

Supporting Information

**P(NMe₂)₃-Mediated Reductive [1 + 4] Annulation of Isatins with
Enones: Facile Synthesis of Spirooxindole-Dihydrofurans**

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Table of Contents

I. General Information	S2
II. The Detailed Rationale about the Stereochemical Outcome	S3
III. Typical Procedure for the [1 + 4] Annulation Reaction	S5
IV. Analytical Data for Compounds 3 and 4	S5
V. ORTEP Drawings for 3b , 3v , and 3w	S15
VI. ¹ H and ¹³ C NMR Spectra of 3 and 4	S18

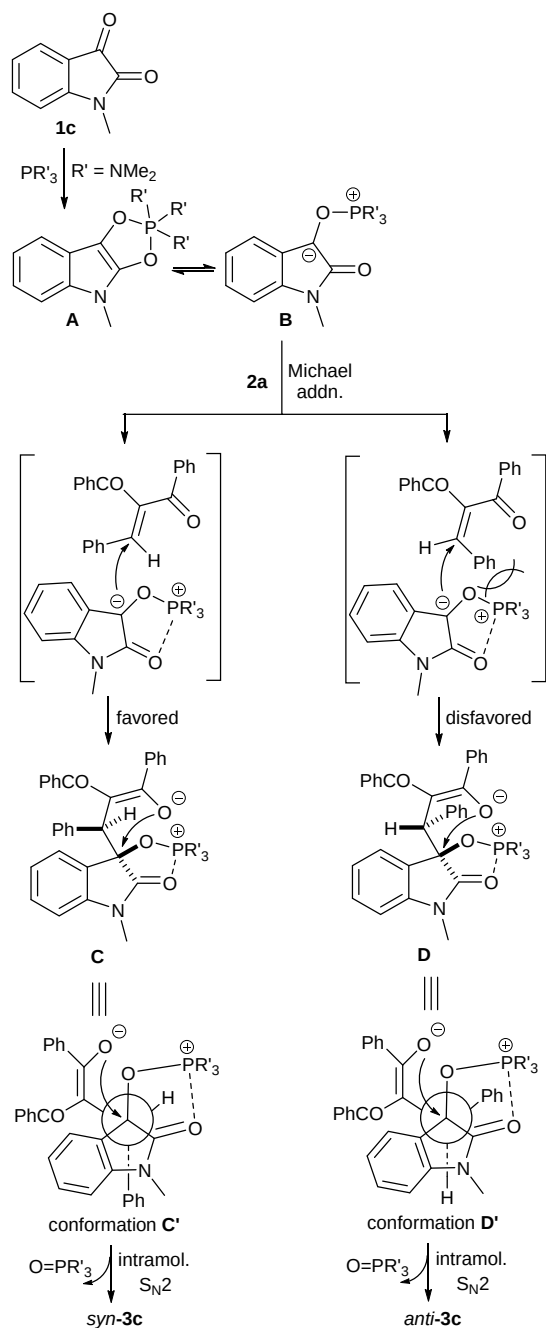
I. General Information

Unless otherwise noted, all reactions were carried out in nitrogen atmosphere under anhydrous conditions. Solvents were purified prior to use according to standard procedures. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 with tetramethylsilane (TMS) as the internal standard. Column chromatography was performed on silica gel (200-300 mesh) using a mixture of petroleum ether/ethyl acetate as eluant. Isatins **1**¹ and enones **2**² were prepared according to the literature procedures.

1 (a) S.-H. Cao, X.-C. Zhang, Y. Wei and M. Shi, *Eur. J. Org. Chem.*, 2011, 2668; (b) K. Aikawa, S. Mimura, Y. Numata and K. Mikami, *Eur. J. Org. Chem.*, 2011, 62.

2 (a) R. Antonioletti, P. Bovicelli and S. Malancona, *Tetrahedron*, 2002, **58**, 589; (b) F.-L. Hu, Y. Wei and M. Shi, *Chem. Commun.*, 2014, **50**, 8912.

II. The Detailed Rationale about the Stereochemical Outcome

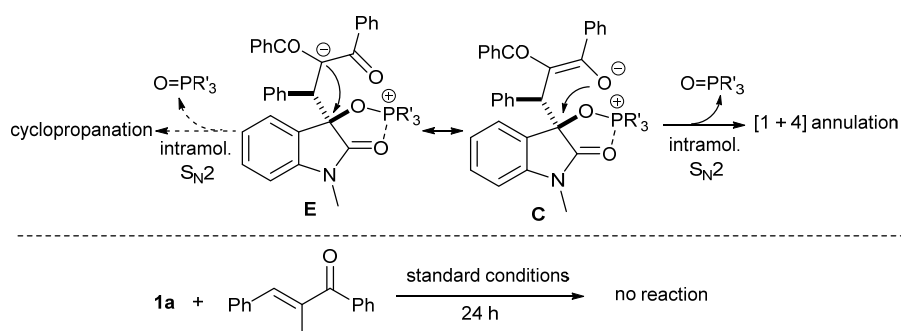


Scheme S1

The detailed rationale about the stereochemical outcome of the [1+4] annulation is presented as follows: presumably, a highly diastereoselective Michael addition step plays a critical role in the overall stereochemistry of the annulation by delivering the predominant intermediate **C**. The stereoselectivity of the Michael step is primarily controlled by the steric effect of the substrates' substituents. As shown in Scheme S1, the planar carbanion intermediate **B** presumably undergoes the Michael addition to the planar olefins such as **2a** in two possible modes: in a favored mode,

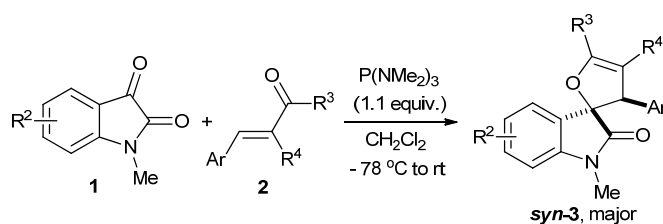
the aryl group like phenyl group in **2a** faces to the benzene ring of the intermediate **B** and the small hydrogen faces to the bulky phosphonium moiety. By this way, the possible π - π stacking interaction between aryl groups and less steric hindrance facilitate the Michael addition leading to a predominant intermediate **C**. In another alternative but disfavored mode, the phenyl group of **2a** faces to the bulky phosphonium moiety and the terminal olefinic hydrogen of **2a** faces to the benzene ring of the intermediate **B**. By this way, the increased steric hindrance disfavors the Michael addition of intermediate **B** to alkene **2a** leading to the minor intermediate **D**. Subsequently, intermediate **C** adopts the preferred conformation **C'** to accomplish the cyclization through an intramolecular S_N2 displacement to give the major annulation product *syn*-**3c**. The minor intermediate **D** cyclizes by the same way via the preferred conformation **D'** to give out the minor product *anti*-**3c**. In the course of the annulation, the Coulombic interaction between phosphonium cation and the carbonyl oxygen atom presumably stabilizes the relevant intermediates. Accordingly, the stereochemistry outcome of the annulation reaction should be governed together by the steric effect of substrates' substituents, the stereochemistry requirement of an S_N2 displacement, and the Coulombic interaction.

By the plausible mechanism, the role of the electron-withdrawing group at the α position of keto group in enones **2** may be interpreted as follows: an electron-withdrawing group like a benzoyl group in intermediate **C** can substantially stabilize the enolate intermediate like **C**, which thereby tends to engage in an intramolecular S_N2 displacement as an oxygen nucleophile to lead to a [1 + 4] annulation mode; meanwhile, the electron-withdrawing group at the α position imposes an increased steric hindrance on the mesomeric structure of the delocalized enolate intermediate like tertiary carbanion **E** (Scheme S2). Consequently, the increased steric hindrance inhibits the enolate intermediate in the form of carbanion **E** from undergoing cyclopropanation via an intramolecular S_N2 displacement. As a supportive evidence for this hypothesis, in our control experiments, when isatin **1a** was reacted with (*E*)-2-methyl-1,3-diphenylprop-2-en-1-one under the standard conditions, no cyclopropanation reaction occurred after 24 h (Scheme S2, bottom). This result is in sharp contrast with that shown in Scheme 4, and implies that the increased steric hindrance at the α position of the enones significantly retards the [1+2] annulation mode of the enolate intermediate **C**.



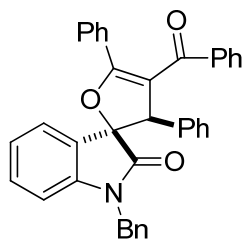
Scheme S2

III. Typical Procedure for the [1 + 4] Annulation Reaction



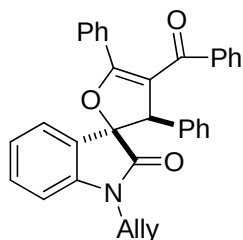
Under N_2 atmosphere and at $-78\text{ }^{\circ}\text{C}$, a solution of $\text{P(NMe}_2)_3$ (0.22 mmol, 40 μL) in CH_2Cl_2 (0.5 mL) was added dropwise by means of syringe to a solution of isatin **1** (0.2 mmol) and enone **2** (0.22 mmol) in CH_2Cl_2 (1.5 mL). The resulting reaction mixture was then slowly warmed up to room temperature and stirred at rt until **1** was completely consumed, as monitored by TLC. The solvent was removed on a rotary evaporator under reduced pressure and the residue was subjected to column chromatography isolation on silica gel by gradient elution with petroleum ether/ ethyl acetate (20:1-5:1) to give product **3**.

IV. Analytical Data for Compounds **3** and **4**

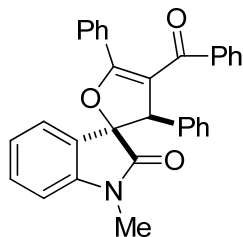


3a. Yield 74% as an isomeric mixture (dr 89:11) with **syn-3a** being the major. Data for **syn-3a**: white solid; mp $227\text{--}229\text{ }^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.94 – 7.87 (m, 2H), 7.72 (dd, $J = 7.3$, 1.0 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.33 – 7.27 (m, 1H), 7.24 – 7.01 (m, 15H), 6.49 (d, $J = 7.6$ Hz, 1H), 6.44 (d, $J = 7.2$ Hz, 2H), 5.64 (s, 1H), 5.11 (d, $J = 15.9$ Hz, 1H), 4.17 (d, $J = 15.9$ Hz, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.7, 172.7, 164.7, 143.7, 138.2, 134.7, 133.9, 132.1, 130.9, 130.4, 129.7, 129.6, 129.3, 128.8, 128.6, 128.4, 128.0, 127.8, 127.7, 127.2, 126.8, 126.5, 124.7,

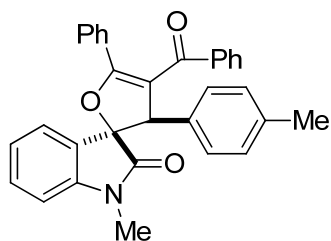
123.4, 114.9, 109.5, 89.6, 62.5, 43.6; HRMS–ESI $[M + H]^+$ Calcd for $C_{37}H_{28}NO_3$ 534.2064, found 534.2056.



3b. Yield 72% as an isomeric mixture (dr 88:12) with *syn*-**3b** being the major. Data for *syn*-**3b**: white solid; mp 231-232 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.5 Hz, 2H), 7.71 (d, J = 7.4 Hz, 1H), 7.42 – 7.27 (m, 4H), 7.24 – 7.15 (m, 4H), 7.14 – 7.04 (m, 5H), 6.96 (d, J = 7.2 Hz, 2H), 6.68 (d, J = 7.8 Hz, 1H), 5.56 (s, 1H), 5.29 – 5.15 (m, 1H), 4.86 (d, J = 10.4 Hz, 1H), 4.49 (d, J = 17.2 Hz, 1H), 4.36 – 4.23 (m, 1H), 3.71 (dd, J = 16.5, 5.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 172.3, 164.9, 143.6, 138.3, 133.9, 132.1, 130.8, 130.4, 130.3, 129.8, 129.7, 129.4, 128.5, 128.2, 128.0, 127.7, 127.6, 126.8, 124.6, 123.3, 116.9, 114.7, 109.1, 89.8, 62.9, 41.9; HRMS–ESI $[M + H]^+$ Calcd for $C_{33}H_{26}NO_3$ 484.1907, found 484.1907.

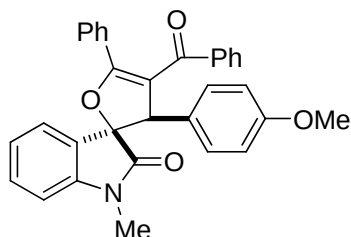


3c. Yield 94% as an isomeric mixture (dr 91:9) with *syn*-**3c** being the major. Data for *syn*-**3c**: white solid; mp 186-187 °C; 1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.4 Hz, 2H), 7.69 (d, J = 7.3 Hz, 1H), 7.45 – 7.33 (m, 3H), 7.30 (t, J = 7.4 Hz, 1H), 7.24 – 7.14 (m, 4H), 7.14 – 7.03 (m, 5H), 6.94 (d, J = 6.8 Hz, 2H), 6.71 (d, J = 7.8 Hz, 1H), 5.53 (s, 1H), 2.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 172.5, 164.9, 144.3, 138.2, 133.9, 132.1, 130.9, 130.4, 129.7, 129.6, 129.4, 128.3, 128.0, 127.9, 127.7, 127.6, 127.1, 124.5, 123.3, 114.7, 108.3, 89.7, 62.6, 25.6; HRMS–ESI $[M + H]^+$ Calcd for $C_{31}H_{24}NO_3$ 458.1751, found 458.1766.

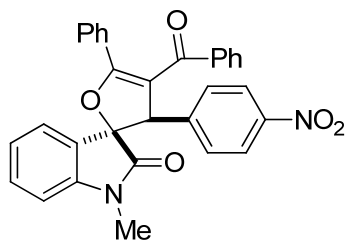


3d. Combined yield 93%, dr 90:10, and 84% yield for *syn*-**3d**. Data for *syn*-**3d**: pale red; 210-212

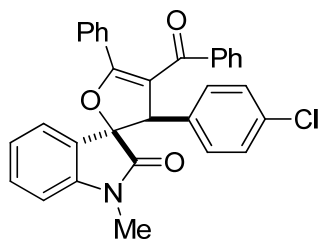
°C; ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J = 7.4$ Hz, 2H), 7.68 (d, $J = 7.3$ Hz, 1H), 7.43 – 7.33 (m, 3H), 7.29 (t, $J = 7.4$ Hz, 1H), 7.24 – 7.13 (m, 4H), 7.09 (t, $J = 7.6$ Hz, 2H), 6.86 (q, $J = 8.1$ Hz, 4H), 6.72 (d, $J = 7.8$ Hz, 1H), 5.49 (s, 1H), 2.86 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.8, 172.6, 164.7, 144.3, 138.3, 137.0, 132.0, 130.9, 130.8, 130.3, 129.7, 129.5, 128.8, 128.2, 127.9, 127.7, 127.3, 124.5, 123.3, 114.9, 108.2, 89.6, 62.3, 25.7, 21.0; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{32}\text{H}_{26}\text{NO}_3$ 472.1907, found 472.1909.



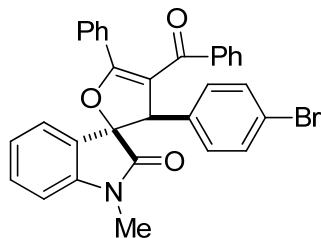
3e. Yield 87% as an isomeric mixture (dr 95:5) with *syn*-**3e** being the major. Data for *syn*-**3e**: yellow solid; mp 187-189 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, $J = 7.4$ Hz, 2H), 7.67 (d, $J = 7.3$ Hz, 1H), 7.42 – 7.34 (m, 3H), 7.30 (t, $J = 7.4$ Hz, 1H), 7.23 – 7.14 (m, 4H), 7.09 (t, $J = 7.7$ Hz, 2H), 6.88 (d, $J = 8.6$ Hz, 2H), 6.72 (d, $J = 7.8$ Hz, 1H), 6.62 (d, $J = 8.7$ Hz, 2H), 5.48 (s, 1H), 3.66 (s, 3H), 2.87 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.8, 172.7, 164.7, 158.8, 144.3, 138.3, 132.1, 130.8, 130.4, 129.7, 129.6, 129.4, 127.9, 127.7, 127.2, 125.9, 124.5, 123.3, 114.9, 113.5, 108.2, 89.6, 61.9, 55.0, 25.7; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{32}\text{H}_{26}\text{NO}_4$ 488.1856, found 488.1859.



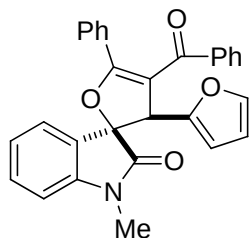
3f. Yield 82% as an isomeric mixture (dr 95:5) with *syn*-**3f** being the major. Data for *syn*-**3f**: white solid; mp 244-245 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.98 (d, $J = 8.0$ Hz, 2H), 7.80 (d, $J = 7.3$ Hz, 2H), 7.71 (d, $J = 7.1$ Hz, 1H), 7.44 (t, $J = 7.5$ Hz, 1H), 7.39 – 7.29 (m, 3H), 7.28 – 7.04 (m, 9H), 6.77 (d, $J = 7.6$ Hz, 1H), 5.59 (s, 1H), 2.89 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.3, 171.8, 166.1, 147.4, 144.1, 142.2, 137.9, 132.4, 131.4, 130.8, 129.9, 129.5, 129.4, 128.9, 128.1, 127.8, 126.5, 124.5, 123.8, 123.3, 113.9, 108.7, 89.1, 61.8, 25.9; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{23}\text{N}_2\text{O}_5$ 503.1601, found 503.1608.



3g. Combined yield 99%, dr 93:7, and 92% yield for *syn*-**3g**. Data for *syn*-**3g**: white solid; mp 255-256 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 7.2 Hz, 2H), 7.67 (d, J = 7.2 Hz, 1H), 7.40 (td, J = 7.8, 0.9 Hz, 1H), 7.35 (d, J = 7.2 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.23 – 7.14 (m, 4H), 7.13 – 7.03 (m, 4H), 6.90 (d, J = 8.5 Hz, 2H), 6.74 (d, J = 7.8 Hz, 1H), 5.49 (s, 1H), 2.88 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.5, 172.3, 165.3, 144.2, 138.1, 133.4, 132.7, 132.2, 131.1, 130.5, 129.7, 129.5, 129.2, 128.3, 128.0, 127.7, 126.7, 124.5, 123.5, 114.3, 108.4, 89.4, 61.8, 25.8; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{23}\text{ClNO}_3$ 492.1361, found 492.1372.

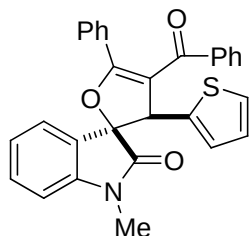


3h. Combined yield 99%, dr 93:7, and 92% for *syn*-**3h**. Data for *syn*-**3h**: white solid; mp 248-250 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, J = 7.4 Hz, 2H), 7.67 (d, J = 7.3 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.35 (d, J = 7.5 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.24 – 7.14 (m, 6H), 7.09 (t, J = 7.6 Hz, 2H), 6.85 (d, J = 8.3 Hz, 2H), 6.74 (d, J = 7.8 Hz, 1H), 5.47 (s, 1H), 2.89 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.5, 172.3, 165.3, 144.2, 138.1, 133.3, 132.2, 131.2, 131.1, 130.5, 130.1, 129.7, 129.5, 129.2, 128.0, 127.8, 126.8, 124.5, 123.5, 121.6, 114.3, 108.4, 89.3, 61.9, 25.8; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{23}\text{BrNO}_3$ 536.0856, found 536.0866.

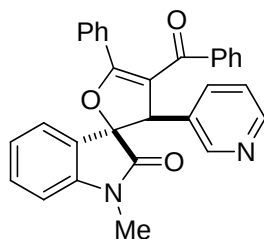


3i. Yield 99% as an isomeric mixture (dr 95:5) with *syn*-**3i** being the major. Data for *syn*-**3i**: yellow solid; mp 189-191 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (d, J = 7.4 Hz, 2H), 7.62 (d, J = 7.4 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.34 (d, J = 7.4 Hz, 2H), 7.29 (t, J = 7.4 Hz, 1H), 7.22 – 7.13 (m, 5H), 7.08 (t, J = 7.6 Hz, 2H), 6.82 (d, J = 7.8 Hz, 1H), 6.17 (dd, J = 3.0, 1.8 Hz, 1H), 6.05 (d,

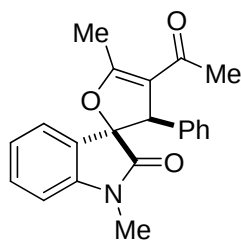
$J = 3.2$ Hz, 1H), 5.56 (s, 1H), 3.06 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.7, 172.2, 164.4, 148.9, 144.1, 142.0, 138.2, 132.1, 130.9, 130.5, 129.6, 129.5, 129.0, 127.9, 127.7, 127.5, 124.5, 123.4, 112.8, 110.5, 108.4, 108.3, 87.8, 55.2, 26.0; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{29}\text{H}_{22}\text{NO}_4$ 448.1543, found 448.1550.



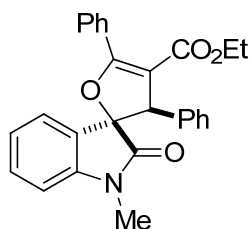
3j. Combined yield 80%, dr 89:11, and 71% for *syn*-**3j**. Data for *syn*-**3j**: yellow solid; mp 216–217 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.92 – 7.85 (m, 2H), 7.65 (dd, $J = 7.4, 0.7$ Hz, 1H), 7.41 (td, $J = 7.8, 1.2$ Hz, 1H), 7.38 – 7.34 (m, 2H), 7.33 – 7.28 (m, 1H), 7.24 – 7.15 (m, 4H), 7.13 – 7.06 (m, 2H), 7.01 (dd, $J = 5.1, 1.2$ Hz, 1H), 6.81 – 6.75 (m, 2H), 6.74 – 6.71 (m, 1H), 5.76 (s, 1H), 2.97 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.7, 172.3, 164.3, 144.5, 138.1, 136.5, 132.2, 131.1, 130.5, 129.7, 129.6, 129.1, 128.0, 127.7, 126.7, 126.6, 126.5, 124.7, 124.5, 123.4, 114.8, 108.4, 89.2, 57.2, 25.9; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{29}\text{H}_{22}\text{NO}_3\text{S}$ 464.1315, found 464.1322.



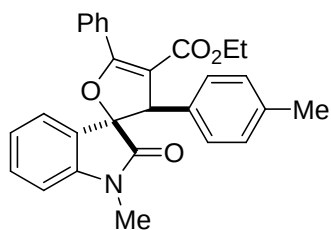
3k. Yield 99% as an isomeric mixture (dr 91:9) with *syn*-**3k** being the major. Data for *syn*-**3k**: white solid; mp 177–178 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (dd, $J = 4.8, 1.5$ Hz, 1H), 8.09 (d, $J = 2.1$ Hz, 1H), 7.86 – 7.77 (m, 2H), 7.69 (d, $J = 7.1$ Hz, 1H), 7.49 – 7.44 (m, 1H), 7.43 – 7.33 (m, 3H), 7.30 (t, $J = 7.4$ Hz, 1H), 7.24 – 7.14 (m, 4H), 7.13 – 7.03 (m, 3H), 6.74 (d, $J = 7.8$ Hz, 1H), 5.53 (s, 1H), 2.85 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.3, 171.9, 165.8, 149.5, 148.9, 143.9, 137.9, 135.9, 132.2, 131.2, 130.6, 130.1, 129.6, 129.4, 128.9, 128.0, 127.7, 126.2, 124.5, 123.6, 123.0, 113.6, 108.6, 89.2, 59.5, 25.7; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{30}\text{H}_{23}\text{N}_2\text{O}_3$ 459.1703, found 459.1710.



3l. Combined yield 84%, dr 86:14, and 72% for *syn*-**3l**. Data for *syn*-**3l**: white solid; mp 197-198 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.51 (dd, $J = 7.4, 0.7$ Hz, 1H), 7.39 (td, $J = 7.8, 1.2$ Hz, 1H), 7.25 – 7.20 (m, 3H), 7.16 (td, $J = 7.6, 0.8$ Hz, 1H), 7.01 (br s, 2H), 6.76 (d, $J = 7.8$ Hz, 1H), 4.86 (d, $J = 1.5$ Hz, 1H), 2.83 (s, 3H), 2.49 (d, $J = 1.6$ Hz, 3H), 1.94 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 194.6, 171.5, 169.5, 143.4, 136.2, 130.7, 129.3, 128.2, 128.1, 127.8, 123.4, 123.3, 114.5, 108.4, 89.1, 59.8, 29.6, 25.9, 15.2; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{20}\text{NO}_3$ 334.1438, found 334.1443.

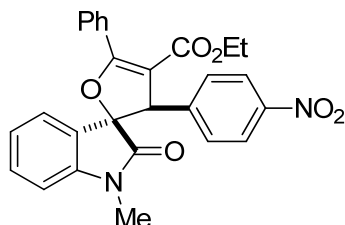


3m. Combined yield 92%, dr 88:12, and 81% for *syn*-**3m**. Data for *syn*-**3m**: white solid; mp 144-147 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.94 (dd, $J = 7.9, 1.4$ Hz, 2H), 7.61 (d, $J = 7.2$ Hz, 1H), 7.50 – 7.34 (m, 4H), 7.24 – 7.13 (m, 4H), 7.13 – 7.04 (m, 2H), 6.77 (d, $J = 7.8$ Hz, 1H), 5.04 (s, 1H), 4.10 – 4.00 (m, 1H), 4.00 – 3.90 (m, 1H), 2.87 (s, 3H), 0.92 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.7, 165.8, 164.3, 143.6, 136.5, 130.8, 130.7, 129.6, 129.5, 129.2, 128.2, 127.8, 127.7, 127.4, 123.6, 123.3, 108.3, 105.8, 88.2, 60.5, 59.9, 25.9, 13.7; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{24}\text{NO}_4$ 426.1700, found 426.1707.

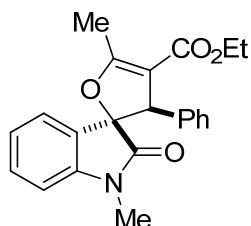


3n. Combined yield 60%, dr 80:20, and 48% for *syn*-**3n**. Data for *syn*-**3n**: white solid; mp 188-189 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.96 – 7.90 (m, 2H), 7.59 (dd, $J = 7.4, 0.7$ Hz, 1H), 7.48 – 7.34 (m, 4H), 7.15 (td, $J = 7.7, 0.8$ Hz, 1H), 7.00 (dd, $J = 18.2, 8.0$ Hz, 4H), 6.76 (d, $J = 7.8$ Hz, 1H), 5.00 (s, 1H), 4.09 – 3.92 (m, 2H), 2.89 (s, 3H), 2.28 (s, 3H), 0.95 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR

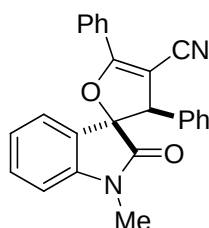
(101 MHz, CDCl₃) δ 171.8, 165.6, 164.3, 143.6, 136.9, 133.4, 130.7, 130.6, 129.7, 129.6, 129.3, 128.6, 128.0, 127.7, 123.5, 123.3, 108.3, 106.0, 88.2, 60.1, 59.9, 25.9, 21.2, 13.8; HRMS–ESI [M + H]⁺ Calcd for C₂₈H₂₆NO₄ 440.1856, found 440.1847.



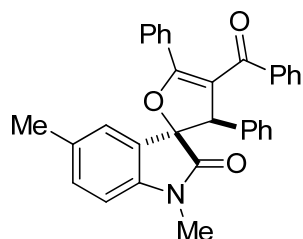
3o. Yield 78% as an isomeric mixture (dr 90:10) with *syn*-**3o** being the major. Data for *syn*-**3o**: white solid; mp 166-168 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (dd, *J* = 7.7, 1.2 Hz, 2H), 7.98 – 7.90 (m, 2H), 7.63 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.53 – 7.38 (m, 4H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.20 (td, *J* = 7.7, 0.8 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 5.10 (s, 1H), 4.10 – 3.93 (m, 2H), 2.91 (s, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 171.0, 166.8, 163.7, 147.3, 144.5, 143.3, 131.3, 131.2, 129.6, 129.3, 128.9, 128.7, 127.8, 123.7, 123.6, 123.1, 108.7, 104.9, 87.7, 60.1, 59.8, 26.1, 13.8; HRMS–ESI [M + H]⁺ Calcd for C₂₇H₂₃N₂O₆ 471.1551, found 471.1554.



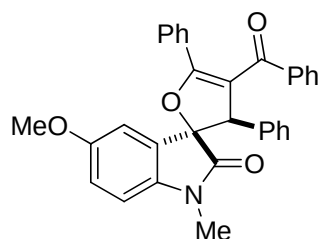
3p. Yield 62% as an isomeric mixture (dr 90:10) with *syn*-**3p** being the major. Data for *syn*-**3p**: pale yellow solid; mp 127-128 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.51 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.37 (td, *J* = 7.8, 1.2 Hz, 1H), 7.22 – 7.11 (m, 4H), 7.02 – 6.92 (m, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 4.83 (d, *J* = 1.6 Hz, 1H), 4.11 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.99 (dq, *J* = 10.8, 7.1 Hz, 1H), 2.83 (s, 3H), 2.47 (d, *J* = 1.7 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 171.7, 169.4, 164.9, 143.5, 136.4, 130.6, 129.5, 128.0, 127.7, 127.3, 123.5, 123.3, 108.3, 105.3, 88.9, 59.5, 59.1, 25.8, 14.5, 14.0; HRMS–ESI [M + H]⁺ Calcd for C₂₂H₂₂NO₄ 364.1543, found 364.1545.



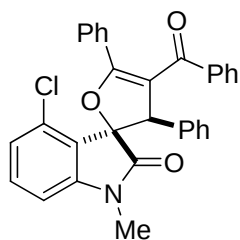
3q. Yield 93% as an isomeric mixture (dr 91:9) with *syn*-**3q** being the major. Data for *syn*-**3q**: white solid; mp 180-181 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.78 – 7.71 (m, 2H), 7.61 – 7.53 (m, 1H), 7.48 – 7.35 (m, 6H), 7.32 – 7.26 (m, 2H), 7.06 – 6.96 (m, 2H), 6.49 (d, *J* = 7.4 Hz, 1H), 4.29 (s, 1H), 3.16 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 185.2, 169.9, 144.5, 134.5, 133.6, 130.2, 129.5, 129.1, 129.0, 128.9, 128.8, 128.6, 125.4, 122.6, 120.0, 114.4, 108.7, 42.9, 38.5, 37.4, 26.8; HRMS–ESI [*M* + *H*]⁺ Calcd for C₂₅H₁₉N₂O₂ 379.1441, found 379.1445.



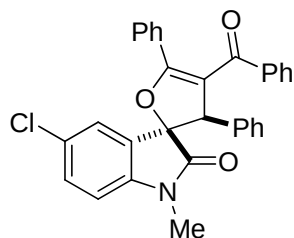
3r. Combined yield 82%, dr 86:14, and 71% yield for *syn*-**3r**. Data for *syn*-**3r**: yellow solid; mp 214-216 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.92 – 7.82 (m, 2H), 7.52 (dd, *J* = 1.1, 0.5 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.33 – 7.27 (m, 1H), 7.22 – 7.14 (m, 4H), 7.13 – 7.04 (m, 5H), 6.95 (dd, *J* = 7.8, 1.6 Hz, 2H), 6.60 (d, *J* = 7.9 Hz, 1H), 5.52 (s, 1H), 2.79 (s, 3H), 2.40 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 192.7, 172.5, 164.9, 141.9, 138.2, 134.1, 133.0, 132.1, 131.1, 130.3, 129.7, 129.6, 129.4, 128.3, 127.9, 127.7, 127.5, 127.1, 125.2, 114.6, 108.0, 89.8, 62.6, 25.6, 21.1; HRMS–ESI [*M* + *H*]⁺ Calcd for C₃₂H₂₆NO₃ 472.1907, found 472.1910.



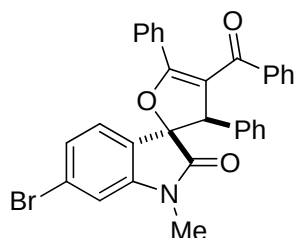
3s. Combined yield 69%, dr 88:12, and 61% for *syn*-**3s**. Data for *syn*-**3s**: yellow solid; mp 187-188 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.94 – 7.83 (m, 2H), 7.41 – 7.34 (m, 2H), 7.33 – 7.27 (m, 2H), 7.24 – 7.15 (m, 3H), 7.14 – 7.04 (m, 5H), 6.96 (dd, *J* = 7.8, 1.3 Hz, 2H), 6.91 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.62 (d, *J* = 8.5 Hz, 1H), 5.52 (s, 1H), 3.85 (s, 3H), 2.79 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 192.8, 172.3, 164.8, 156.4, 138.1, 137.5, 133.9, 132.1, 130.4, 129.7, 129.6, 129.3, 128.2, 128.1, 127.9, 127.7, 127.5, 115.9, 114.6, 110.8, 108.9, 89.9, 62.7, 55.8, 25.7; HRMS–ESI [*M* + *H*]⁺ Calcd for C₃₂H₂₆NO₄ 486.1856, found 486.1857.



3t. Yield 90% as an isomeric mixture (dr 90:10) with *syn*-**3t** being the major. Data for *syn*-**3t**: yellow solid; mp 255-257 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 7.8 Hz, 2H), 7.36 – 7.27 (m, 2H), 7.24 – 7.04 (m, 9H), 6.97 (d, J = 6.8 Hz, 2H), 6.63 (d, J = 7.8 Hz, 1H), 5.93 (s, 1H), 2.79 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.4, 171.9, 165.5, 145.8, 138.4, 134.5, 132.1, 131.9, 130.3, 129.6, 129.5, 129.4, 128.4, 128.0, 127.9, 127.7, 127.6, 124.3, 123.8, 114.5, 106.7, 89.6, 58.6, 25.8; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{23}\text{ClNO}_3$ 492.1361, found 492.1371.

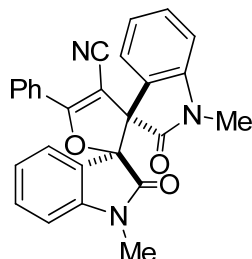


3u. Combined yield 91%, dr 90:10, and 82% yield for *syn*-**3u**. Data for *syn*-**3u**: yellow solid; mp 226-227 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.91 – 7.82 (m, 2H), 7.68 (d, J = 2.1 Hz, 1H), 7.38 – 7.32 (m, 3H), 7.32 – 7.26 (m, 1H), 7.23 – 7.14 (m, 3H), 7.13 – 7.04 (m, 5H), 6.96 (dd, J = 7.9, 1.4 Hz, 2H), 6.62 (d, J = 8.3 Hz, 1H), 5.51 (s, 1H), 2.77 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 192.4, 172.1, 164.6, 142.7, 138.0, 133.6, 132.1, 130.7, 130.5, 129.6, 129.5, 129.0, 128.7, 128.6, 128.2, 128.0, 127.9, 127.7, 127.6, 124.9, 114.4, 109.3, 89.2, 62.7, 25.7; HRMS–ESI $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{23}\text{ClNO}_3$ 492.1361, found 492.1366.

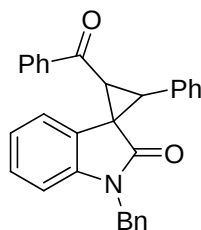


3v. Combined yield 94%, dr 90:10, and 85% yield for *syn*-**3v**. Data for *syn*-**3v**: pale yellow solid; mp 193-194 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, J = 7.3 Hz, 2H), 7.54 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 7.1 Hz, 3H), 7.30 (t, J = 7.4 Hz, 1H), 7.24 – 7.14 (m, 3H), 7.14 – 7.04 (m, 5H), 6.94 (d, J = 6.6 Hz, 2H), 6.87 (d, J = 1.3 Hz, 1H), 5.49 (s, 1H), 2.79 (s, 3H); ^{13}C NMR (101 MHz,

CDCl₃) δ 192.5, 172.4, 164.7, 145.5, 138.1, 133.7, 132.2, 130.5, 129.7, 129.6, 129.2, 128.2, 128.1, 128.0, 127.8, 127.7, 126.2, 126.1, 125.8, 124.7, 114.5, 111.9, 89.2, 62.6, 25.7; HRMS–ESI [M + H]⁺ Calcd for C₃₁H₂₃BrNO₃ 536.0856, found 536.0859.



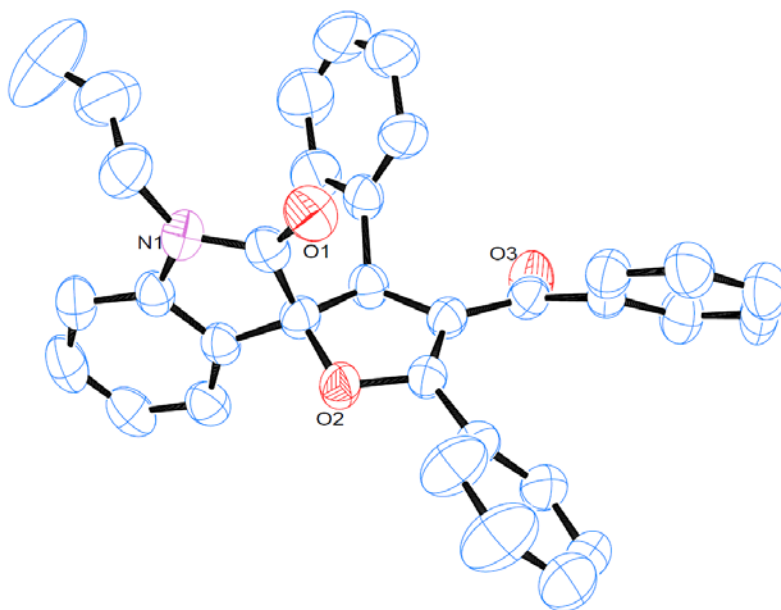
3w. Yield 62% as an isomeric mixture (dr 10:1) with *anti*-**3w** being the major. Data for *anti*-**3w**: white solid; mp 255-257 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.12 – 8.05 (m, 2H), 7.74 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.58 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.51 – 7.44 (m, 2H), 7.35 – 7.24 (m, 2H), 7.05 (tdd, *J* = 7.7, 3.2, 0.9 Hz, 2H), 6.64 (dd, *J* = 10.5, 7.8 Hz, 2H), 3.01 (s, 3H), 2.95 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 172.9, 172.1, 171.3, 144.6, 144.5, 132.3, 131.7, 130.5, 128.7, 127.8, 127.3, 127.2, 126.6, 123.3, 123.1, 121.3, 121.0, 115.0, 108.4, 90.7, 84.6, 64.6, 26.3, 25.9; HRMS–ESI [M + H]⁺ Calcd for C₂₇H₂₀N₃O₃ 434.1499, found 434.1502.



4. Yield 70% as an isomeric mixture (dr 6:1). Data for the major isomer: white solid; mp 203-204 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.83 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.39 – 7.29 (m, 5H), 7.29 – 7.24 (m, 2H), 7.21 – 7.06 (m, 4H), 6.98 (d, *J* = 7.0 Hz, 2H), 6.83 – 6.67 (m, 2H), 6.15 (d, *J* = 7.2 Hz, 1H), 5.14 (d, *J* = 15.6 Hz, 1H), 4.57 (d, *J* = 15.6 Hz, 1H), 4.22 (d, *J* = 8.3 Hz, 1H), 3.69 (d, *J* = 8.3 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 191.5, 172.5, 143.1, 136.4, 135.7, 133.6, 133.3, 129.8, 128.7, 128.6, 128.5, 128.3, 127.7, 127.6, 127.3, 127.1, 125.3, 121.9, 121.1, 109.1, 43.9, 41.8, 39.3, 37.4; HRMS–ESI [M + H]⁺ Calcd for C₃₀H₂₄NO₂ 430.1802, found 430.1802.

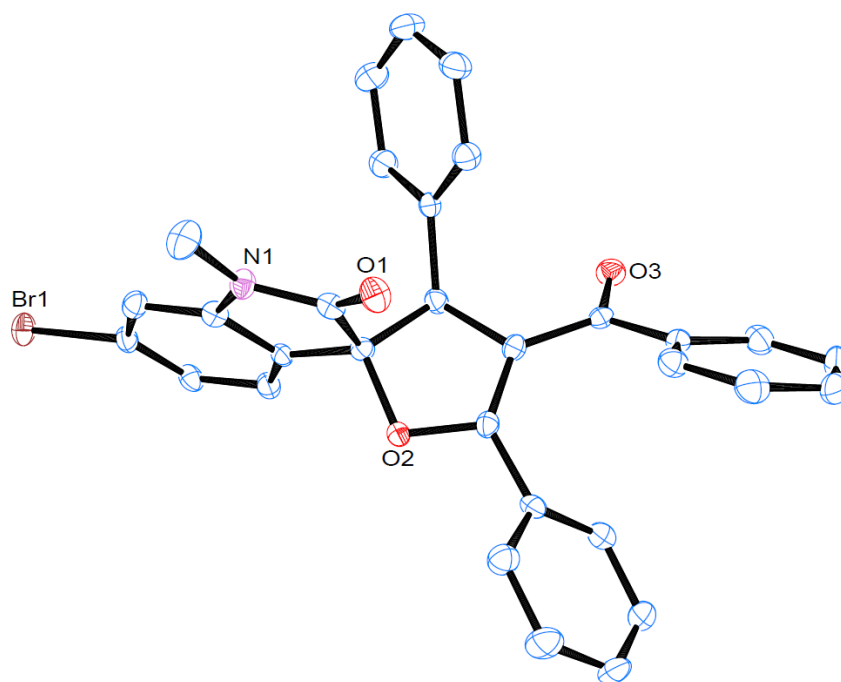
V. ORTEP Drawings for 3b, 3v, and 3w.

Table 1. Crystal data and structure refinement for 3b.



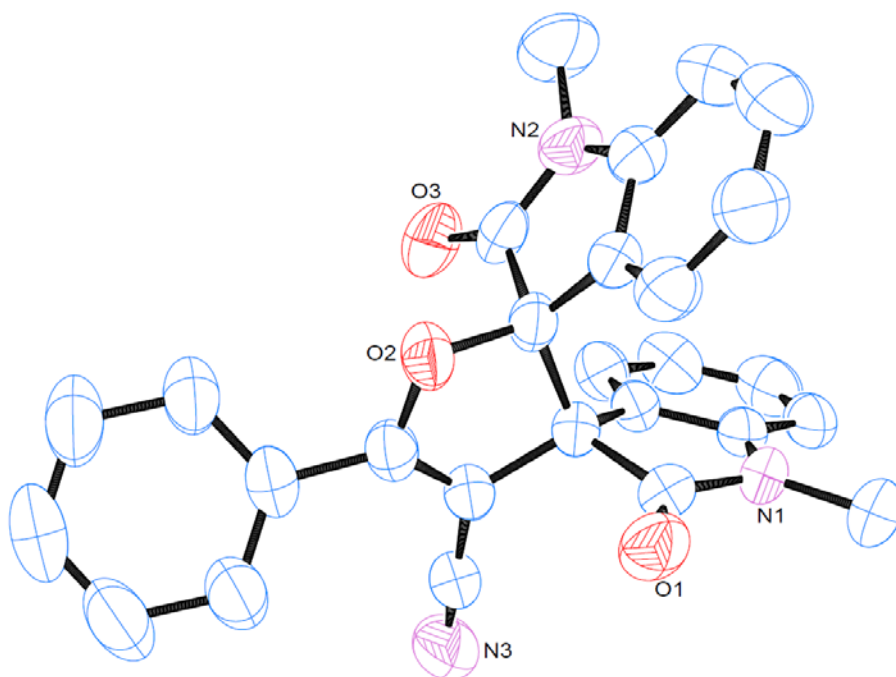
Identification code	3b
Empirical formula	C ₃₃ H ₂₅ NO ₃
Formula weight	483.54
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 15.116(2) Å α = 90° b = 11.4640(17) Å β = 105.324(3)° c = 15.484(2) Å γ = 90°
Volume	2587.8(7) Å ³
Z, Calculated density	4, 1.241 Mg/m ³
Absorption coefficient	0.079 mm ⁻¹
F(000)	1016
Crystal size	0.50 x 0.31 x 0.20 mm ³
Theta range for data collection	1.67 to 25.04°
Limiting indices	-11 ≤ h ≤ 18, -13 ≤ k ≤ 13, -18 ≤ l ≤ 18
Reflections collected / unique	14072 / 4568 [R(int) = 0.0664]
Completeness to the θ = 25.04°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9843 and 0.9615
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4568 / 0 / 345
Goodness-of-fit on F ²	0.982
Final R indices [I > 2σ(I)]	R1 = 0.0517, wR2 = 0.1247
R indices (all data)	R1 = 0.1100, wR2 = 0.1608
Largest diff. peak and hole	0.156 and -0.254 e. Å ⁻³

Table 2. Crystal data and structure refinement for 3v.



Identification code	3v
Empirical formula	C ₃₁ H ₂₂ BrNO ₃
Formula weight	536.41
Temperature	113(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, 2(1)/n
Unit cell dimensions	a = 15.016(3) Å α = 90° b = 11.906(2) Å β = 100.25(3)° c = 15.221(3) Å γ = 90°
Volume	2677.7(9) Å ³
Z, Calculated density	4, 1.331 Mg/m ³
Absorption coefficient	1.567 mm ⁻¹
F(000)	1096
Crystal size	0.24 x 0.20 x 0.18 mm ³
Theta range for data collection	1.76 to 28.01°
Limiting indices	-18 ≤ h ≤ 19, -15 ≤ k ≤ 14, -20 ≤ l ≤ 19
Reflections collected / unique	26056 / 6429 [R(int) = 0.0683]
Completeness to the θ = 28.01°	99.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7657 and 0.7049
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	6429 / 0 / 327
Goodness-of-fit on F ²	1.004
Final R indices [I > 2σ(I)]	R1 = 0.0458, wR2 = 0.0970
R indices (all data)	R1 = 0.0616, wR2 = 0.1033
Largest diff. peak and hole	0.489 and -0.780 e. Å ⁻³

Table 3. Crystal data and structure refinement for 3w.



Identification code	3w
Empirical formula	$C_{27}H_{19}N_3O_3$
Formula weight	433.45
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, C2/c
Unit cell dimensions	$a = 21.917(6)$ Å $\alpha = 90^\circ$ $b = 9.529(2)$ Å $\beta = 115.112(4)^\circ$ $c = 23.123(8)$ Å $\gamma = 90^\circ$
Volume	$4373(2)$ Å ³
Z, Calculated density	8, 1.317 Mg/m ³
Absorption coefficient	0.088 mm ⁻¹
F(000)	1808
Crystal size	$0.35 \times 0.31 \times 0.31$ mm ³
Theta range for data collection	1.95 to 25.05°
Limiting indices	$-26 \leq h \leq 26$, $-11 \leq k \leq 11$, $-27 \leq l \leq 27$
Reflections collected / unique	22685 / 3880 [R(int) = 0.0346]
Completeness to the $\theta = 25.05^\circ$	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9734 and 0.9700
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3880 / 0 / 301
Goodness-of-fit on F ²	0.989
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0382, wR2 = 0.0794
R indices (all data)	R1 = 0.0572, wR2 = 0.0894
Largest diff. peak and hole	0.149 and -0.123 e. Å ⁻³

VI. ^1H and ^{13}C NMR Spectra of 3 and 4

