us to calculate the concentration of **3b**.

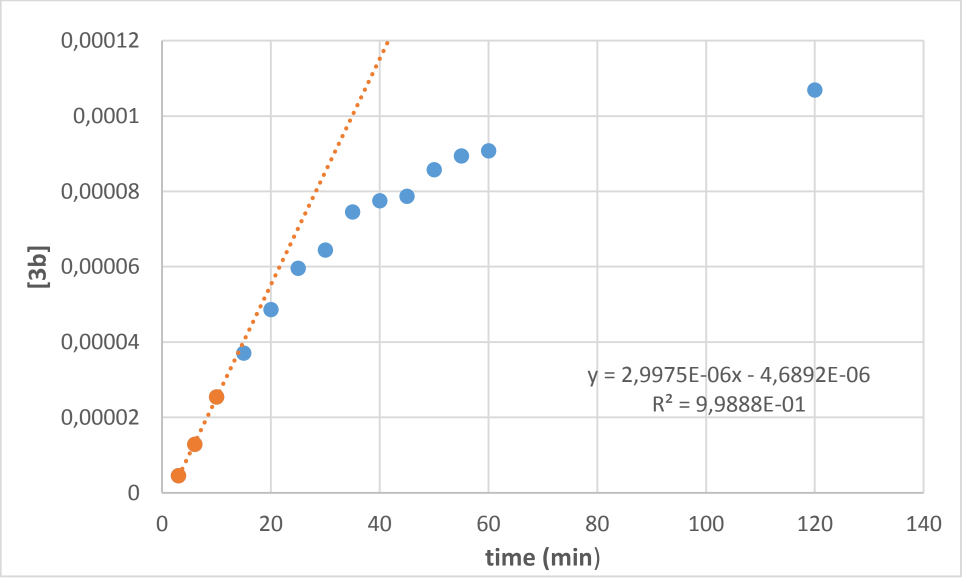
Calibration curve



Rate constants were calculated for each reaction using the initial rates method.

Representative initial rates data





The plot between the initial rate constant versus the concentration of FeCl$_3$ was then drawn.

II.4 *In-situ* IR monitoring

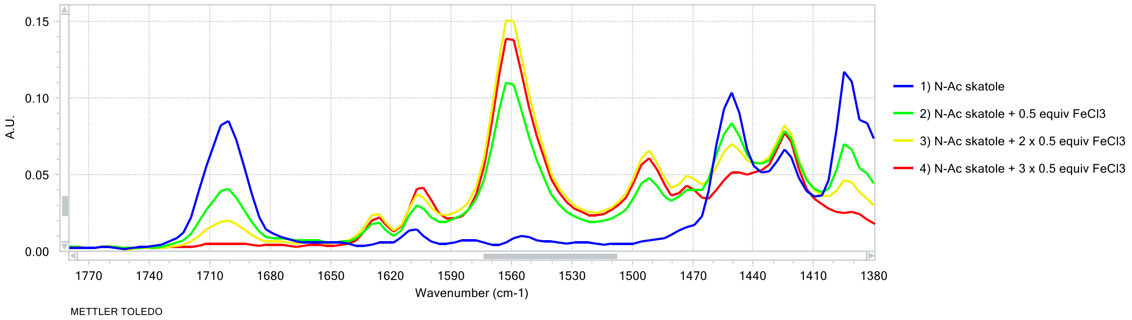
Reaction setup: React IR 15 with MCT Detector using HappGenzel apodization was used to collect IR reaction spectra. The instrument was fitted with a DiComp (Diamond) probe connected via AgX 6mm x 1.5m silver halide fiber. All data were collected at 8 cm^{-1} resolution from 2500 to 650 cm^{-1}. 125 scans were collected to obtain 1 spectrum. An air background was collected prior to the experiments and Mettler Toledo iCIR version 4.3 was used for instrument control and data analysis. Baseline offset correction was applied.

IR monitoring of the reaction between N-Ac skatole and $FeCl_3$ in CH_2Cl_2 (0.2 M):

Procedure:

Under nitrogen atmosphere, CH_2Cl_2 (2.0 mL) was introduced intro a three-necked round-flask equipped with the DiComp probe. N-Ac skatole (69 mg, 0.4 mmol) was introduced. After stabilization of the system, $FeCl_3$ was added in 3 successive portions: 1) 33 mg, 0.2 mmol, 2) 33 mg, 0.2 mmol, 0.2 mmol and 3) 33 mg, 0.2 mmol, 0.2 mmol. Evolution of the system was monitored at 1 min intervals and the subsequent portion was introduced when no further evolution was noted.

Selected IR spectra [1770–1380 cm^{-1}]:

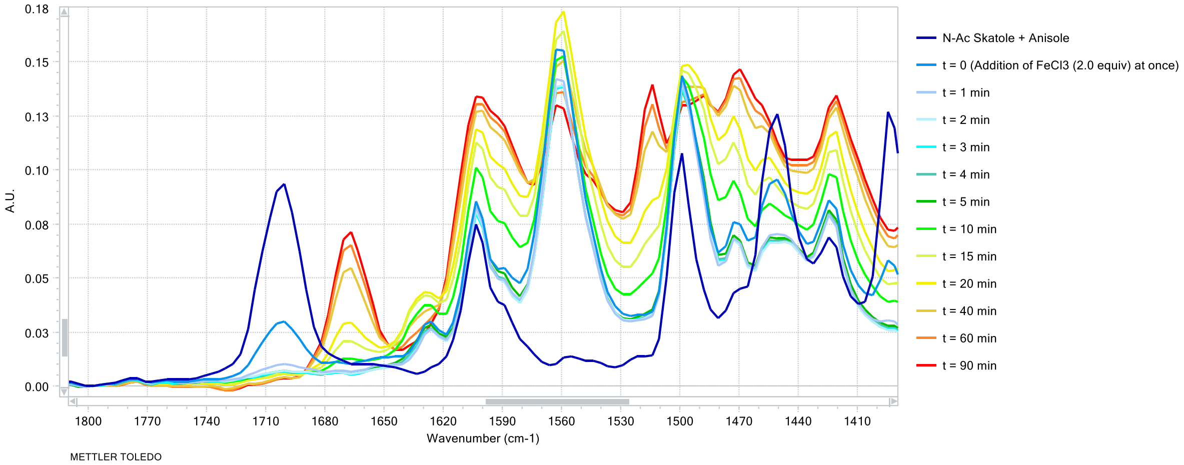


IR monitoring of the reaction between N-Ac skatole and anisole (2.0 equiv) in the presence of $FeCl_3$ (2.0 equiv) in CH_2Cl_2 (0.2 M)

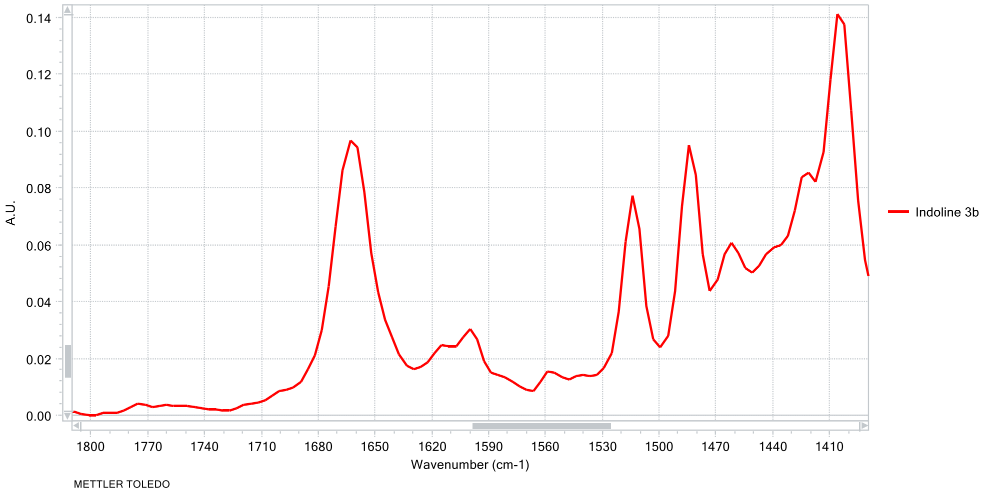
Procedure:

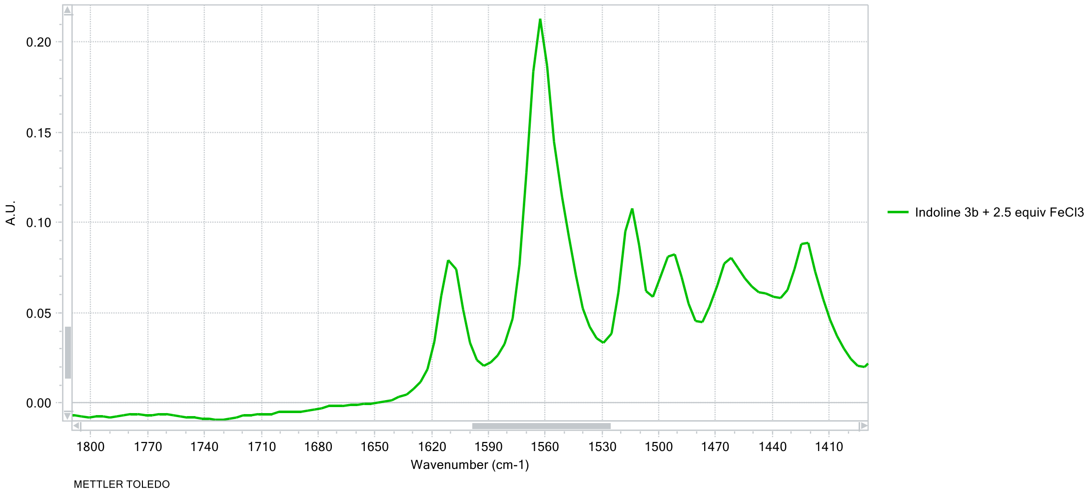
Under nitrogen atmosphere, CH_2Cl_2 (2.0 mL) was introduced intro a three-necked round-flask equipped with the DiComp probe. N-Ac skatole (69 mg, 0.4 mmol) followed by anisole (87 µL, 0.8 mmol) was introduced. After stabilization of the system, $FeCl_3$ (130 mg, 0.8 mmol) was added at once. The end of the addition was taken as reference time (t = 0).

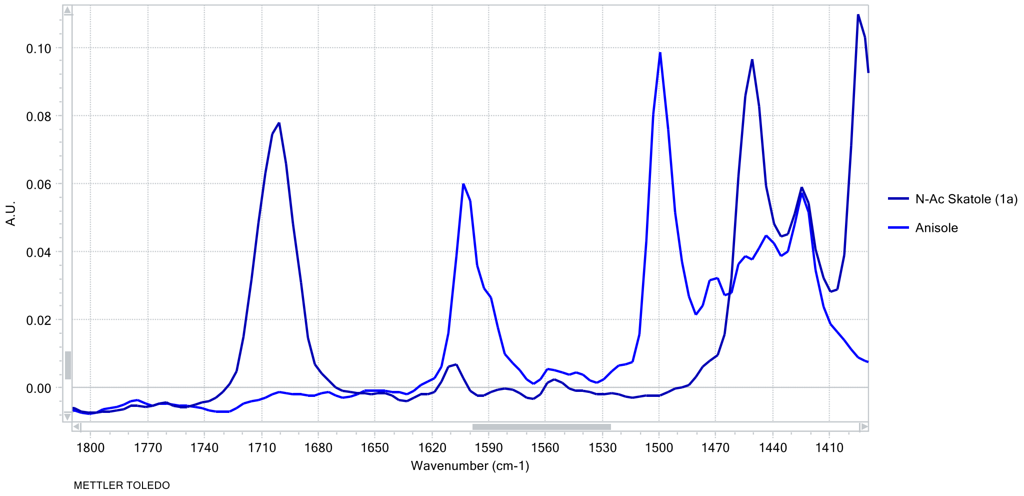
Selected IR spectra [1800–1400 cm^{-1}] region



Reference Spectra [1800–1400 cm^{-1}] region (0.2 M solutions in CH_2Cl_2)

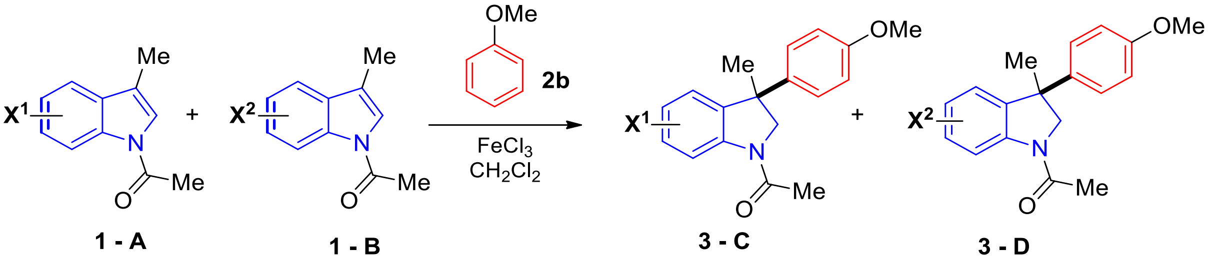






II.5 Hammett study at the C_5- and C_6-positions

The Hammett study was conducted through competitive experiments involving two N-Ac skatoles derivatives **1** as follows:



Typical procedure

To a solution of 5- or 6-substituted N-Ac indole derivatives **1 - A** (0.173 mmol) and **1 - B** (0.173 mmol) in CH_2Cl_2 (1.7 mL), was successively added anisole **2b** (0.693 mmol) and $FeCl_3$ (0.832 mmol) in one portion. The reaction was stirred until it reaches a 10-20% conversion. The reaction was quenched with a saturated NaCl aqueous solution and was then diluted with EtOAc. The phases were separated. The aqueous phase was then extracted twice with EtOAc. The combined organic phases were then dried over Na_2SO_4, filtered and concentrated under vacuum. The mixture of **3 - C** and **3 - D** were then separated from **1 - A** and **1 - B** by flash column chromatography.

The ratio of the two hydroarylated compounds **3 - C** and **3 - D** was determined by relative integration by ^1H NMR in order to obtain the kX/kH ratio.

k_H = rate constant of the reaction with anisole and N-Ac skatole **1a** (X = H).

k_X = rate constant of the reaction with anisole and a 5 or 6 substituted N-Ac skatole **1** ($X \neq H$).

Product ratio obtained from competing experiments

X^1	X^2	Ratio C/D
5-OMe	H	1.14
5-Me	H	1.876
5-Br	H	0.13
5-CO_2Et	**5-Br**	0.526
5-CN	**5-Br**	0.357
5-NO_2	**5-CN**	0.344
6-Me	H	1.63
6-F	H	1.505
6-Br	H	0.446
6-Cl	**6-Br**	1.447
6-NO_2	**5-NO_2**	0.125

The integration ratio of **3** ($X \neq H$) / **3a** (X = H) was equal to k_X/k_H and $\log(k_X/k_H)$ was then determined. Hammett σ_p values were obtained from Taft and co-workers.[17]

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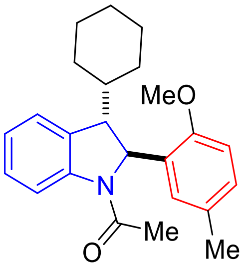
[17] Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.

Hammett relationship from 5- and 6-substituted N-Ac skatole

Substituent	σ_p	k_X/k_H	$\log(k_X/k_H)$
5-OMe	-0,27	1.14	0,0569
5-Me	-0,15	1.876	0,273
5-H	0	1	0
5-Br	0,23	0.13	-0,886
5-CO_2Et	0,45	0.0684	-1,163
5-CN	0,66	0.0464	-1,333
5-NO_2	0,78	0.0244	-1,6126
6-Me	-0,15	1.63	0,212
6-H	0	1	0
6-F	0,06	1.505	0,177
6-Cl	0,23	0.646	-0,189
6-Br	0,23	0.446	-0,35
6-NO_2	0,78	0.00305	-2,51

II.6 Influence of the C3-substituent

***N*-Acetyl-2-(2-methoxy-5-methylphenyl)-3-cyclohexylindoline (8aa)**



70% (48 h)

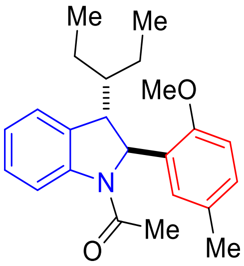
8aa was prepared from 1-Acetyl-3-cyclohexylindole **1f** (80 mg, 0.330 mmol) following ***General Procedure E*** using 4-methylanisole **2a** as electron-rich arene (89 mg, 0.729 mmol) and $FeCl_3$ (130 mg, 0.796 mmol) in 0.5 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 9/1 to 8/2) led to **8aa** as colorless solid (84 mg, 0.231mmol, 70%).

The *trans* stereochemistry was assigned based on the small coupling constant between the protons at the 2 and 3 positions of the N-Ac indoline.[19]

*Data for **8aa***

R_f: 0.35 (Cyclohexane/EtOAc: 8/2); **^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm):** 8.33 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.11 – 6.98 (m, 3H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.62 (d, *J* = 1.4 Hz, 1H), 5.44 (br s, 1H), 3.87 (s, 3H), 2.88 (d, *J* = 3.3 Hz, 1H), 2.11 (s, 3H), 2.04 (s, 3H), 1.78 – 1.59 (m, 6H), 1.29 – 1.08 (m, 5H); **^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm):** 169.3, 153.5, 143.6, 132.7, 130.4, 130.3, 128.9, 127.9, 125.8, 125.7, 123.6, 116.8, 110.4, 62.2, 56.0, 55.3, 44.4, 29.8, 29.3, 26.7, 26.6, 26.5, 23.8, 20.7; **IR (NaCl), ν (cm^{-1}):** 2925, 2851, 1663, 1597, 1499, 1479, 1461, 1396, 1246, 1112, 1031, 756; **HRMS (ESI^+):** calculated: 386.2091 ($[C_{24}H_{29}NNaO_2]^+$;$[M+Na]^+$); found: 386.2075.

***N*-Acetyl-2-(2-methoxy-5-methylphenyl)-3-(pentan-3-yl)indoline (8ab)**



36% (48 h)

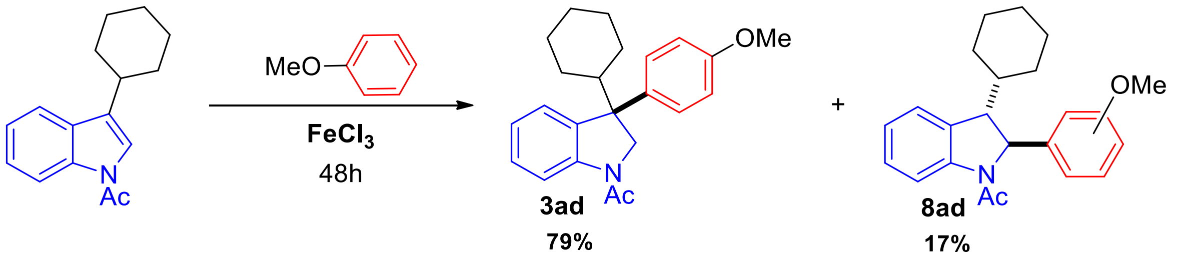
8ab was prepared from 1-Acetyl-3-(pentan-3-yl)indole **1j** (80 mg, 0.348 mmol) following ***General Procedure E*** using 4-methylanisole **2a** as electron-rich arene (94 mg, 0.767 mmol) and $FeCl_3$ (135 mg, 0.837 mmol) in 0.5 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 9/1 to 8/2) led to **8ab** as colorless oil (44 mg, 0.125 mmol, 36%).

The *trans* stereochemistry was assigned based on the small coupling constant between the protons at the 2 and 3 positions of the N-Ac indoline.[19]

*Data for **8ab***

Rf: 0.33 (Cyclohexane/EtOAc: 8/2); **^{1}H NMR (250 MHz, CDCl$_3$) δ (ppm):** 8.33 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.25 (m, 1H), 7.08 (m, 3H), 6.79 (d, *J* = 8.3 Hz, 1H), 6.66 (d, *J* = 1.6 Hz, 1H), 5.38 (d, *J* = 1.8 Hz, 1H), 3.90 – 3.79 (m, 1H), 3.86 (s, 3H), 3.20 (t_{app}, *J* = 2.6 Hz, 1H), 2.13 (s, 3H), 2.01 (s, 3H), 1.60 – 1.43 (m, 2H), 1.35 – 1.22 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 6H); **^{13}C NMR (62.9 MHz, CDCl$_3$) δ (ppm)**: 169.5, 153.4, 144.1, 133.1, 130.9, 130.5, 128.9, 127.9, 125.9, 125.2, 123.9, 116.9, 110.3, 61.8, 55.3, 52.1, 48.4, 23.9, 23.0, 22.3, 20.8, 12.4, 12.2; **IR (NaCl), ν (cm^{-1}):** 2960, 2931, 2873, 1664, 1596, 1499, 1479, 1460, 1395, 1246, 1031, 754; **HRMS (ESI^{+}):** calculated: 374.2091 ([$C_{23}H_{29}NNaO_2$]$^{+}$;[M+Na]$^{+}$); found: 374.2072.

N-Acetyl-3-(4-methoxyphenyl)-3-cyclohexylindoline (3ad)

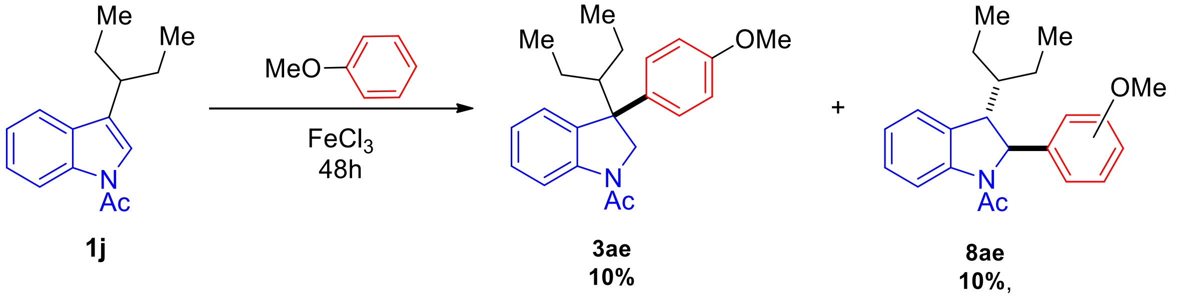


3ad was prepared from 1-Acetyl-3-cyclohexylindole **1f** (62.7 mg, 0.260 mmol) following ***General Procedure E*** using anisole **2b** (87 mg, 0.785 mmol) as electron-rich arene and $FeCl_3$ (101.6 mg, 0.626 mmol) in 0.5 mL of CH_2Cl_2. Flash column chromatography purification (Cyclohexane/EtOAc: 8/2) led to **3ad** as a pale brown oil (72.5 mg, 0.207 mmol, 79%) along with **8ad** (16.1 mg, 0.046 mmol, 17%) as an inseparable mixture of *ortho/para* regioisomers.

*Data for **3ad***

R$_f$: 0.17 (Cyclohexane/EtOAc: 8/2); **^{1}H NMR (250 MHz, CDCl$_3$) δ (ppm)**: 8.29 (d, *J* = 8.2 Hz, 1H), 7.28 – 7.22 (m, 3H), 7.18 – 7.14 (m, 1H), 7.05 (td, *J* = 7.3, 0.9 Hz, 1H), 6.85 (d, *J* = 8.9 Hz, 2H), 4.18 (d, *J* = 10.8 Hz, 1H), 4.04 (d, *J* = 10.8 Hz, 1H), 3.77 (s, 3H), 2.22 (s, 3H), 1.74 – 1.51 (m, 6H), 1.31 – 1.15 (m, 2H), 1.14 – 0.99 (m, 2H), 0.69 – 0.60 (m, 1H); **^{13}C NMR (62.9 MHz, CDCl$_3$) δ (ppm)**: 168.2, 158.0, 143.5, 137.6, 134.7, 128.0, 127.6 (2C), 126.0, 123.2, 117.0, 114.0 (2C), 61.9, 55.3, 55.1, 47.1, 28.1, 27.9, 26.8, 26.8, 26.4, 24.5; **IR (NaCl), ν (cm^{-1})**: 3039, 3001, 2930, 2852, 1662, 1609, 1595, 1512, 1482, 1401, 1251, 757; **HRMS (ESI^{+})**: calculated: 350.2115 ([$C_{23}H_{28}NO_2$]$^{+}$;[M+H]$^{+}$); found: 350.2100.

N-Acetyl-3-(4-methoxyphenyl)-3-(pentan-3-yl)indoline (3ae)



3ae was prepared from 1-Acetyl-3-(pentan-3-yl)indole **1j** (60.0 mg, 0.261 mmol) using anisole **2b** (87 mg, 0.785 mmol) as electron-rich arene and $FeCl_3$ (101.6 mg, 0.626 mmol) in 0.5 mL of CH_2Cl_2 following ***General Procedure E***. Preparative TLC purification (Petroleum ether/EtOAc: 8/2) led to **3ae** as a gummy oil (9.0 mg, 0.0267 mmol, 10%) along with **8ae** (9.0 mg, 0.0267 mmol, 10%) as an inseparable mixture of *ortho/para* regioisomers

*Data for **3ae***

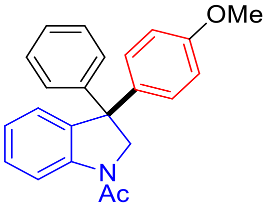
Rf: 0.37 (Petroleum ether/EtOAc: 8/2); **^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm):** 8.28 (d, *J* = 7.8 Hz, 1H), 7.29 – 7.15 (m, 4H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 2H), 4.17 (s, 2H), 3.78 (s, 3H), 2.26 (s, 3H), 2.14 – 2.07 (m, 1H), 1.56 – 1.41 (m, 2H), 1.29 – 1.18 (m, 1H), 1.12 – 1.02 (m, 1H), 0.95 – 0.87 (m, 6H); **^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm)**: 168.4, 158.1, 143.1, 138.8, 136.3, 128.1, 127.3 (2C), 125.1, 123.6, 117.2, 114.1 (2C), 60.9, 56.3, 55.3, 49.6, 25.0, 24.7, 24.6, 15.0, 13.6; **IR (NaCl), ν (cm^{-1}):** 2961, 1665, 1510, 1399, 1252, 666.; **HRMS (ESI$^+$):** calculated: 360.1934 ($[C_{22}H_{27}NNaO_2]^+$; $[M+Na]^+$); found: 360.1928

N-Acetyl-2-((2/4)-methoxyphenyl)-3-(pentan-3-yl)indoline (8ae)

*Data for **8ae***

R$_f$: 0.52 (Petroleum ether/EtOAc: 8/2); **^{1}H NMR (360 MHz, $CDCl_3$) δ (ppm):** 8.33 (d, *J* = 7.9 Hz, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.32 – 7.21 (m, 3H), 7.12 – 7.01 (m, 6H), 6.92 – 6.79 (m, 5H), 5.42 (d, *J* = 1.8 Hz, 1H, C2 H of *ortho* isomer), 4.97 (d, *J* = 1.8 Hz, 1H, C2 H of *para* isomer), 3.91 (s, 3H), 3.78 (s, 3H), 3.26 (s, 1H), 3.20 (s, 2H), 2.04 (s, 3H), 2.01 (s, 3H), 1.54 – 1.24 (m, 10H), 0.92 – 0.82 (m, 12H); **^{13}C NMR (90 MHz, $CDCl_3$) δ (ppm)**: 168.3, 155.5, 143.9, 135.5, 132.9, 130.9, 128.5, 127.9,127.8, 126.0, 125.3, 125.1,124.9, 123.9, 123.8,121.1, 116.8, 116.7, 114.4, 110.2, 66.0, 61.7, 55.2, 55.0, 53.3, 51.8, 48.2, 47.9, 29.7, 24.1, 23.7, 23.3, 22.7, 22.1, 21.9, 12.3, 12.2, 12.1, 12.0; **IR (NaCl), ν (cm^{-1}):** 2960, 1664, 1512, 1479, 1461, 1248, 1030, 753; **HRMS (ESI$^+$):** calculated: 360.1934 ($[C_{22}H_{27}NNaO_2]^+$; $[M+Na]^+$); found: 360.1936

N-Acetyl-3-(4-methoxyphenyl)-3-phenylindoline (3af)



90% (12 h)

We reported the synthesis of **3af** with $FeCl_3$ with ***General Procedure E*** in ref **15**.

See ref **15** for full characterization of **3af.**

II.7 Taft study at C_3 position

The goal is to determine the Taft equation which take into account the steric and electronic factors of the substituent at the C3-position of the indole nucleus.

$$\log(k_R/k_{Me}) = \rho^*\sigma^* \text{ and } \delta Es$$

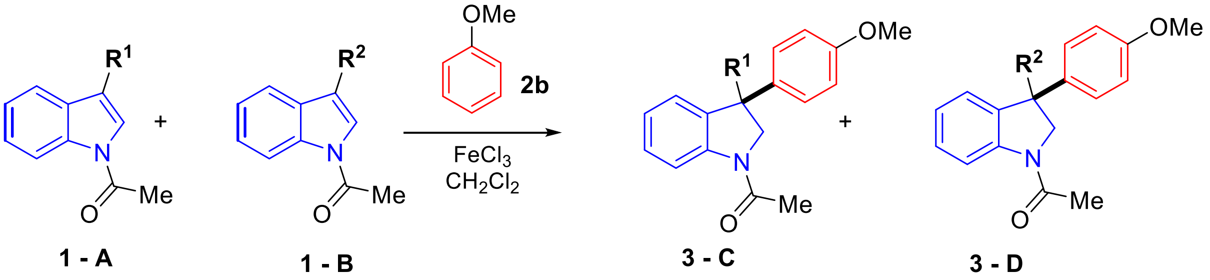
$\mathbf{k_R}$ = rate constant of the reaction with anisole and 3-substituted N-Ac indole **1** ($R \neq Me$).

$\mathbf{k_{Me}}$ = rate constant of the reaction with anisole and N-Ac skatole **1a** (R = Me).

σ* and **Es** are respectively the Taft's polar and steric substituent parameters.

ρ* and **δ** are respectively the polar and steric constants

The Taft study was undertaken through competitive experiments involving two 3-substituted N-Ac indoles derivatives **1** as follows:



Typical procedure

To a solution of 3-substituted N-Ac indole derivatives **1 - A** (0.173 mmol) and **1 - B** (0.173 mmol) in CH_2Cl_2 (1.7 mL), was successively added anisole **2b** (0.693 mmol) and $FeCl_3$ (0.832 mmol) in one portion. The reaction was stirred until it reaches a 10-20% conversion. The reaction was quenched with a saturated NaCl aqueous solution and was then diluted with EtOAc. The phases were separated. The aqueous phase was then extracted twice with EtOAc. The combined organic phases were then dried over Na_2SO_4, filtered and concentrated under vacuum. The mixture of **3 - C** and **3 - D** were then separated from **1 - A** and **1 - B** by flash column chromatography.

The ratio of the two hydroarylated compounds **3 - C** and **3 - D** was determined by relative integration by ^{1}H NMR in order to obtain the k_R/k_{Me} ratio.

k_{Me} = rate constant of the reaction with anisole and N-Ac skatole **1a** (R = Me).
k_R = rate constant of the reaction with anisole and 3-substituted N-Ac indole **1** ($R \neq Me$).

Product ratio obtained from competing experiments

R^1	R^2	Ratio C/D
Et	Me	1.25
***n*-Bu**	Me	0.555
Bn	Me	0.1299
***cyclo*-Hexyl**	**Bn**	0.59
***iso*-Pentyl**	***cyclo*-Hexyl**	0.035
Ph	Me	0.01

The integration ratio of **3** (R ≠ Me) / **3a** (R = Me) was equal to k_R/k_{Me} and $\log(k_R/k_{Me})$ was then determined. $\sigma*$ and Es are respectively the Taft's polar[18] and steric substituent[19] parameters.

Taft relationship from 3-substituted N-Ac indoles with $FeCl_3$

R	**$\sigma*$**	**Es**	**k_R/k_{Me}**	**$\log(k_R/k_{Me})$**
Me	0	0	1	0
Et	-0,1	-0,07	1.25	0,0969
***n*-Bu**	-0,13	-0,39	0.555	-0,2557
Bn	0,225	-0,38	0.1299	-0,8864
***cyclo*-Hexyl**	-0,15	-0,79	0.01	-1,1155
***iso*-Pentyl**	-0,225	-1,98	0.0766	-2,57
Ph	0,6	-2,55	0.00268	-2

The polar ($\rho* = 1.05$) and steric ($\delta = 0.84$) constants were determined by multiple linear regression.

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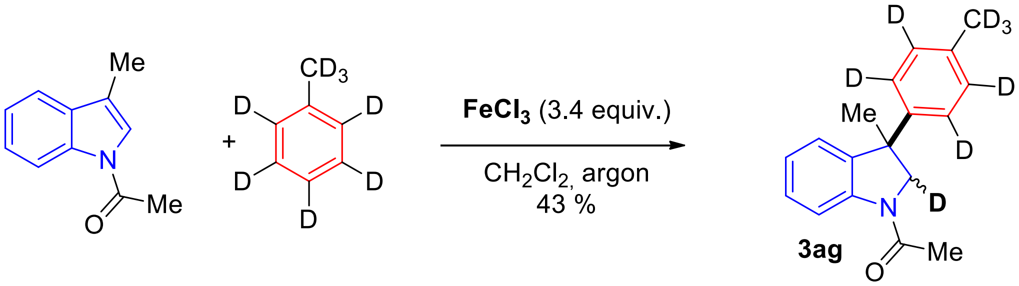
[18] Obtained from: (a) Taft, R. W. *J. Am. Chem. Soc.* **1953**, *75*, 4231-4238; (b) Taft, R.; Kreevoy, M. M. W. *J. Am. Chem. Soc.* **1957**, *79*, 4011-4015;

[19] Obtained from: (a) Taft, R. W. *J. Am. Chem. Soc.* **1952**, *74*, 3120-3128; (b) Wang, B.-Y.; Rieth, S.; Badjić, J. D. *J. Am. Chem. Soc.* **2009**, *131*, 7250-7252.

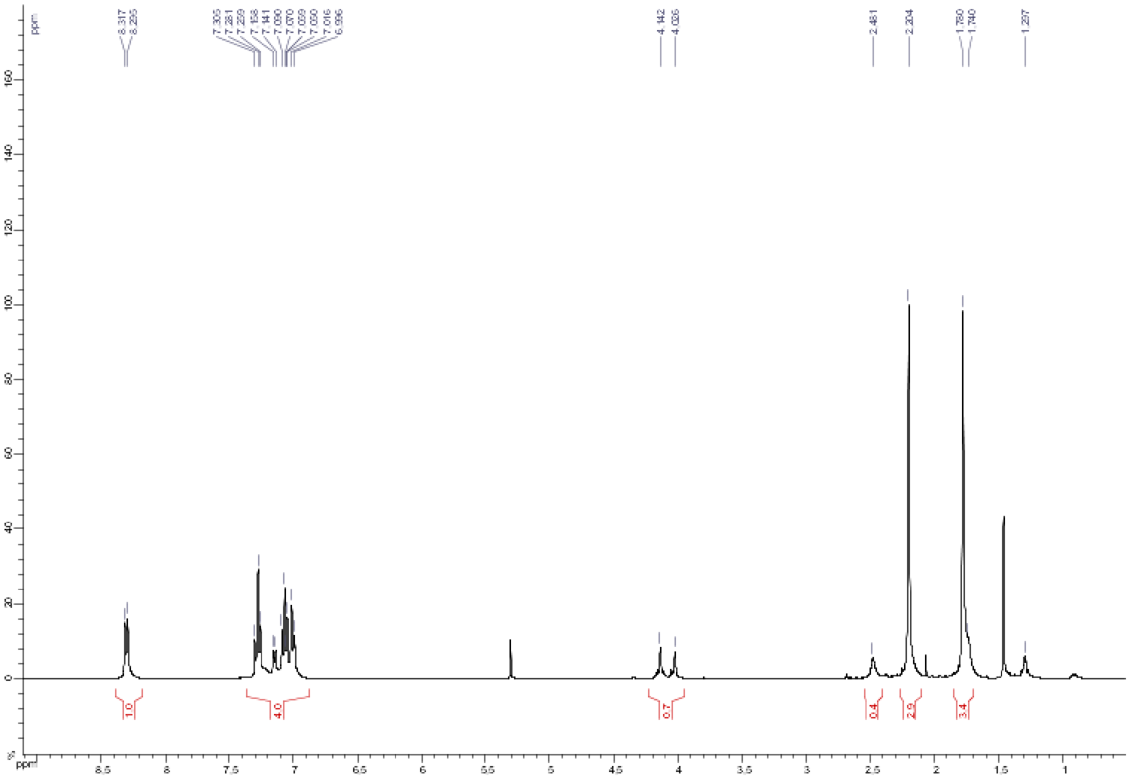
II.8 Deuterated experiments

Hydroarylation with d8-toluene

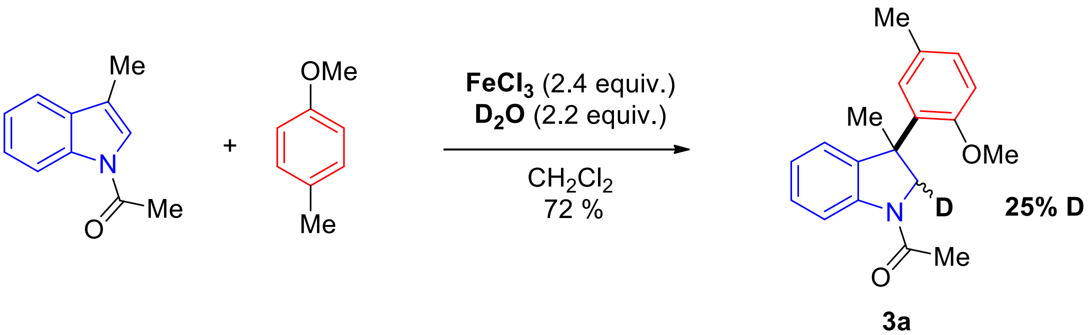


Deuterated **3g** was prepared from 1-Acetyl-3-methylindole **1a** (100.0 mg, 0.578 mmol), d8-toluene (173.6 mg, 1.733 mmol) as electron-rich arene and $FeCl_3$ (318.0 mg, 1.965 mmol) in 0.7 mL of CH_2Cl_2 following ***general procedure E***. Flash column chromatography purification (Petroleum ether/EtOAc: 8/2) led to to **3ag** with almost complete incorporation of deuterium at C2 (68.5 mg, 0.25 mmol, 43%).

^{1}H NMR ($CDCl_3$, 300 MHz) of deuterated 3ag



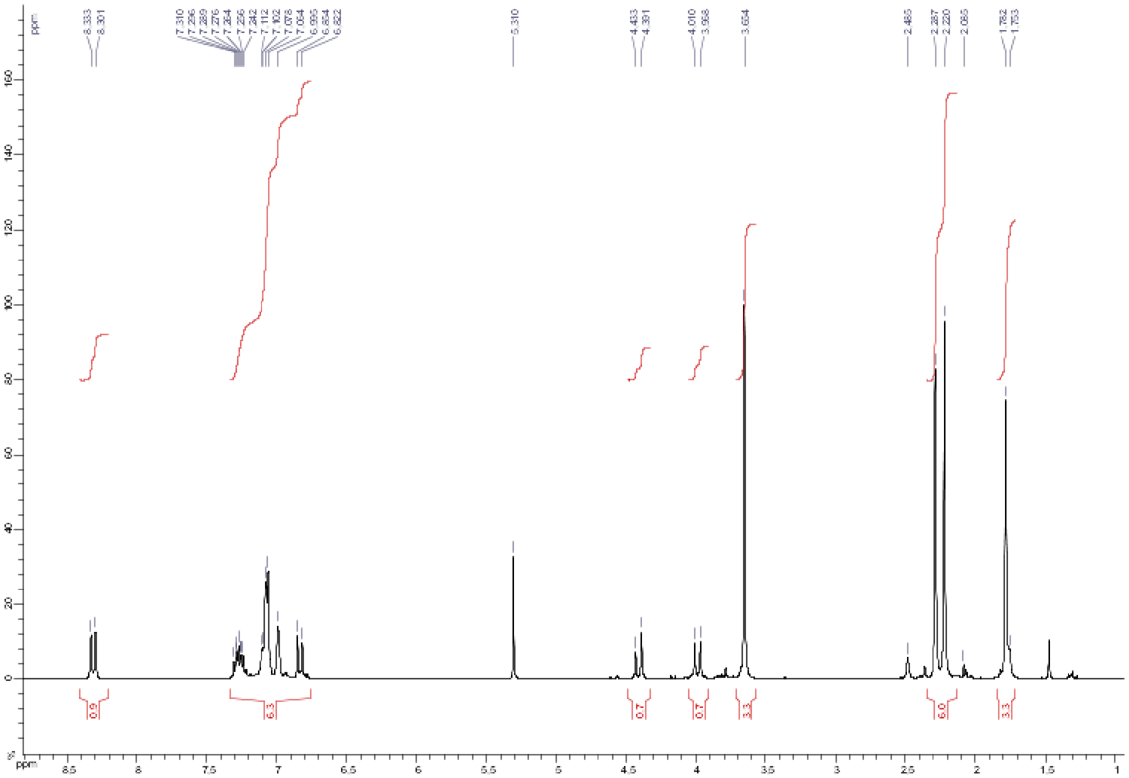
Hydroarylation with D_2O and $FeCl_3$



3a

Partially deuterated **3a** was prepared from 1-Acetyl-3-methylindole **1a** (150.0 mg, 0.866 mmol), 4-methylanisole (230.0 mg, 1.88 mmol) as electron-rich arene and $FeCl_3$ (337.1 mg, 2.08 mmol) with **D**$_2$O (37.6 mg, 1.88 mmol) in 1 mL of CH_2Cl_2 following ***general procedure E***. Flash column chromatography purification (Petroleum ether/EtOAc: 8/2) led to **3a** with 25% incorporation of deuterium at C2 (184 mg, 0.62 mmol, 72%).

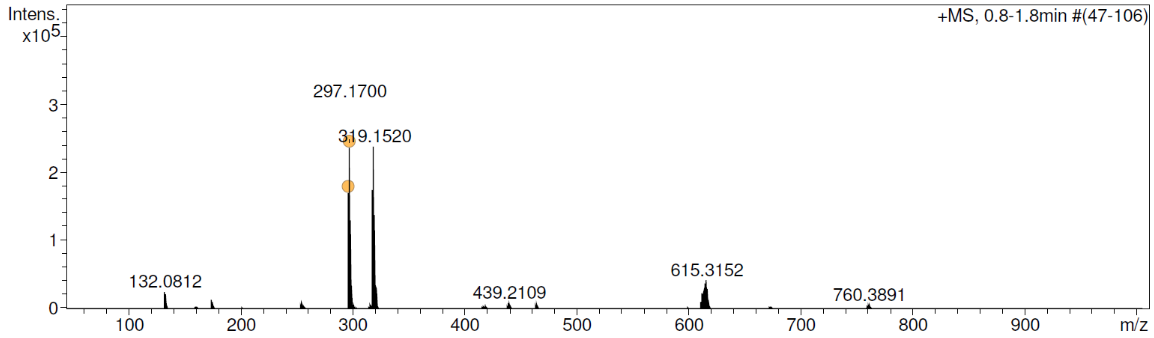
^{1}H NMR ($CDCl_3$, 300 MHz) of partially deuterated 3a



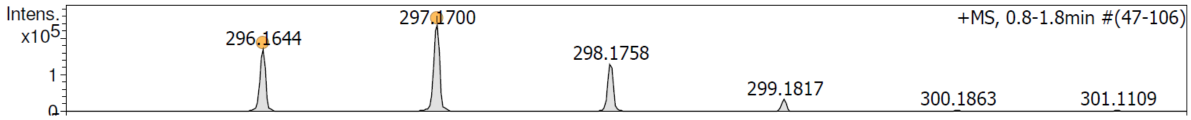
MS trace (ESI$^+$) of partially deuterated 3ae

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.8 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	9.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	100.0 Vpp	Set Divert Valve	Waste



Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma
296.164353	1	C19H22NO2	296.164505	0.2	0.5	571.8
297.169982	1	C19H21DNO2	297.170782	0.8	2.7	208.7



III. DFT Coordinates (x,y,z) of the M06-2X computed intermediates

A1 E(RM062X) = -2369.49716354				**TS_{A1B1}** E(RM062X) = -2369.49098694 Frequency -209.0056			
C	-2.591679000	-0.655649000	-1.605887000	C	-2.682178000	-0.440662000	-1.281457000
C	-2.821342000	0.781566000	0.878603000	C	-2.659987000	0.652202000	0.537624000
C	-4.295957000	0.616981000	0.910330000	C	-4.141581000	0.748550000	0.781897000
H	-4.374796000	-1.453830000	1.569489000	H	-4.482469000	-1.194532000	1.677890000
H	-4.596664000	1.055653000	1.876993000	H	-4.225690000	1.296400000	1.732008000
H	-4.746656000	1.254294000	0.142596000	H	-4.591451000	1.394898000	0.020990000
C	-4.866489000	-0.810324000	0.829136000	C	-4.906065000	-0.567836000	0.883545000
H	-5.919193000	-0.754007000	1.118212000	H	-5.941076000	-0.357135000	1.162764000
C	-4.751008000	-1.443304000	-0.569849000	C	-4.874673000	-1.341577000	-0.453050000
H	-5.246471000	-0.796937000	-1.302673000	H	-5.392599000	-0.758754000	-1.221810000
H	-5.290517000	-2.394790000	-0.562679000	H	-5.397314000	-2.294391000	-0.342696000
C	-3.308576000	-1.657072000	-0.943638000	C	-3.443110000	-1.555949000	-0.826027000
H	-3.123444000	0.209660000	-1.997572000	H	-3.212546000	0.388131000	-1.745113000
C	-2.622111000	-2.795367000	-0.505020000	C	-2.783315000	-2.752787000	-0.567265000
H	-3.170351000	-3.595850000	-0.014109000	H	-3.342039000	-3.605990000	-0.193872000
C	-1.245346000	-2.909050000	-0.693890000	C	-1.411421000	-2.868818000	-0.809714000
C	-0.529907000	-1.877703000	-1.314695000	C	-0.660461000	-1.788337000	-1.305312000
H	-0.724710000	-3.807552000	-0.373810000	H	-0.912957000	-3.816248000	-0.621387000
H	0.542494000	-1.967193000	-1.464230000	H	0.401961000	-1.900093000	-1.501127000
C	-1.208731000	-0.755796000	-1.780561000	C	-1.295896000	-0.591401000	-1.563098000
H	-0.660100000	0.030186000	-2.291434000	H	-0.731258000	0.248188000	-1.960588000
C	-2.106337000	1.867579000	0.383102000	C	-1.877537000	1.824563000	0.200176000
C	-1.870484000	-0.136602000	1.563327000	C	-1.794175000	-0.171031000	1.462424000
C	-2.553694000	3.012432000	-0.329042000	C	-2.252788000	2.983030000	-0.490305000
H	-3.609073000	3.157996000	-0.533502000	H	-3.264990000	3.110742000	-0.861269000
C	-1.614576000	3.918776000	-0.745696000	C	-1.296938000	3.965165000	-0.689333000
H	-1.908933000	4.805249000	-1.294936000	H	-1.555678000	4.874989000	-1.218306000
C	-0.241383000	3.702386000	-0.465077000	C	0.010158000	3.790955000	-0.209231000
C	0.235246000	2.599401000	0.229924000	C	0.406492000	2.644296000	0.475042000
H	0.479766000	4.434903000	-0.814809000	H	0.743541000	4.572672000	-0.375869000
H	1.290603000	2.471700000	0.415751000	H	1.418914000	2.527977000	0.834826000
C	-0.716117000	1.671483000	0.650718000	C	-0.558835000	1.661986000	0.662189000
N	-0.561213000	0.477386000	1.344806000	N	-0.457649000	0.414176000	1.318266000
H	-2.110102000	-0.196896000	2.634481000	H	-2.159824000	-0.034402000	2.489999000
H	-1.901798000	-1.149335000	1.139115000	H	-1.784377000	-1.239329000	1.233412000
C	0.615809000	-0.168712000	1.593109000	C	0.673745000	-0.234968000	1.646268000
C	0.567475000	-1.497257000	2.272605000	C	0.570170000	-1.559912000	2.335025000
O	1.675368000	0.372456000	1.243022000	O	1.782620000	0.278979000	1.370382000
H	-0.109598000	-1.485546000	3.129476000	H	-0.140813000	-1.524485000	3.163753000
H	1.574304000	-1.764802000	2.588655000	H	1.558518000	-1.840349000	2.695150000
H	0.218474000	-2.247362000	1.552390000	H	0.241446000	-2.318036000	1.614179000
Fe	3.071418000	-0.205439000	-0.107564000	Fe	2.992468000	-0.266099000	-0.117679000

Cl	2.116014000	0.610570000	-1.934842000	Cl	1.943402000	0.621957000	-1.868377000
Cl	2.954226000	-2.403853000	0.007066000	Cl	2.745760000	-2.471902000	-0.123693000
Cl	4.906624000	0.759867000	0.502861000	Cl	4.944926000	0.548324000	0.318506000
B1 E(RM062X) = -2369.49654770				**A2** E(RM062X) = -3873.51738580			
C	-2.591900000	-0.384873000	-0.997208000	C	-4.091004000	0.932047000	0.845694000
C	-2.622224000	0.559885000	0.357377000	C	-3.077550000	-1.418770000	-0.296922000
C	-4.088238000	0.769871000	0.738453000	C	-4.433274000	-1.883772000	-0.673789000
C	-4.837103000	-0.539600000	0.966122000	H	-4.731451000	-0.651408000	-2.438258000
C	-4.788811000	-1.425713000	-0.300650000	H	-4.234733000	-2.820252000	-1.225416000
C	-1.793145000	-0.096620000	1.480980000	H	-4.977459000	-2.184677000	0.227537000
C	-3.367050000	-1.605414000	-0.710533000	C	-5.302044000	-0.977173000	-1.559871000
C	-2.733619000	-2.829530000	-0.706259000	H	-6.129223000	-1.585695000	-1.934206000
C	-1.379873000	-2.921667000	-1.072046000	C	-5.858743000	0.251515000	-0.815709000
C	-0.615923000	-1.802061000	-1.464733000	H	-6.445920000	-0.079533000	0.047483000
C	-1.207388000	-0.569903000	-1.445495000	H	-6.539088000	0.783886000	-1.486277000
C	-1.840268000	1.818119000	0.084247000	C	-4.731096000	1.146107000	-0.381298000
N	-0.448322000	0.475899000	1.320668000	H	-4.531174000	0.243083000	1.564086000
C	-2.205072000	2.940766000	-0.646150000	C	-4.196610000	2.094029000	-1.260880000
C	-1.269658000	3.962863000	-0.803693000	H	-4.696335000	2.288567000	-2.206575000
C	0.004941000	3.850581000	-0.246570000	C	-3.028693000	2.783876000	-0.935978000
C	-0.557902000	1.718436000	0.627176000	C	-2.371897000	2.529836000	0.275113000
C	0.388509000	2.724171000	0.480914000	H	-2.632300000	3.531461000	-1.617225000
C	0.672402000	-0.135738000	1.706658000	H	-1.462071000	3.065980000	0.528733000
O	1.794220000	0.357656000	1.405466000	C	-2.913965000	1.613727000	1.170911000
C	0.578330000	-1.402330000	2.503597000	H	-2.427719000	1.442141000	2.126541000
Fe	2.926670000	-0.266607000	-0.082056000	C	-2.337683000	-1.821281000	0.820952000
Cl	1.950263000	0.626701000	-1.879535000	C	-2.178291000	-0.661992000	-1.210758000
Cl	2.514449000	-2.463929000	-0.075027000	C	-2.722730000	-2.621755000	1.922439000
Cl	4.958868000	0.361128000	0.285653000	H	-3.737236000	-2.996581000	2.006994000
H	-5.268417000	-2.390591000	-0.124799000	C	-1.771514000	-2.916167000	2.871572000
H	-5.335265000	-0.916896000	-1.104198000	H	-2.022440000	-3.530950000	3.727913000
H	-5.880303000	-0.340919000	1.220730000	C	-0.457135000	-2.422105000	2.734254000
H	-4.401715000	-1.087822000	1.810240000	C	-0.047917000	-1.619103000	1.669669000
H	-3.283133000	-3.727977000	-0.444497000	H	0.280057000	-2.673472000	3.491025000
H	-3.128830000	0.260096000	-1.708159000	H	0.971935000	-1.269133000	1.619081000
H	-0.899981000	-3.898293000	-1.062529000	C	-1.008630000	-1.321185000	0.716047000
H	0.420402000	-1.916718000	-1.765530000	N	-0.916172000	-0.568064000	-0.469095000
H	-0.634194000	0.308821000	-1.732915000	H	-2.024199000	-1.234979000	-2.137488000
H	0.292420000	-2.231756000	1.847888000	H	-2.560784000	0.335075000	-1.461683000
H	-1.754008000	-1.185946000	1.426081000	C	0.138483000	0.075729000	-0.953279000
H	1.564553000	-1.623080000	2.909140000	C	0.063867000	0.757698000	-2.273453000
H	-0.152198000	-1.311951000	3.310566000	O	1.220292000	0.094741000	-0.255582000
H	1.380549000	2.637323000	0.902780000	H	-0.232719000	0.043292000	-3.047256000
H	0.721410000	4.652934000	-0.382349000	H	1.043578000	1.171373000	-2.512326000
H	-1.534270000	4.852015000	-1.364539000	H	-0.669643000	1.571624000	-2.223818000
H	-3.195665000	3.031336000	-1.082696000	Fe	1.773425000	1.802944000	0.821057000

H	-4.583560000	1.349880000	-0.049082000	Cl	0.388309000	1.592109000	2.525521000
H	-4.108911000	1.386291000	1.643342000	Cl	1.187675000	3.410643000	-0.552555000
H	-2.204693000	0.198729000	2.453900000	Cl	3.866121000	1.407646000	1.161997000
				Fe	2.728294000	-1.267204000	-0.887419000
				Cl	3.473002000	-2.180214000	0.938457000
				Cl	1.228066000	-2.559169000	-1.942925000
				Cl	3.934688000	-0.099728000	-2.247164000
TS$_{A2B2}$ E(RM062X) = -3873.51429096 Frequency -168.6198				**B2** E(RM062X) = -3873.52201529			
C	-4.023152000	0.690742000	0.684305000	C	-3.857221000	0.332830000	0.454188000
C	-3.149842000	-1.159762000	-0.181095000	C	-3.178895000	-1.044966000	-0.126020000
C	-4.419755000	-1.828266000	-0.615751000	C	-4.311707000	-1.935690000	-0.641381000
H	-4.765539000	-0.780980000	-2.482761000	H	-4.546096000	-1.042729000	-2.604091000
H	-4.074829000	-2.757597000	-1.096218000	H	-3.861867000	-2.855309000	-1.030420000
H	-4.983667000	-2.140155000	0.269258000	H	-4.947765000	-2.228388000	0.202006000
C	-5.321184000	-1.062623000	-1.579930000	C	-5.153970000	-1.256102000	-1.716590000
H	-6.133270000	-1.720184000	-1.899003000	H	-5.962057000	-1.915806000	-2.039475000
C	-5.902012000	0.202994000	-0.913954000	C	-5.765694000	0.062075000	-1.185746000
H	-6.522883000	-0.085788000	-0.059874000	H	-6.479868000	-0.181017000	-0.388967000
H	-6.536139000	0.735589000	-1.626500000	H	-6.306770000	0.589798000	-1.973539000
C	-4.754170000	1.055286000	-0.477413000	C	-4.681840000	0.915541000	-0.622556000
H	-4.504147000	0.059739000	1.428238000	H	-4.499090000	-0.066243000	1.254296000
C	-4.265445000	2.084223000	-1.279494000	C	-4.353433000	2.152342000	-1.136628000
H	-4.803098000	2.363291000	-2.180952000	H	-4.918887000	2.568918000	-1.964188000
C	-3.103118000	2.769087000	-0.920364000	C	-3.302942000	2.891832000	-0.569518000
C	-2.391889000	2.432877000	0.245795000	C	-2.551447000	2.434516000	0.536593000
H	-2.744849000	3.582674000	-1.545430000	H	-3.060105000	3.864406000	-0.992827000
H	-1.494334000	2.979466000	0.519538000	H	-1.763136000	3.047445000	0.959380000
C	-2.862332000	1.416946000	1.054118000	C	-2.827759000	1.198896000	1.044575000
H	-2.332095000	1.162112000	1.967465000	H	-2.254785000	0.816611000	1.886648000
C	-2.363619000	-1.662219000	0.918193000	C	-2.323013000	-1.656438000	0.952306000
C	-2.174245000	-0.617338000	-1.190003000	C	-2.139687000	-0.721269000	-1.217397000
C	-2.761473000	-2.423428000	2.024640000	C	-2.712139000	-2.376803000	2.072220000
H	-3.802599000	-2.690798000	2.174928000	H	-3.757556000	-2.604478000	2.259239000
C	-1.787966000	-2.833858000	2.920386000	C	-1.725356000	-2.818612000	2.953715000
H	-2.061143000	-3.430886000	3.782684000	H	-2.005206000	-3.393528000	3.829225000
C	-0.444757000	-2.487745000	2.715917000	C	-0.381320000	-2.531092000	2.716916000
C	-0.027156000	-1.718967000	1.629094000	C	0.023697000	-1.796239000	1.603093000
H	0.305092000	-2.826641000	3.423058000	H	0.375200000	-2.883038000	3.409317000
H	1.018057000	-1.474474000	1.506980000	H	1.071125000	-1.580085000	1.446833000
C	-1.011340000	-1.309711000	0.741684000	C	-0.973946000	-1.369839000	0.736194000
N	-0.900445000	-0.558154000	-0.458596000	N	-0.854215000	-0.648707000	-0.497621000
H	-2.077957000	-1.338877000	-2.014565000	H	-2.089129000	-1.545610000	-1.938799000
H	-2.439087000	0.360815000	-1.598659000	H	-2.322836000	0.213849000	-1.749993000
C	0.161114000	0.049301000	-0.950049000	C	0.209244000	-0.091153000	-1.022731000
C	0.107351000	0.716232000	-2.281464000	C	0.214294000	0.393604000	-2.434815000

O	1.249538000	0.061553000	-0.246721000	O	1.282628000	0.025358000	-0.287715000
H	-0.257893000	0.018476000	-3.039784000	H	-0.070359000	-0.422977000	-3.104880000
H	1.108966000	1.057394000	-2.545625000	H	1.219352000	0.737060000	-2.684383000
H	-0.557684000	1.586733000	-2.228451000	H	-0.477274000	1.232378000	-2.556392000
Fe	1.724414000	1.732737000	0.878199000	Fe	1.520578000	1.767468000	0.752651000
Cl	0.291997000	1.514202000	2.550023000	Cl	0.255337000	1.502700000	2.551100000
Cl	1.121907000	3.358191000	-0.483078000	Cl	0.521822000	3.192205000	-0.642300000
Cl	3.812869000	1.433750000	1.305621000	Cl	3.639945000	1.965767000	1.038683000
Fe	2.784483000	-1.210777000	-0.943733000	Fe	2.924429000	-1.151330000	-0.818587000
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Cl	1.331533000	-2.511765000	-2.042808000	Cl	1.642849000	-2.706699000	-1.772653000
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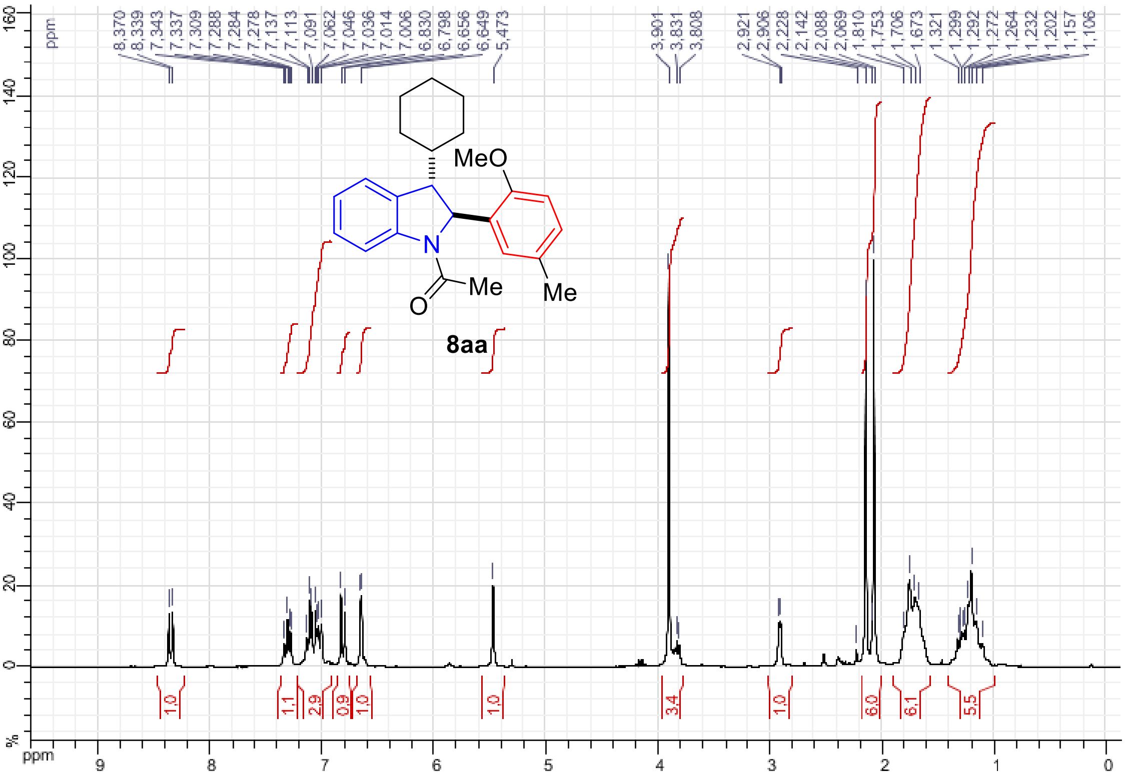
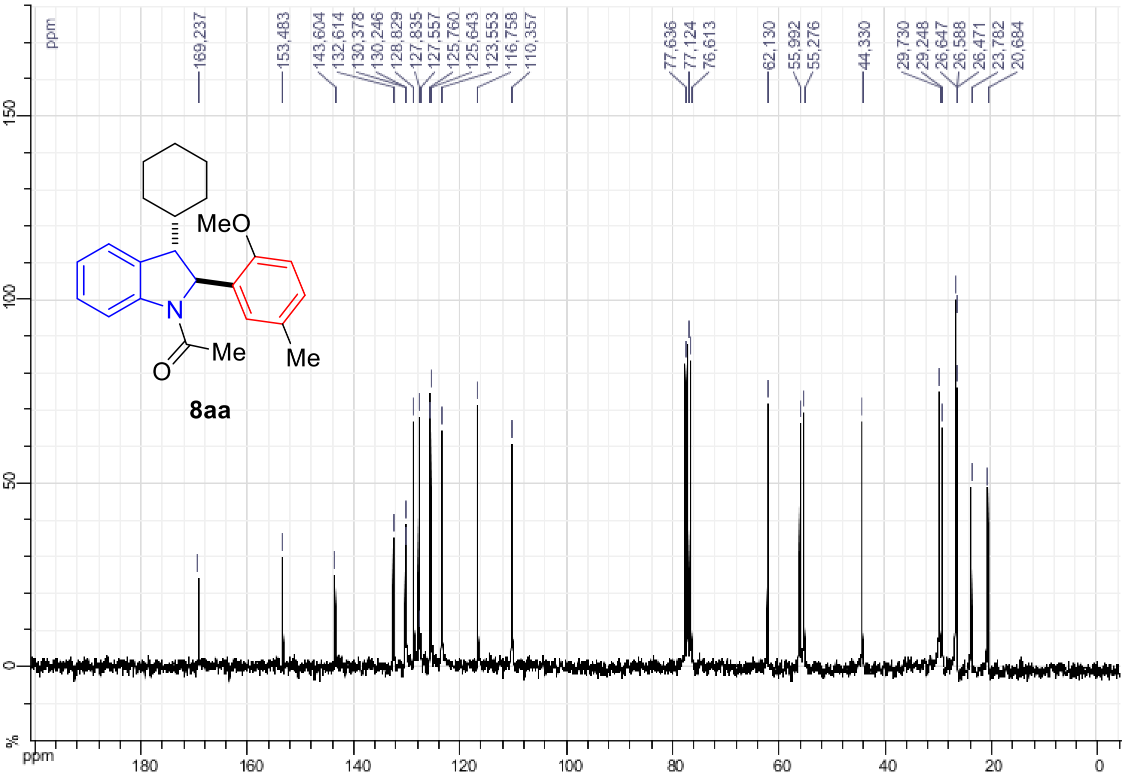
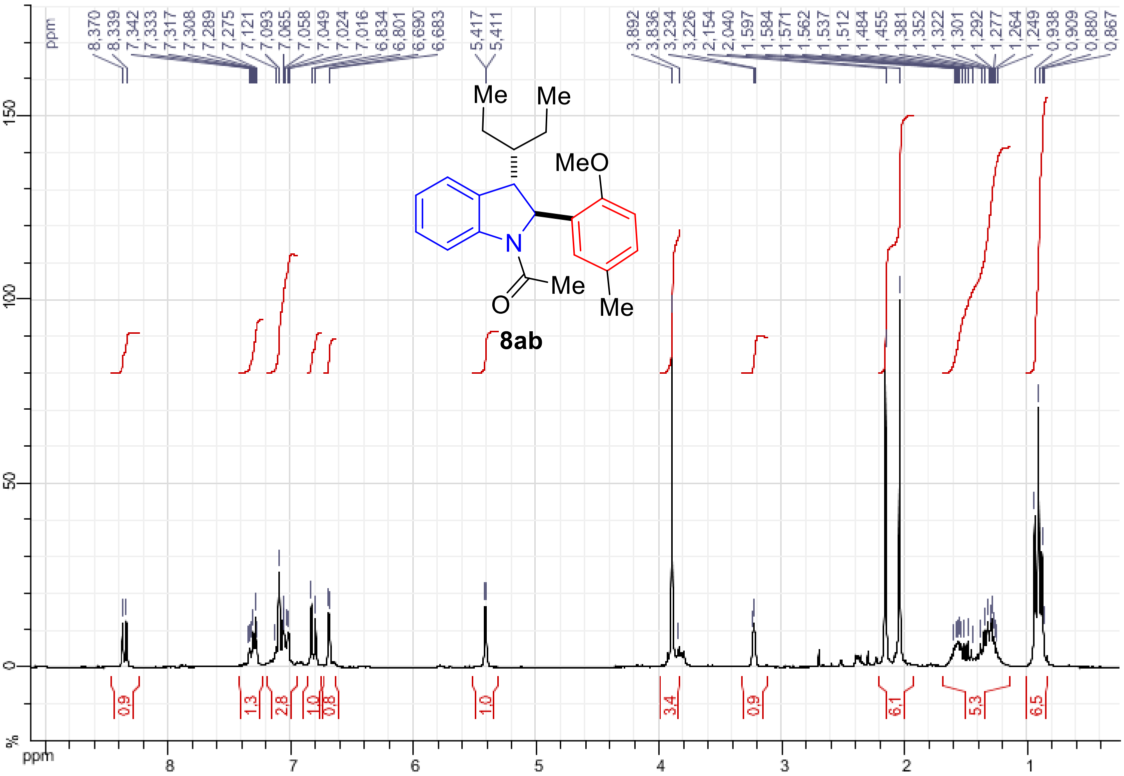
IV. NMR spectra of new compounds



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7,049
7,024
7,016
6,834
6,801
6,690
6,683
5,417
5,411
3,892
3,836
3,234
3,226
2,154
2,040
1,597
1,584
1,571
1,562
1,537
1,512
1,484
1,455
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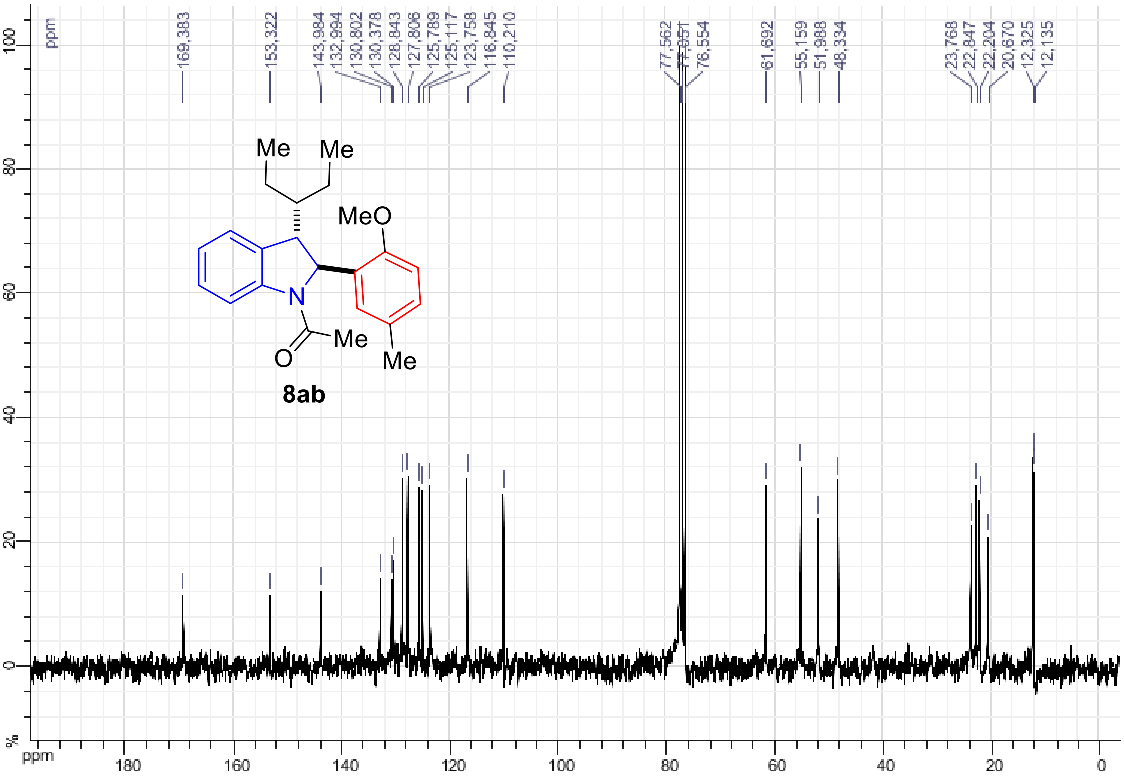
1,249
0,938
0,909
0,880
0,867
Me
Me
MeO
N
O
Me
Me
8ab
150
100
50
0
%
0,9
1,3
2,8
1,0
0,8
1,0
3,4
0,9
6,1
5,3
6,5
ppm
8
7
6
5
4
3
2
1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110,210
77,562
77,057
76,554
61,692
55,159
51,988
48,334
23,768
22,847
22,204
20,670
12,325
12,135
Me
Me
MeO
N
O
Me
Me
8ab
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60
40
20
0
%
ppm
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140
120
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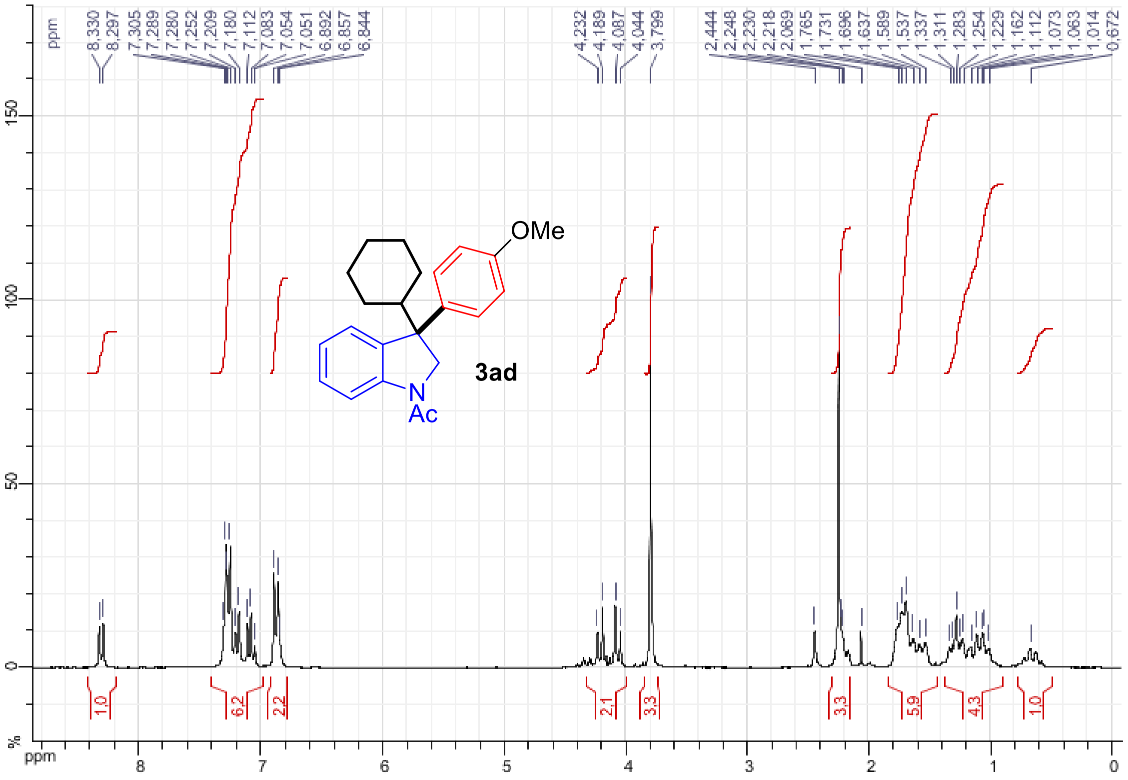
80
60
40
20
0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6,857
6,844
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4,189
4,087
4,044
3,799
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2,248
2,230
2,218
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1,731
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1,589
1,537
1,337
1,311
1,283
1,254
1,229
1,162
1,112
1,073
1,063
1,014
0,672
150
100
50
0
%
OMe
N
Ac
3ad
1,0
6,2
2,2
2,1
3,3
3,3
5,9
4,3
1,0
ppm
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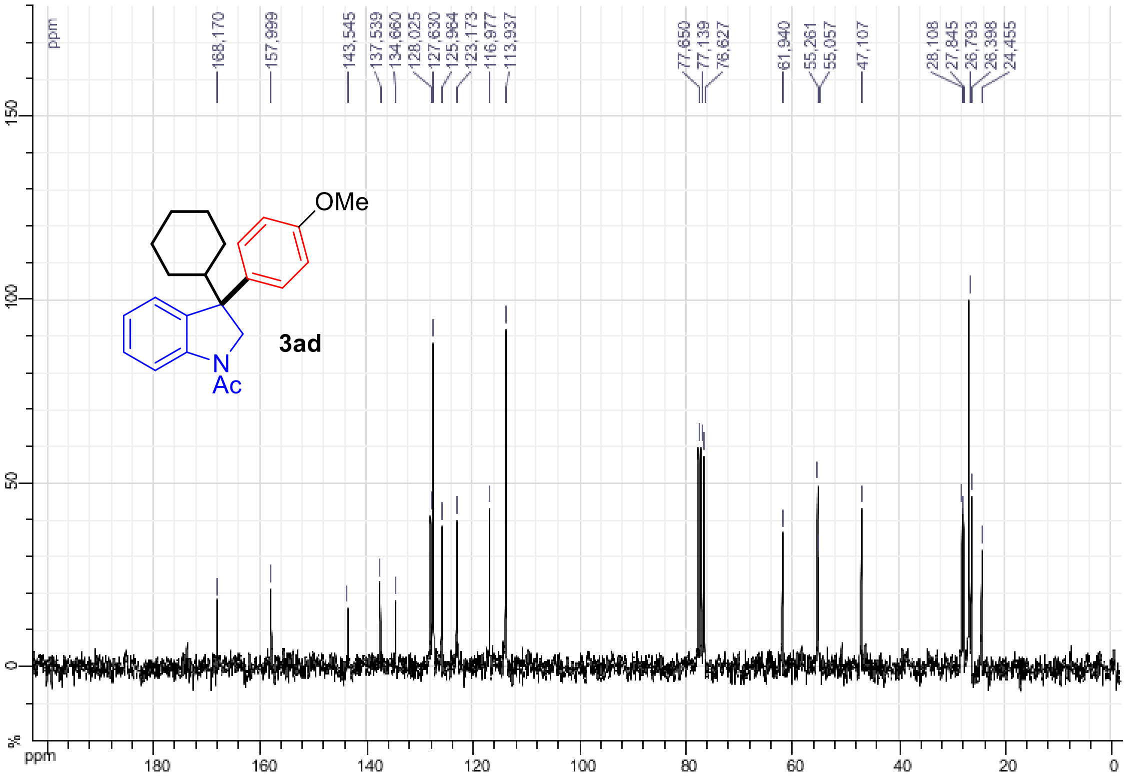
7
6
5
4
3
2
1
0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76,627
61,940
55,261
55,057
47,107
28,108
27,845
26,793
26,398
24,455
150
100
50
0
%
OMe
N
Ac
3ad
ppm
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140
120
100
80
60
40
20
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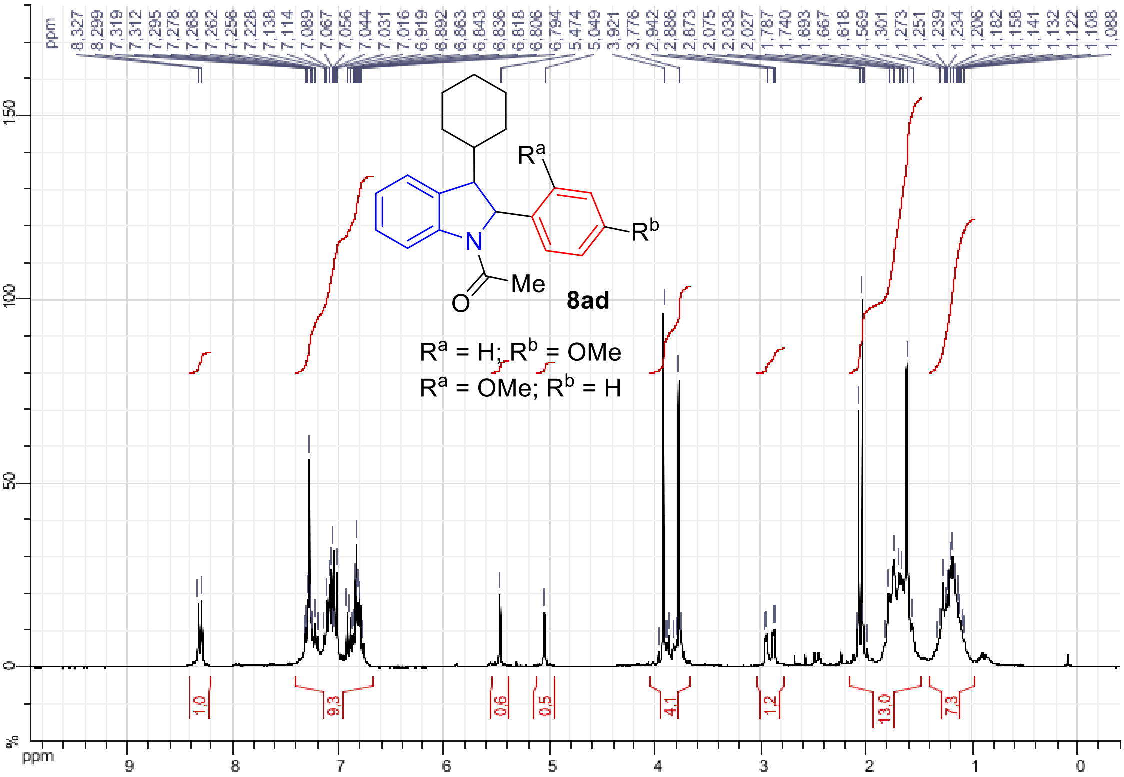
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7,067
7,056
7,044
7,031
7,016
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6,892
6,863
6,843
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6,818
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6,794
5,474
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3,921
3,776
2,942
2,886
2,873
2,075
2,038
2,027
1,787
1,740
1,693
1,667
1,618
1,569
1,301
1,273
1,251
1,239
1,234
1,206
1,182
1,158
1,141
1,132
1,122
1,108
1,088
R^a
R^b
N
O
Me
8ad
R^a = H; R^b = OMe
R^a = OMe; R^b = H
150
100
50
0
%
1,0
9,3
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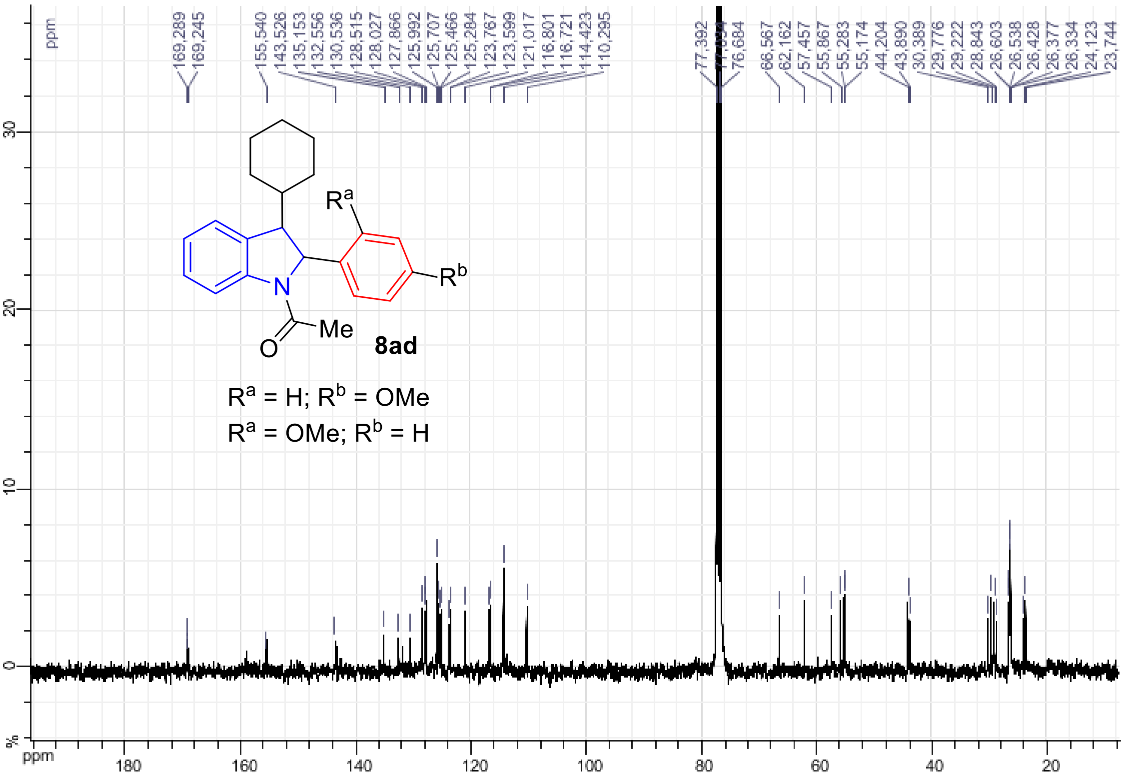
1,2
13,0
7,3
ppm
9
8
7
6
5
4
3
2
1
0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127,866
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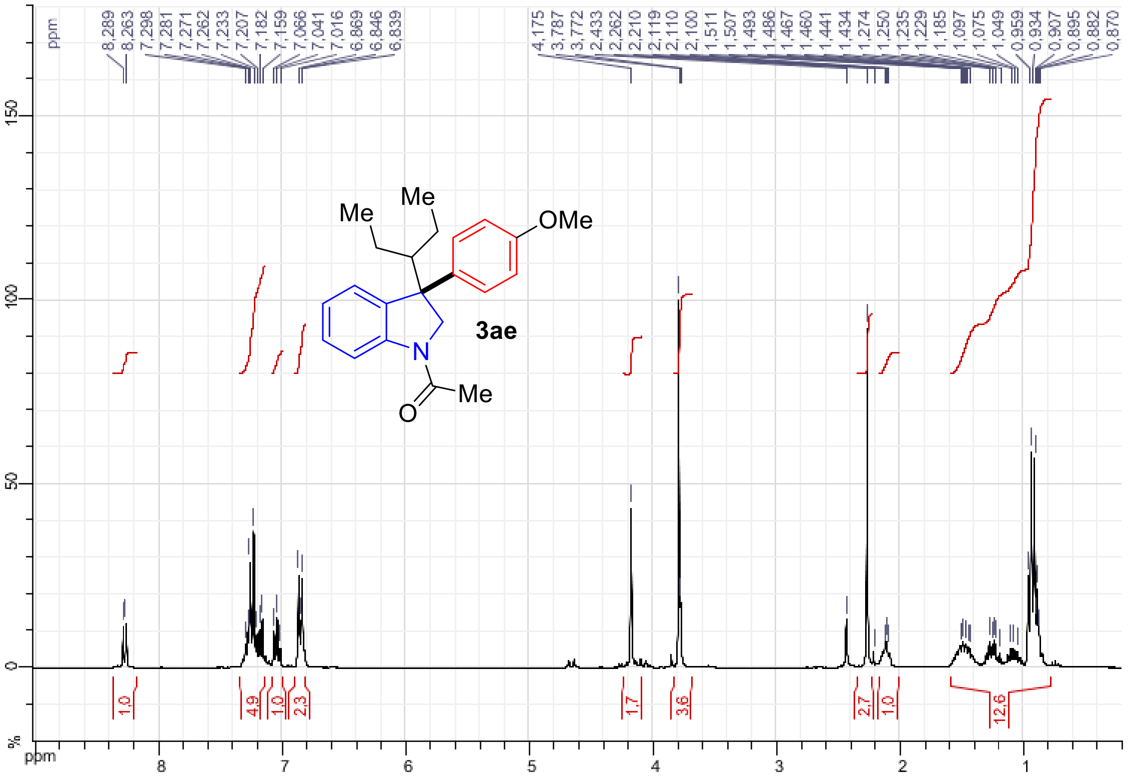
125,284
123,767
123,599
121,017
116,801
116,721
114,423
110,295
77,392
76,684
66,567
62,162
57,457
55,867
55,283
55,174
44,204
43,890
30,389
29,776
29,222
28,843
26,603
26,538
26,428
26,377
26,334
24,123
23,744
R^a
R^b
N
O
Me
8ad
R^a = H; R^b = OMe
R^a = OMe; R^b = H
30
20
10
0
%
ppm
180
160
140
120
100
80
60
40
20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6,846
6,839
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3,787
3,772
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2,262
2,210
2,119
2,110
2,100
1,511
1,507
1,493
1,486
1,467
1,460
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1,229
1,185
1,097
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0,959
0,934
0,907
0,895
0,882
0,870
Me
Me
OMe
N
O
Me
3ae
1,0
4,9
1,0
2,3
1,7
3,6
2,7
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12,6
%
150
100
50
0
ppm
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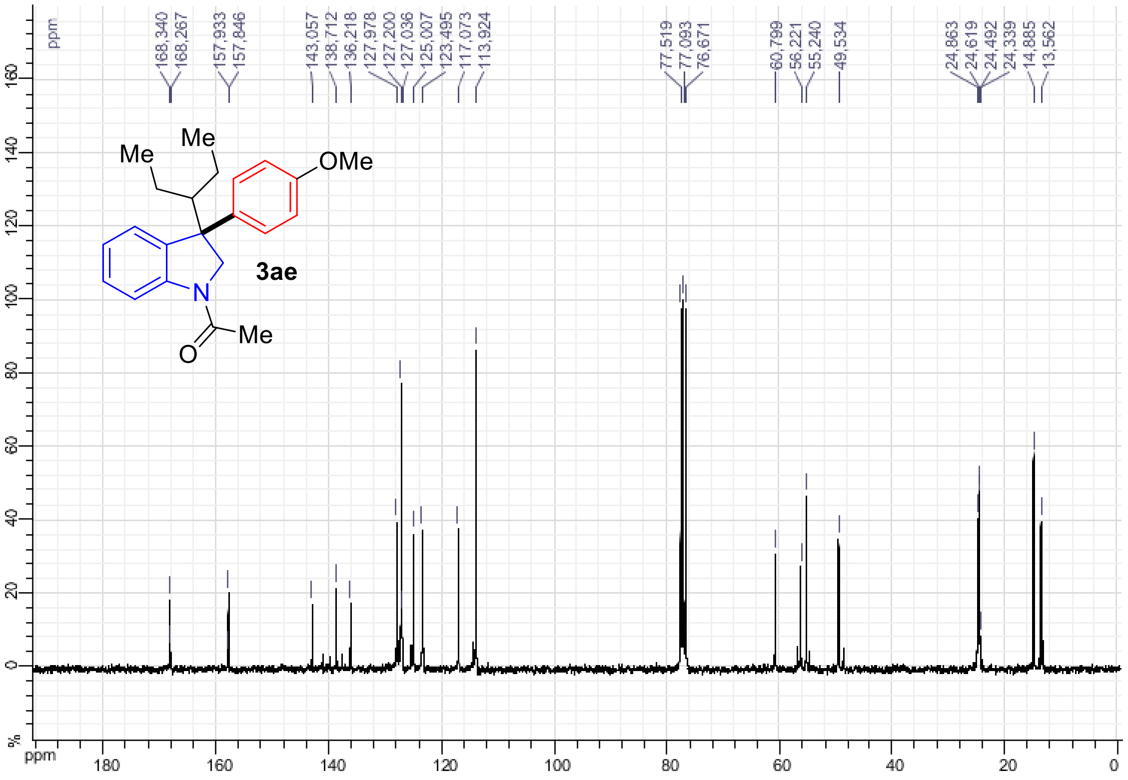
6
5
4
3
2
1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127,036
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113,924
77,519
77,093
76,671
60,799
56,221
55,240
49,534
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24,619
24,492
24,339
14,885
13,562
Me
Me
OMe
N
O
Me
3ae
%
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140
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80
60
40
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0
ppm
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140
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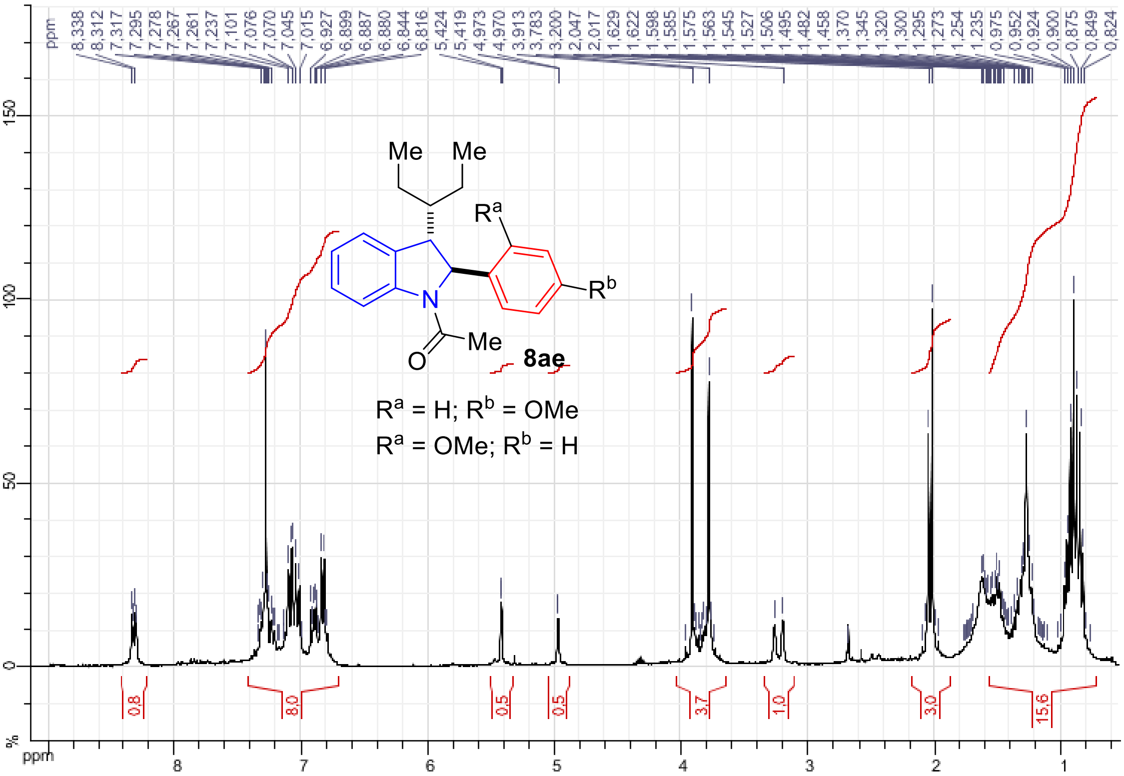
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Me Me
R^a
R^b
N
O
Me
8ae
R^a = H; R^b = OMe
R^a = OMe; R^b = H
0,8
8,0
0,5
0,5
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150
100
50
0
%
ppm
8
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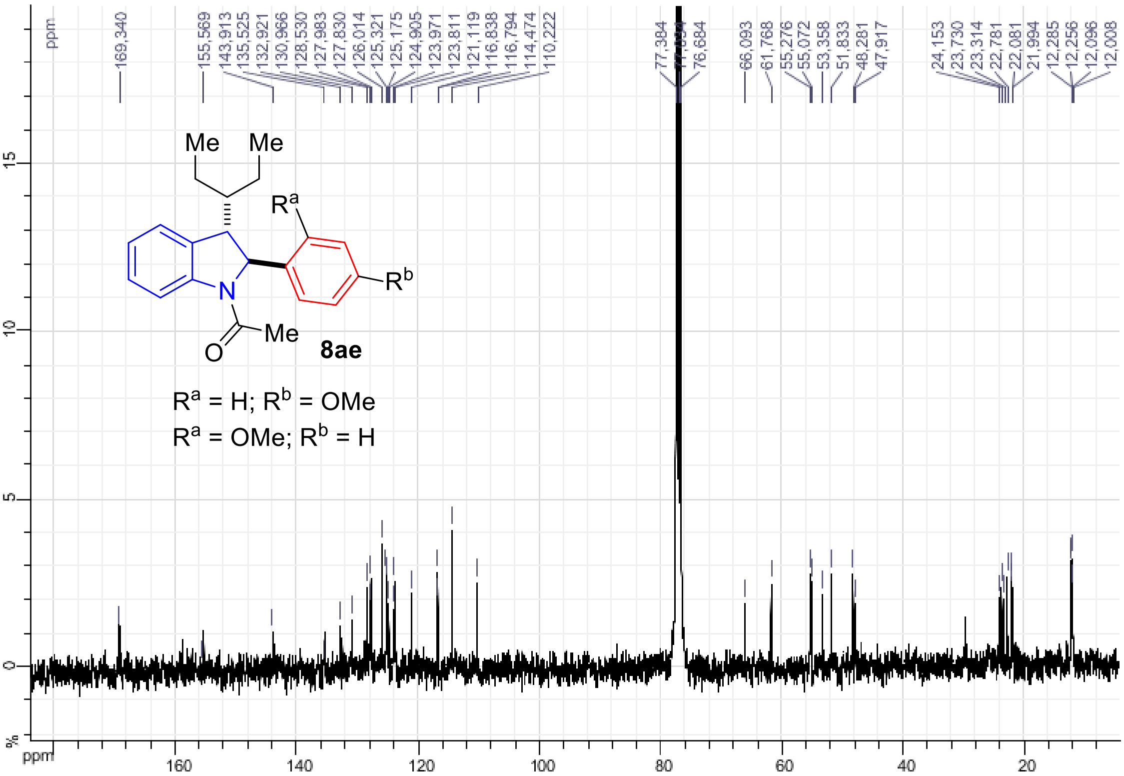
4
3
2
1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Me Me
R^a
R^b
N
O
Me
8ae
R^a = H; R^b = OMe
R^a = OMe; R^b = H
15
10
5
0
%
ppm
160
140
120
100
80
60
40
20