Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

C—ON Bond Homolysis of Alkoxyamines: When Too High Polarity is Detrimental.

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Parameters for correlations

The effects ruling the C—ON bond homolysis of alkoxyamines are described by several multiparameters relationships corresponding to the nitroxyl fragments investigated, eq. 1 for TEMPO-based alkoxyamines and eq. 2 for SG1-based alkoxyamines.

$$\log\left(k_d/s^{-1}\right) = -14.8(\pm 0.7) + 13.9(\pm 0.9)\cdot\sigma_{RS} + 13.6(\pm 3.2)\cdot\sigma_I + 6.6(\pm 0.7)\cdot\upsilon \qquad \text{eq. 1}$$

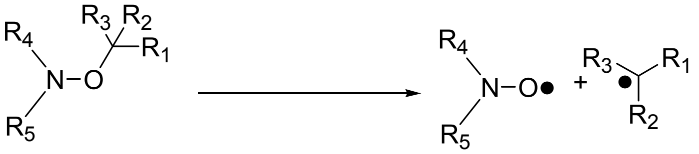
$$\log\left(k_d/s^{-1}\right) = -14.3(\pm 1.3) + 15.3(\pm 2.2)\cdot\sigma_{RS} + 19.5(\pm 3.0)\cdot\sigma_I + 7.0(\pm 1.1)\cdot\upsilon \qquad \text{eq. 2}$$

Parameters σ_{RS}, σ_I and υ are estimated as previously reported[1] and are collected in Table 1. As the various substituents were directly bound to the reactive center (Scheme 1), the value of the electrical Hammett constant σ_I for the alkyl fragment $CR_1R_2R_3$ is given by eqs. 3 - 5 for primary, secondary, and tertiary alkyl groups, respectively.

$$\sigma_{I,CH2R} = 0.416\cdot\sigma_{I,R} - 0.0103 \qquad \text{eq. 3}$$

$$\sigma_{I,CHR1R2} = 0.297\cdot\sum\sigma_{I,R} + 0.00482 \qquad \text{eq. 4}$$

$$\sigma_{I,CR1R2R3} = 0.248\cdot\sum\sigma_{I,R} + 0.00398 \qquad \text{eq. 5}$$



Scheme 1

Taking into account the effect of the penultimate unit,[2] it is assumed that the OAc and Me groups in the **f** and **l** fragments are not sterically more demanding than a hydrogen atom, and thus, $\upsilon_{\mathbf{f}} = \upsilon_{\mathbf{l}} = \upsilon_{\mathbf{h}} = 0.86$. Then, bulkiness of the alkyl fragment is given by eq. 6 assuming υ_l the saturation of the reactive center, i.e., primary, secondary or tertiary carbon atom, υ_2 for the largest substituent attached to the radical center, and υ_3 is used for the group involved as penultimate unit.

$$\upsilon = 0.866 \cdot \upsilon_1 + 0.436 \cdot \upsilon_2 + 0.348 \cdot \upsilon_3 - 0.0455 \qquad \text{eq. 6}$$

The stabilization effect for radicals **a•** – **e•**, **g•** and **k•** is estimated with a good reliability and accuracy using the procedure described previously[1] (Table 1) or based on reasonable assumptions (vide infra). Thus, σ_{RS} are estimated using the RSE values given by Rüchardt et al. which are first reported in eqs. 7 - 9 to give the corrected radical stabilization energy (RSE^{corr}), $RSE(CH3^\bullet) = 0.0$ kJ mol^{-1} being the reference.

$$RSE^{corr}(\text{tertiary}) = \text{RSE} - 18.0\ \text{kJ mol}^{-1} \qquad \text{eq. 7}$$

$$RSE^{corr}(\text{secondary}) = \text{RSE} - 14.2\ \text{kJ mol}^{-1} \qquad \text{eq. 8}$$

$$RSE^{corr}(\text{primary}) = \text{RSE} - 9.6\ \text{kJ mol}^{-1} \qquad \text{eq. 9}$$

To normalize the RSE^{corr} values, the formation enthalpy of the methyl radical ($\Delta H_f(CH3^\bullet)$) -146.3 kJ mol^{-1}) was used as it should contain a minimum of effects due to the saturated ground state of the molecule. The values of σ_{RS} are given by eq. 10. The larger σ_{RS} is, the more stabilized the alkyl radical is.

$$\sigma_{RS} = \frac{RSE^{corr}}{\Delta H_f\left(CH_3^\bullet\right)} \qquad \text{eq. 10}$$

Indeed, for **b•** and **e•**, it is assumed there is no influence of the *t*-Bu group on the stabilization and, hence, $\sigma_{RS,\mathbf{e}\bullet} = \sigma_{RS,\mathbf{b}\bullet}$. The same assumption is done for the Me group and the H atom in **g•** and **k•**, that is, $\sigma_{RS,\mathbf{g}\bullet} = \sigma_{RS,\mathbf{k}\bullet}$. It seems that EPR data of radical **k•** have not been reported. However, the EPR features of •CHPhCOOMe have been reported, and as **a•** is less stabilized than **b•**, its RSE is likely to be the lower limit for radical **k•**.[3] Unless it escapes our scrutiny, EPR features of radical **d•** have not been reported. Thus, it is assumed that the stabilization effect of the C(O)NMeOMe group should not be very different from that of the COOMe group, and consequently, $\sigma_{\mathrm{RSE},\mathbf{d}\bullet} = \sigma_{\mathrm{RS},\mathbf{a}\bullet}$.[4] The effect of EWG in the alkyl fragment is described by σ_{I}, and reliable and accurate estimates are obtained using the reported procedures (Table 1SI).[1] Similarly, the use of previously reported procedure to estimate υ (vide supra) would afford values of $\upsilon_{\mathbf{a\text{-}e}}$ spanning from $\upsilon_{\mathbf{a\text{-}e}} = 1$ (assuming the COO*t*Bu group is not sterically more demanding than the methyl group) to $\upsilon_{\mathbf{a\text{-}e}} = 1.32$ (assuming $\upsilon_1 = \upsilon_{i\mathrm{Pr}} = 0.76$ and $\upsilon_2 = \upsilon_3 = \upsilon_{\mathrm{COO}t\mathrm{Bu}} = \upsilon_{\mathrm{COOMe}} = 0.9$). As lower υ values for $\mathrm{CMe_2COO}t\mathrm{Bu}$, CHMeCOO*t*Bu, and $\mathrm{CH_2COO}t\mathrm{Bu}$ (vide supra) afford a good correlation and to make our purpose clearer, the steric hindrance is assumed as low as possible, and thus, assuming that the COOMe group is not more sterically demanding than the methyl group ($\upsilon_{\mathrm{COOMe}} = 0.50$ and $\upsilon_{\mathrm{Me}} = 0.52$), $\upsilon_{\mathbf{a\text{-}e}} = \upsilon_{\mathbf{i}} = 0.83$, which is the lowest value of υ which can be expected for the bulkiness of groups **a** – **e** (Table 1SI).[5-6]

For the sake of simplicity, in eqs 1 and 2 a single value υ for the bulkiness of the COOMe group was applied, although the experimental results suggested the use of a lower value for **1**-derivatives and a larger one for **2**-derivatives. Thus, the coefficients ineq. 1 are re-estimated using $\upsilon = 0.58$ for $\mathrm{CH_2COOMe}$,[7] $\upsilon_1 = \upsilon_{i\mathrm{Pr}} = 0.76$ for $\mathrm{CHCH_3COOMe}$, $\upsilon_1 = \upsilon_{t\mathrm{Bu}} = 1.24$ for $\mathrm{CMe_2COOMe}$, and $\upsilon_{\mathrm{COOMe}} = 0.5$,[10] affording $\upsilon_{\mathrm{CHMeCOOMe}} = 0.83$ and $\upsilon_{\mathrm{CMe2COOMe}} = 1.25$. Therefore, using these new values and implementing **1f** and **1l** in eq. 1, which are expected to be included in the correlation, very good statistical outputs (eq. 11)[8] are obtained, supporting our new assumptions (Figure 2 main manuscript). The weight of each effect is estimated as previously reported[1] and affords 39%, 20%, and 41% for the stabilization, polar, and steric effects, respectively. These values are very close to those previously reported (44%, 16%, and 40%, respectively)[1] and do not deserve more comments.

$$\log\left(k_{\mathrm{d}}/s^{-1}\right) = -14.8(\pm 0.4) + 12.4(\pm 0.9)\cdot\sigma_{\mathrm{RS}} + 17.7(\pm 2.2)\cdot\sigma_{\mathrm{I}} + 7.1(\pm 0.5)\cdot\upsilon \qquad \text{eq. 11}$$

Table 1SI. Radical Stabilization Energy (RSE), its corrected value (RSE^{corr}) and its Hammett-type constant σ_{RS}, Electrical Hammett constant σ_{I}, and steric constant υ for fragments **a** - **l**.

	RSE[a]	RSE^{corr}[b]	σ_{RS}[b]	σ_{I}[c]	υ[d]
a	-16.10[e]	-30.3	0.21	0.20[f,g]	0.83
b	-33.85	-48.1	0.33	0.18[g,h]	0.83
c	-24.31[i]	-38.5	0.26	0.19[f,g,h]	0.83
d	-16.10[j]	-30.3	0.21	0.22[f,g,k]	0.83
e	-24.31[l]	-38.5	0.26	0.19[f,g,m]	0.83
f			0.34[n]	0.09[g,o]	0.86[p]
g	-42.1 to -53.7[q]	-56.3 to -67.9	0.38-0.46	0.13[g,rs]	0.86[s]
h[t]			0.34	0.07	0.86
i[t]			0.18	0.09	0.83
j[t]			0.15	0.15	0.58[u]
k	-42.1 to -53.7[q]	-56.3 to -67.9	0.38-0.46	0.13[g,r]	0.86[s]
l			0.34	0.07	0.86

[a] Given in ref. 5, unless otherwise mentioned. In kJ/mol. [b] Using equations 15 - 17 reported in ref. [9], unless otherwise mentioned (see SI). In kJ/mol. [c] Using equations 10-12 reported in ref. 12, as suitable, unless otherwise mentioned. [d] See text unless otherwise mentioned. [e] $a_{\mathrm{H}\alpha}$ = 20.15 G and using eq. 3 provided in ref. 5. [f] $\sigma_{\mathrm{I,COOMe}} = 0.32$. [g] Given in ref. 6. [h] $\sigma_{\mathrm{I,Ac}} = 0.30$. [i] $a_{\mathrm{H}\alpha}$ = 18.96 G and using eq. 3 provided in ref. 5. [j] $a_{\mathrm{H}\alpha}$ = 21.5 G for both •CH_2COOMe and •CH_2NH_2, meaning that the stabilization of the odd electron is the same for these two groups. It is assumed that the stabilization should be very similar for the CONMeOMe group. Consequently, $\sigma_{\mathrm{RSE},\mathbf{d}\bullet} = \sigma_{\mathrm{RSE},\mathbf{a}\bullet}$. See ref. 8. [k] $F_{\mathrm{CONHMe}} = 0.35$ providing $\sigma_{\mathrm{I}} = 0.38$ using eq. 8 in ref. 7. It must be mentioned that the true value of σ_{I} is likely higher. [l] $a_{\mathrm{H}\alpha}$ = 19.9 G for *t*BuCOCH$_2$ and $a_{\mathrm{H}\alpha}$ = 19.5 G for MeCOCH$_2$, meaning that these two radicals are similarly stabilized. Thus, it was assumed that $\sigma_{\mathrm{RS},\mathbf{e}\bullet} \approx \sigma_{\mathrm{RS},\mathbf{c}\bullet}$ or slightly lower. See ref. 8. [m] It was assumed that $\sigma_{\mathrm{I,CO}t\text{-}\mathrm{Bu}} = \sigma_{\mathrm{I,Ac}}$. See footnote *h*. [n] It was assumed $\sigma_{\mathrm{RS},\mathbf{f}} = \sigma_{\mathrm{RS,PhMeCH}}$. [o] $\sigma_{\mathrm{I,Ph}} = 0.12$ and $\sigma_{\mathrm{I,CH2OAc}} = 0.15$. [p] Assuming that the effect of the OAc group is not larger than that of a hydrogen atom. See ref. 10. [q] As EPR features for radicals **g**• or **k**• are not reported, it was assumed that the RSE of PhC•MeCOOMe may afford some clue on the stabilization of **g**• and **k**•. That is, $a_{\mathrm{H}\beta}$ = 16.6 G for PhMeC•COOMe was used to estimate the lower limit of RSE for **g**• and **k**•. The upper limit is given by radical Ph$_2$HC• with $\alpha_{\mathrm{H}\alpha}$ = 14.7 G, as radicals PhMeHC• and MeCOMeHC• exhibit very similar RSE. $a_{\mathrm{H}\beta}$ = 16.6 G for PhMeC•COOMe is used to estimate the lower limit of RSE for **g**• and **k**•. See refs. 5. [r] $\sigma_{\mathrm{I,CHO}} = 0.30$ and $\sigma_{\mathrm{I,Ph}} = 0.12$. [s] Assuming that the effect of the Ac group is not larger that of the methyl group. See ref. 13. [t] Given in ref. 12. [u] Given in ref. 10.

Kinetics measurements

For experiment details, see the experimental section in main article. In figure 1SI are displayed two examples of kinetics in water/methanol mixture (blue symbols) and in t-BuPh (black symbols).

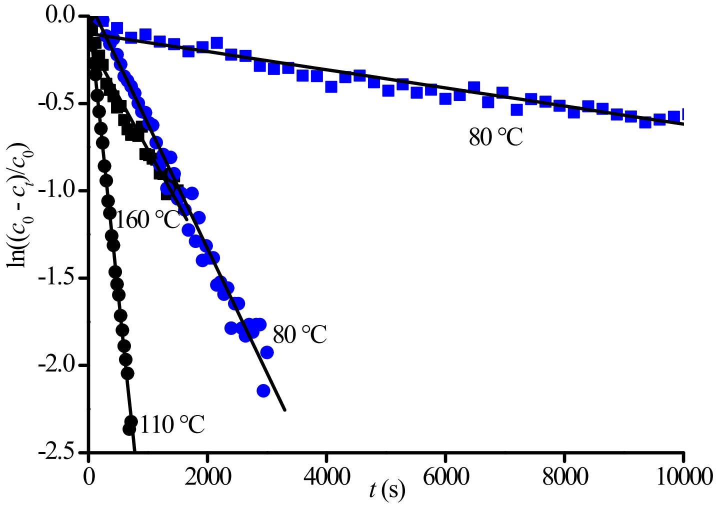


Figure 1SI. Decays of **1a** (squares) and **2a** (circles) in water/methanol mixture (blue symbols) and in *tertio*-butylbenzene (black) symbols at various temperatures.

p*K*a measurement

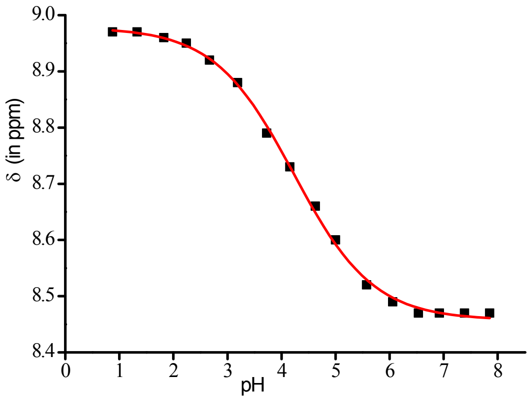
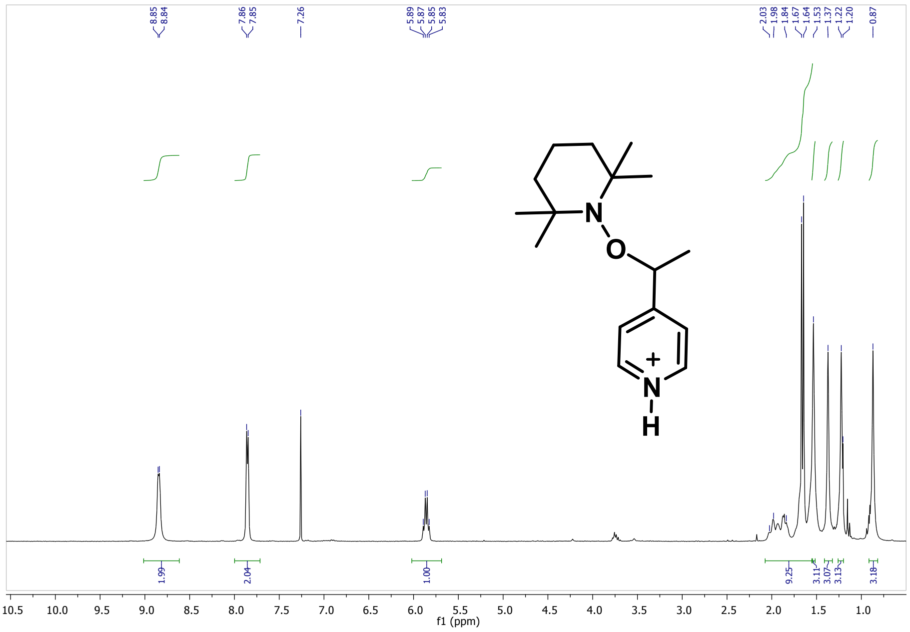


Figure 2SI. Titration curve of **1m**

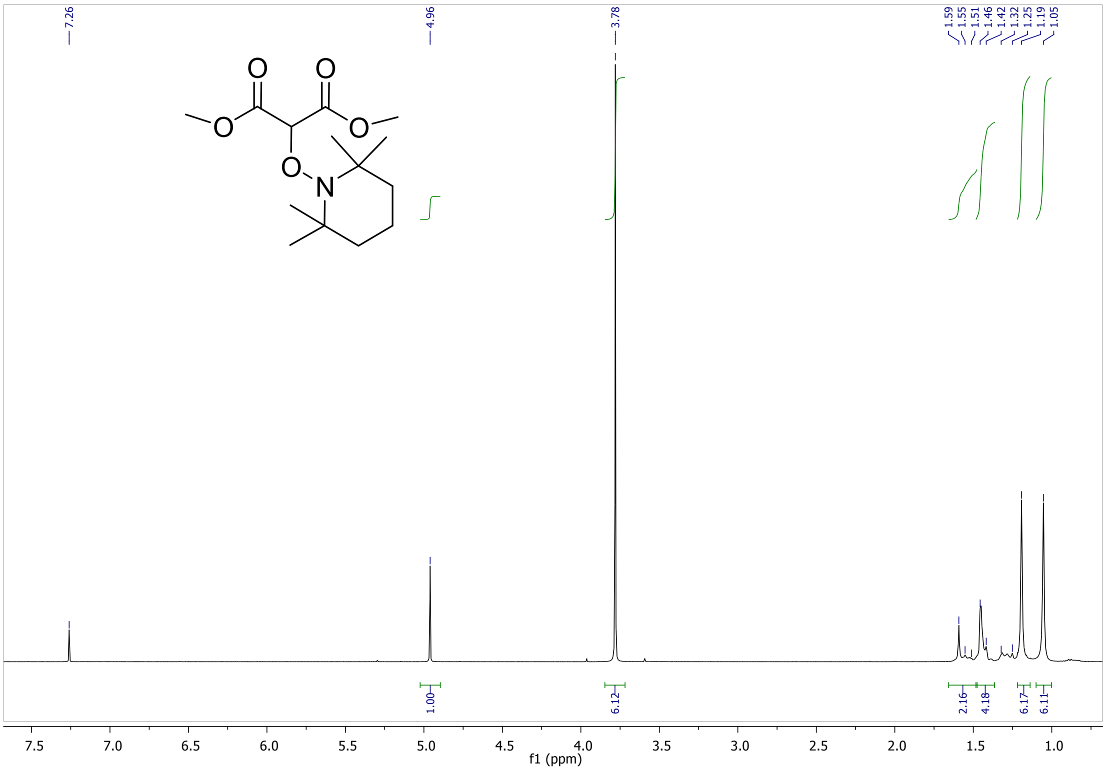
pK_a value of **1m** was measured by monitoring the dependency of ^{1}H NMR chemical shift in various pH*. A solution of 0.01 M **1m** in D_2O/CD_3OD (1/1) was used. The pH* values were adjusted with DCl and NaOD and converted to pH values with the equation pH = 0.929 pH* + 0.42.[11] ^{1}H-NMR spectra were recorded on 400 MHz spectrometer. pK_a value was determined by fitting the curve using the Henderson-Hasselbach equation:[12]

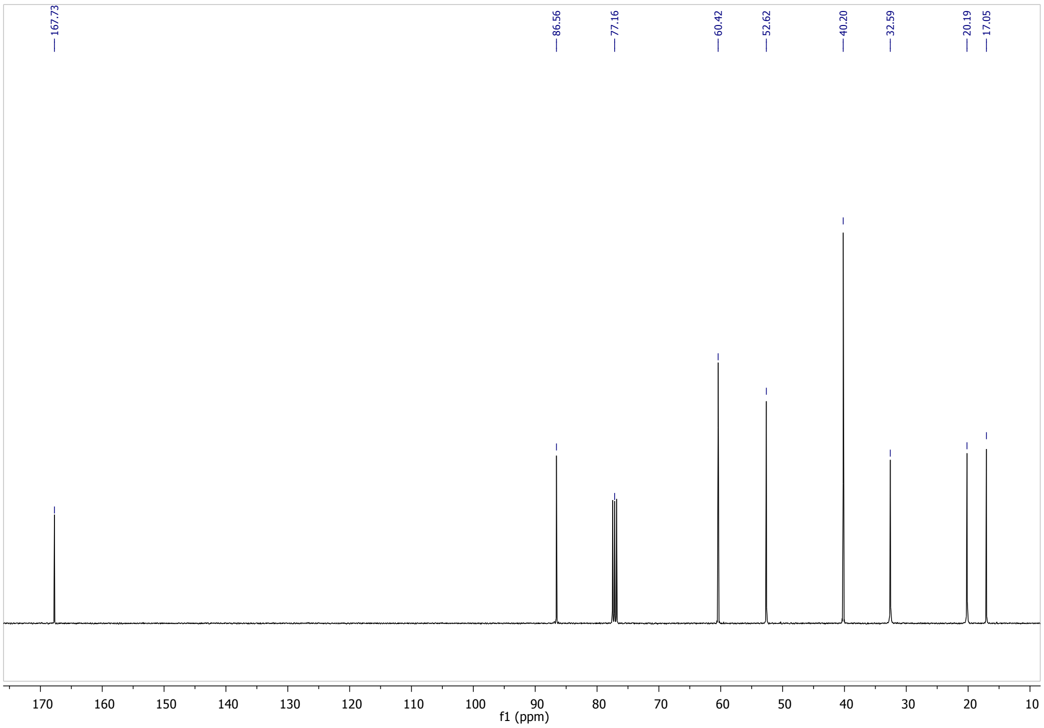
$$\delta_{\mathrm{pH}} = \delta_{\mathbf{1m}} + \frac{\delta_{\mathbf{1mH+}} - \delta_{\mathbf{1m}}}{1 + 10^{\mathrm{p}K_a - \mathrm{pH}}}$$



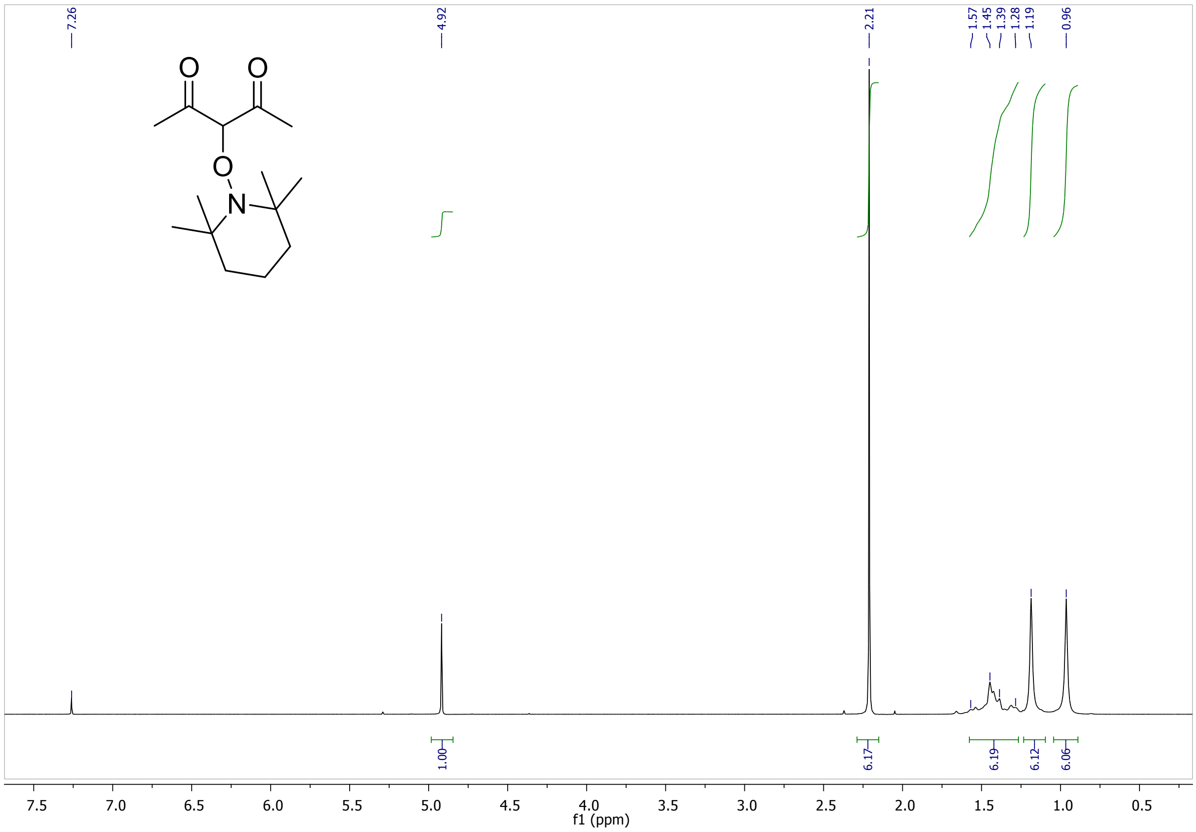
<u>^{1}H NMR</u> (300 MHz, $CDCl_3$) δ 8.85 (d, *J* = 4.4 Hz, 2H), 7.86 (d, *J* = 5.1 Hz, 2H), 5.86 (q, *J* = 6.5 Hz, 1H), 2.23 – 1.61 (m, 9H), 1.53 (s, 3H), 1.37 (s, 3H), 1.22 (s, 3H), 0.87 (s, 3H).

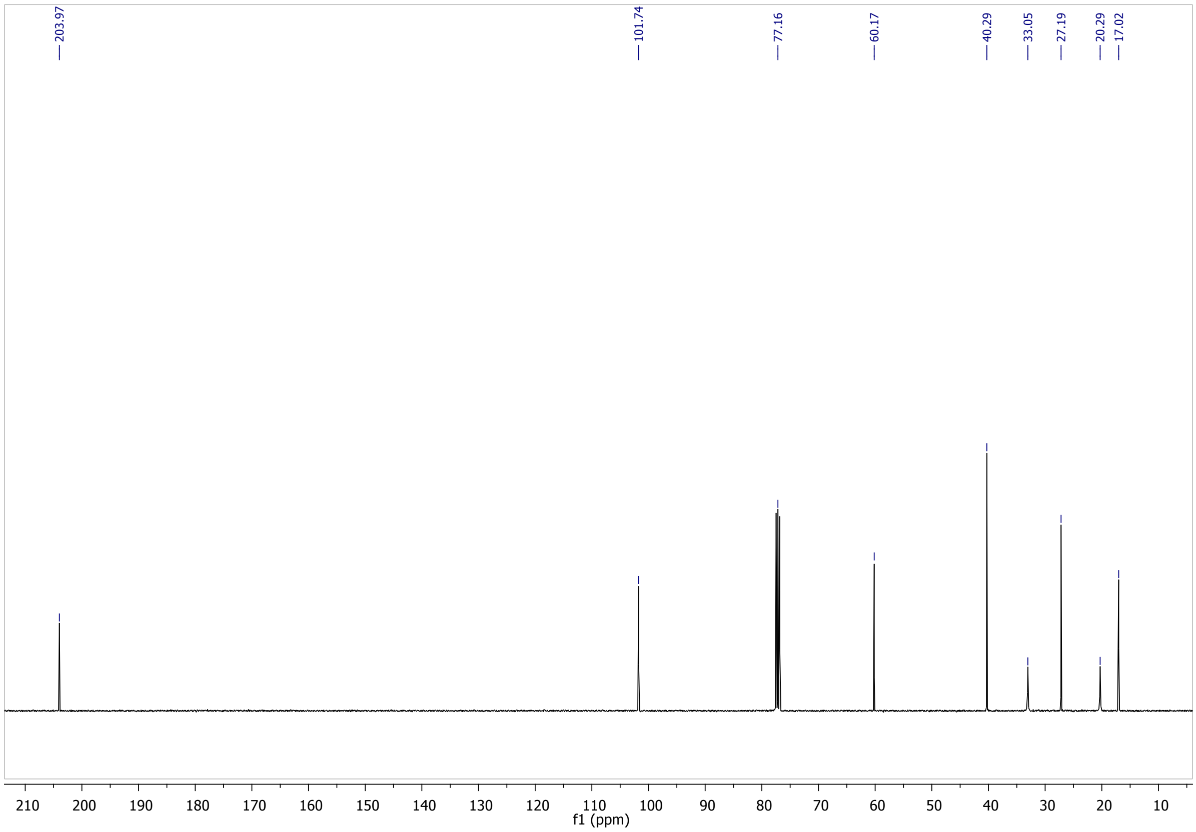
Dimethyl 2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)malonate 1a.



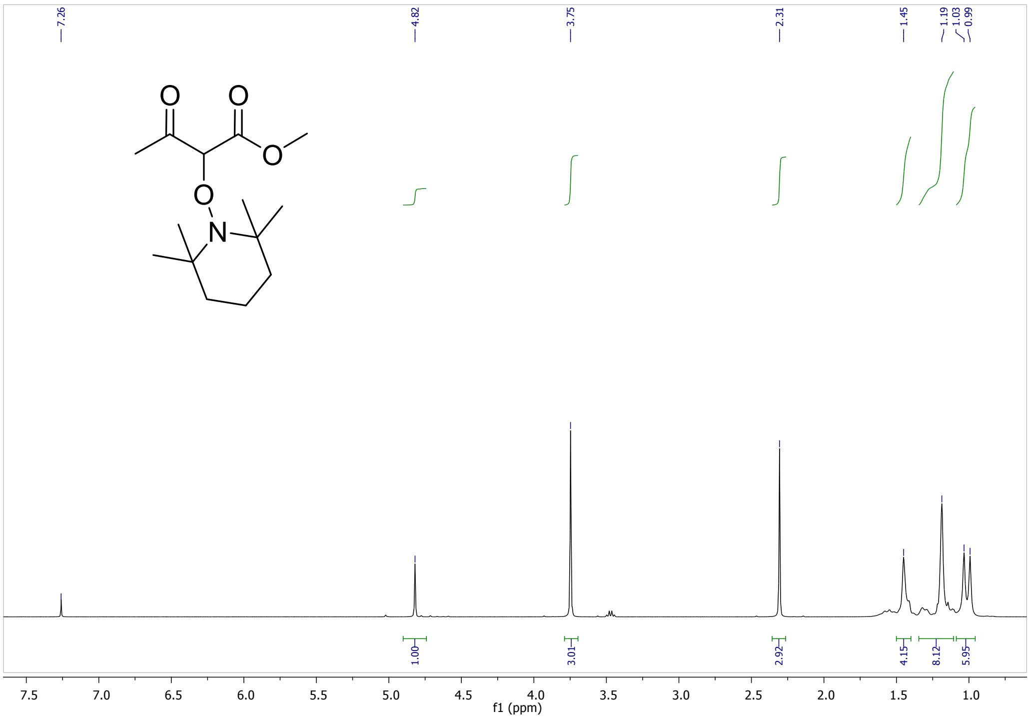


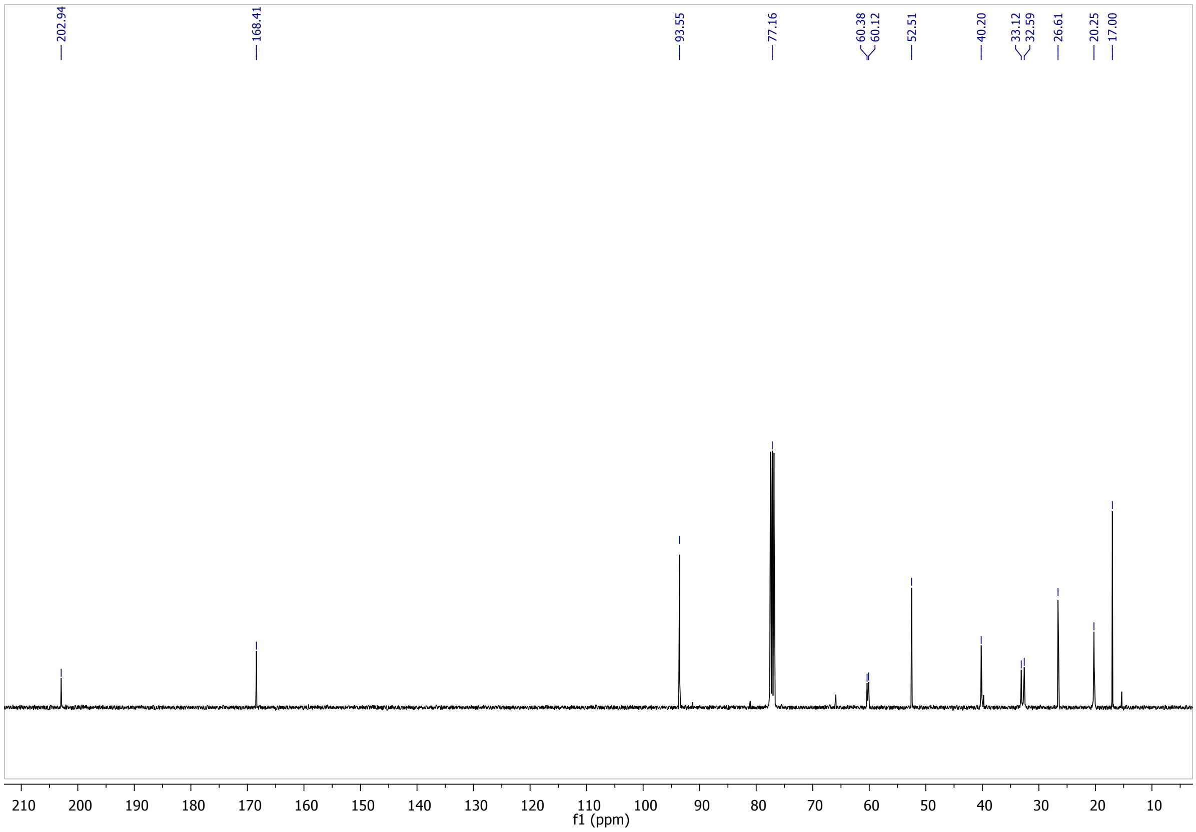
3-((2,2,6,6-tetramethylpiperidin-1-yl)oxyl)pentane-2,4-dione 1b.



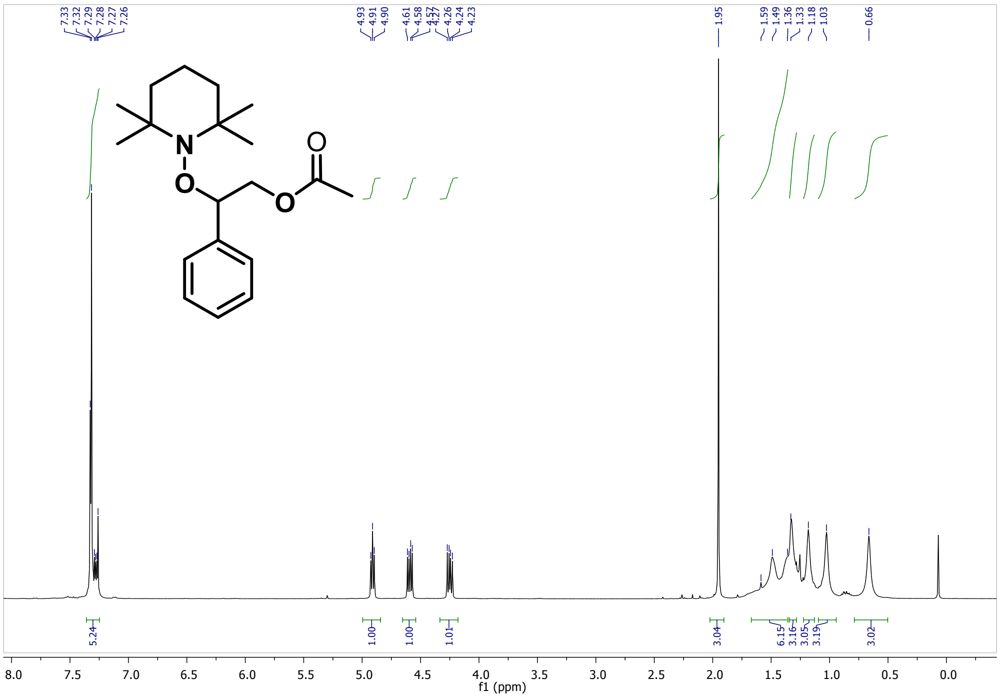


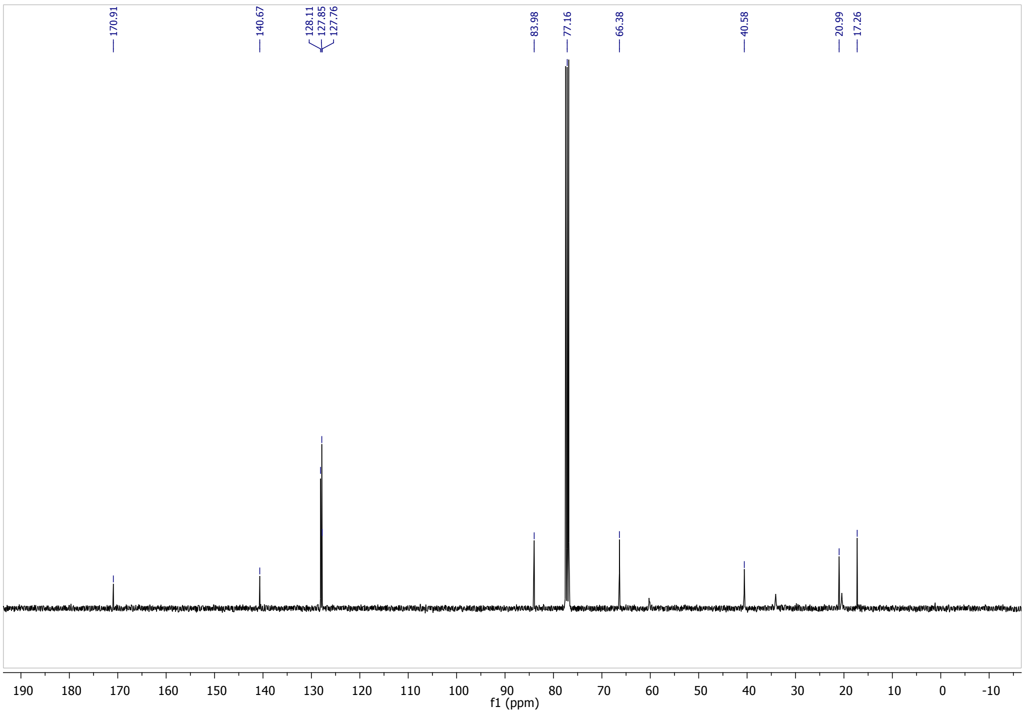
Methyl 3-oxo-2((2,2,6,6-tetramethyl piperidine-1-yl)butanoate 1c.



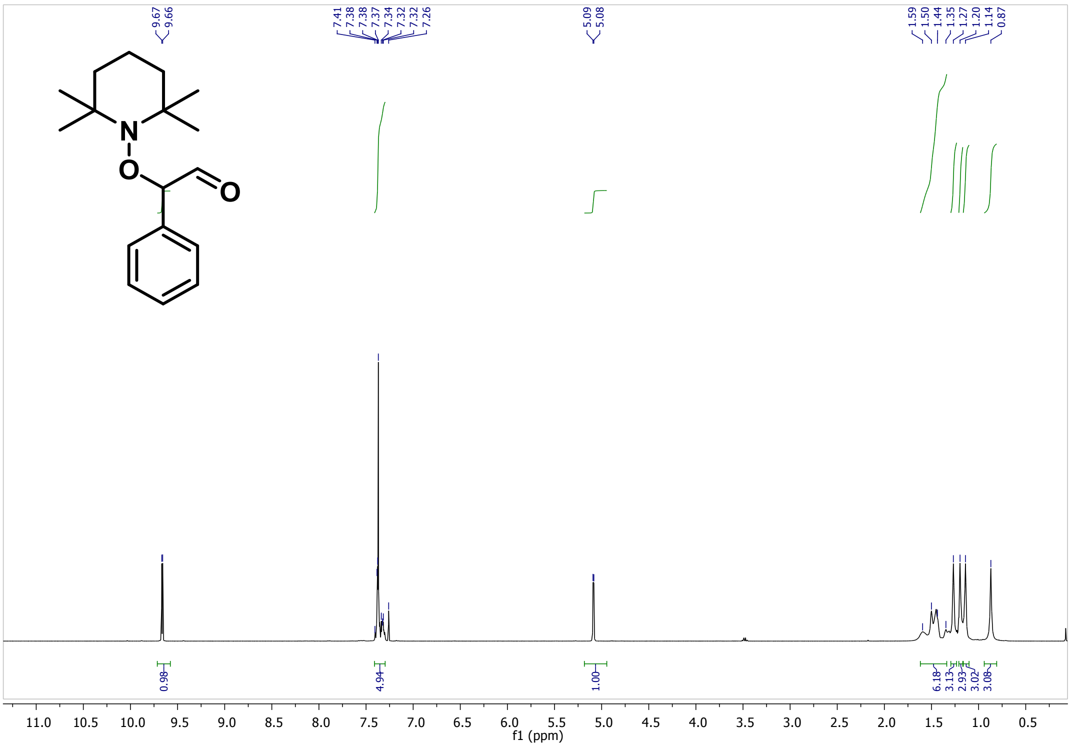


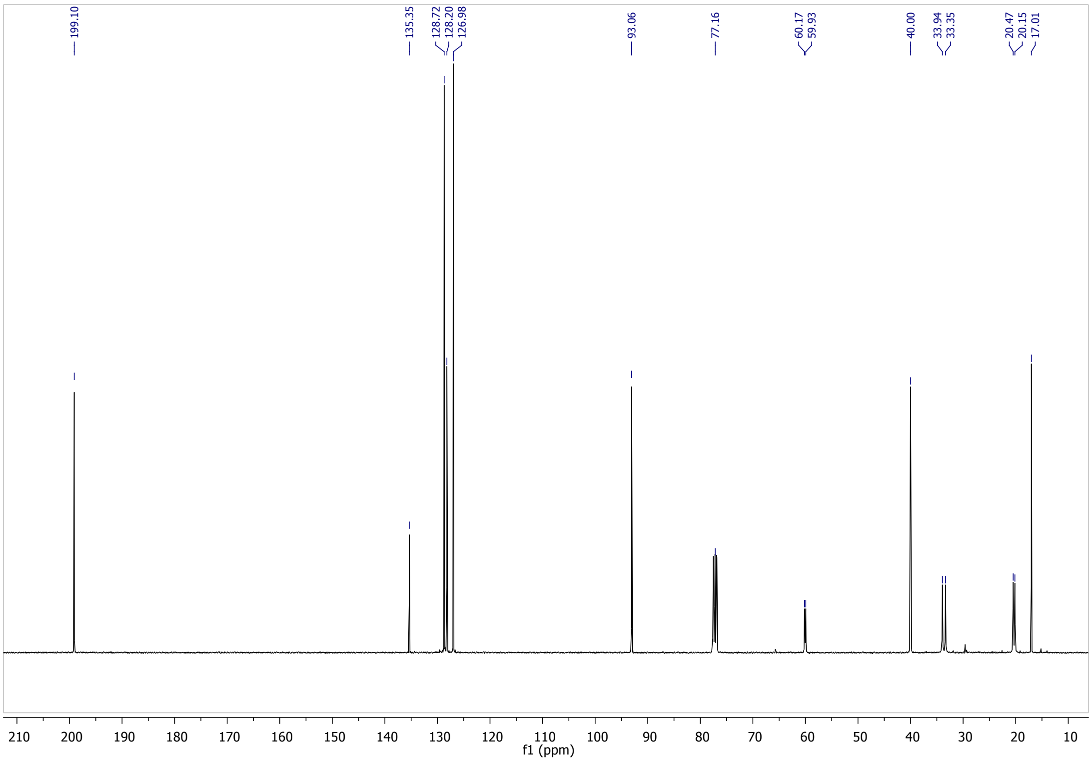
2-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxyl)ethyl acetate 1f.



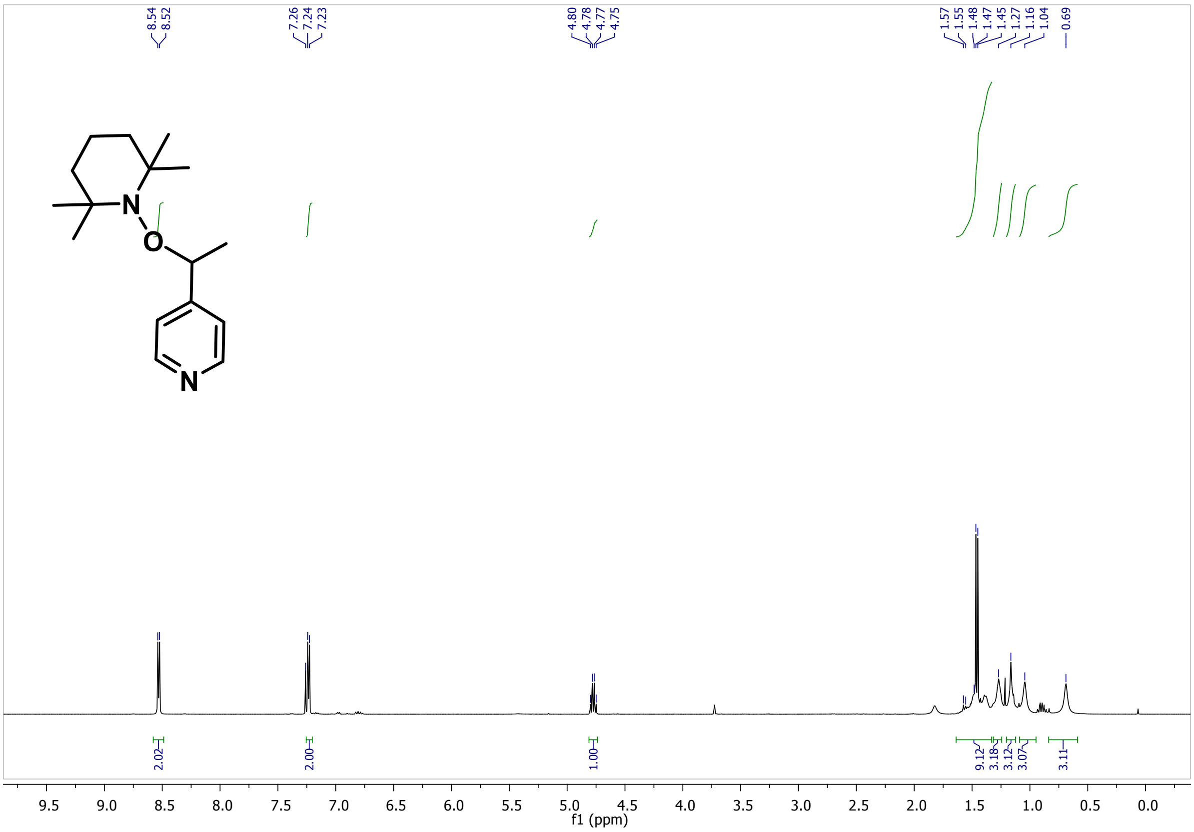


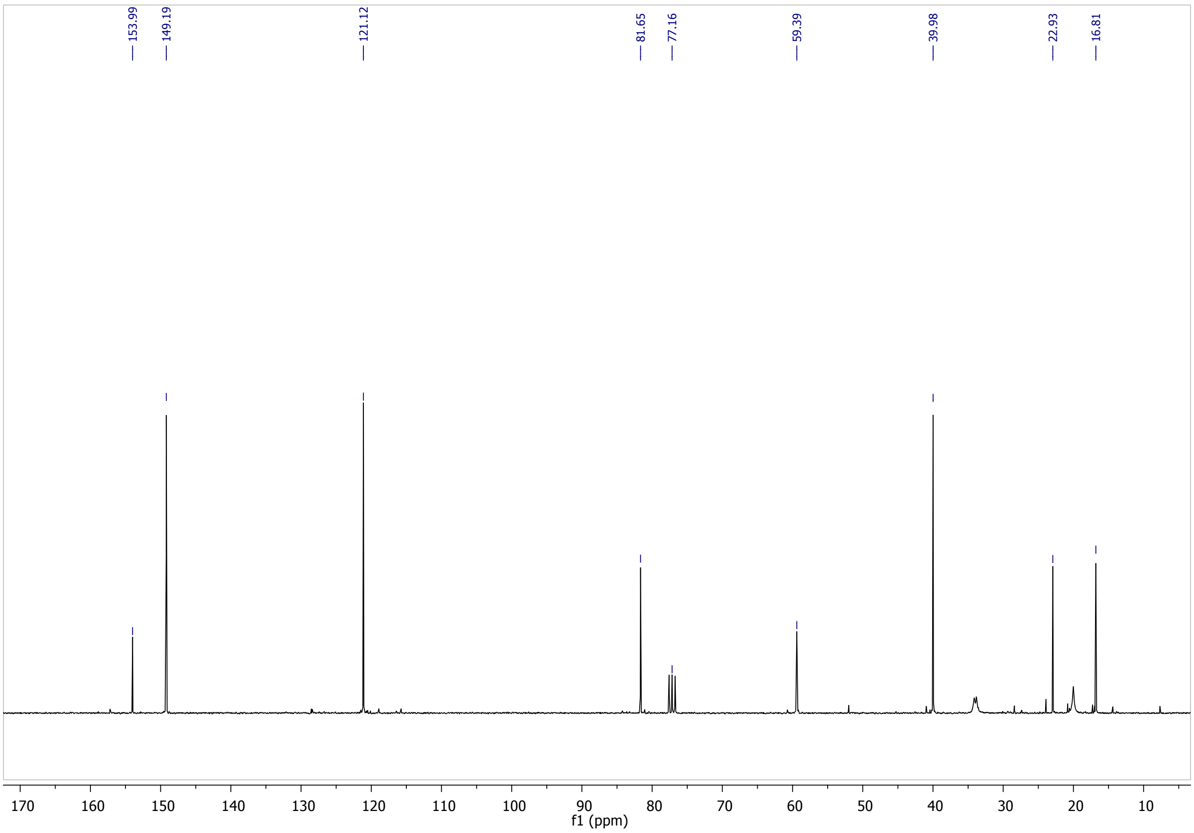
2-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxyl)acetaldehyde 1g.



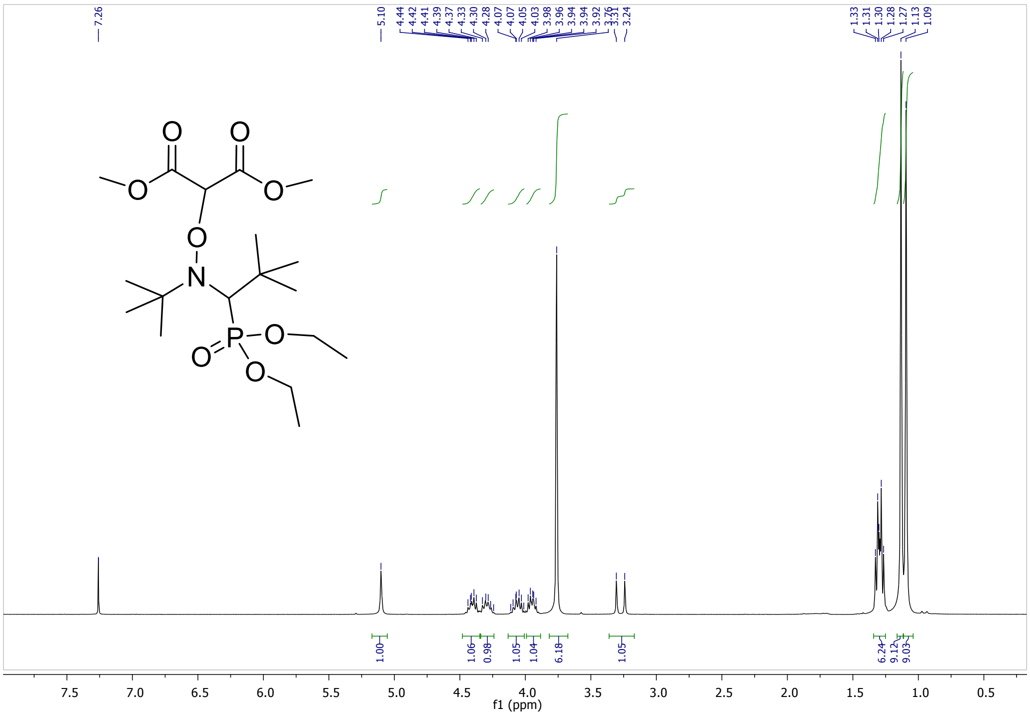


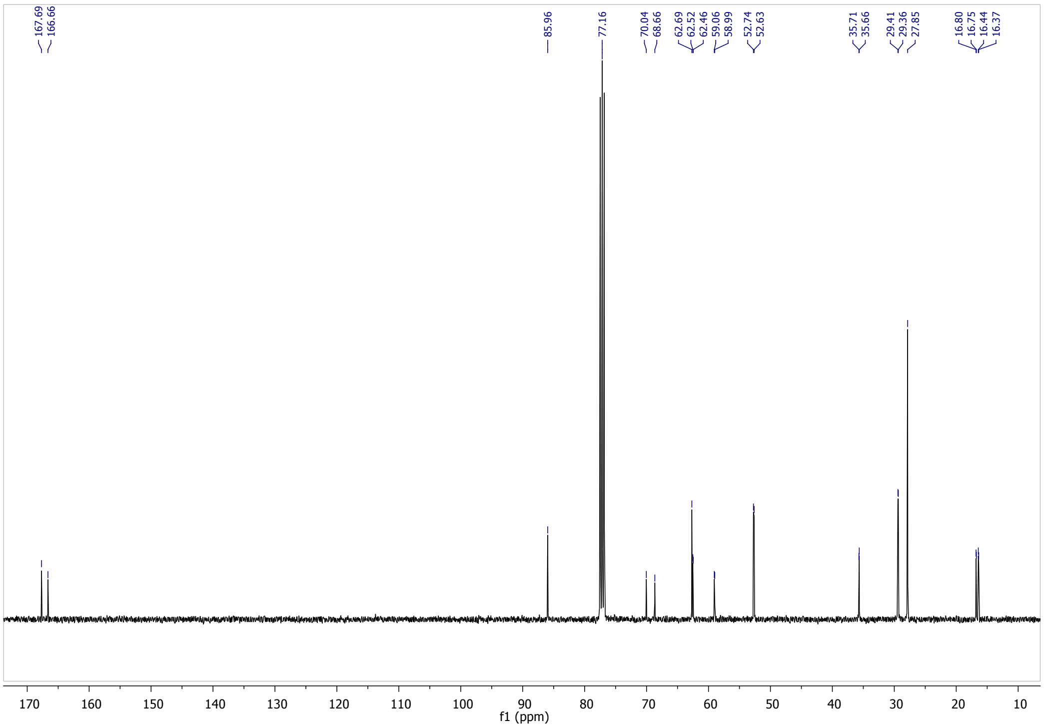
4-[1-(2,2,6,6-tetramethylpiperidin-1-yloxy)-ethyl]-pirydine 1m.





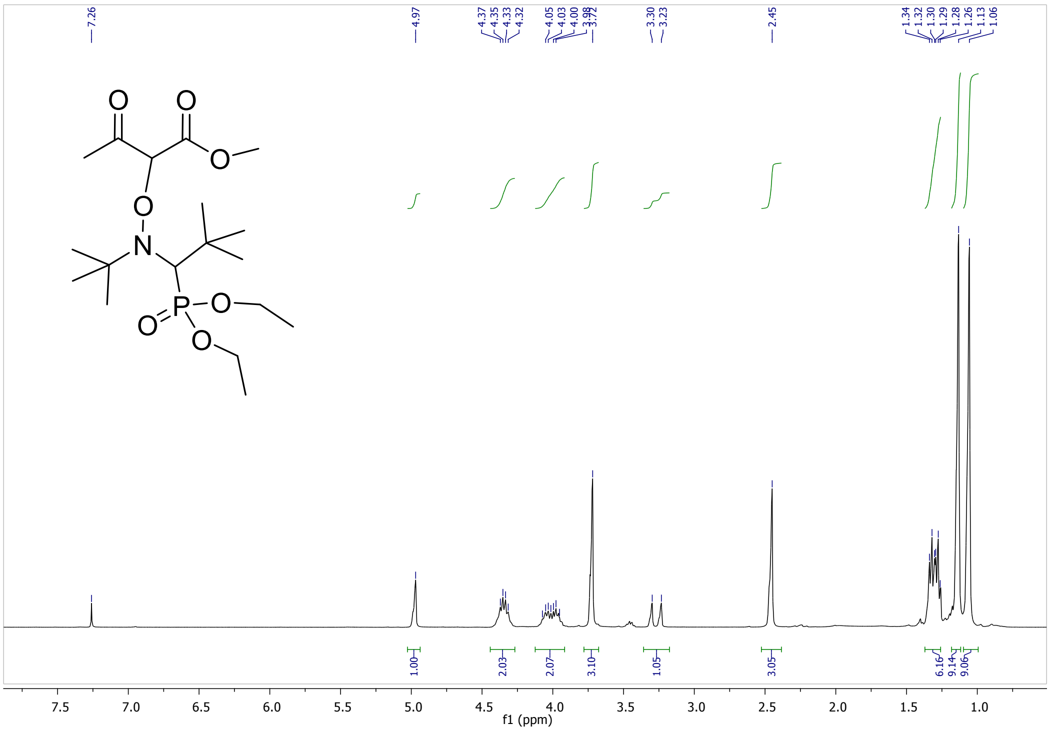
Dimethyl 2-((*tert*-butyl(1-(diethoxyphosphoryl)-2,2-dimethylpropyl)amino)oxy) malonate 2a.

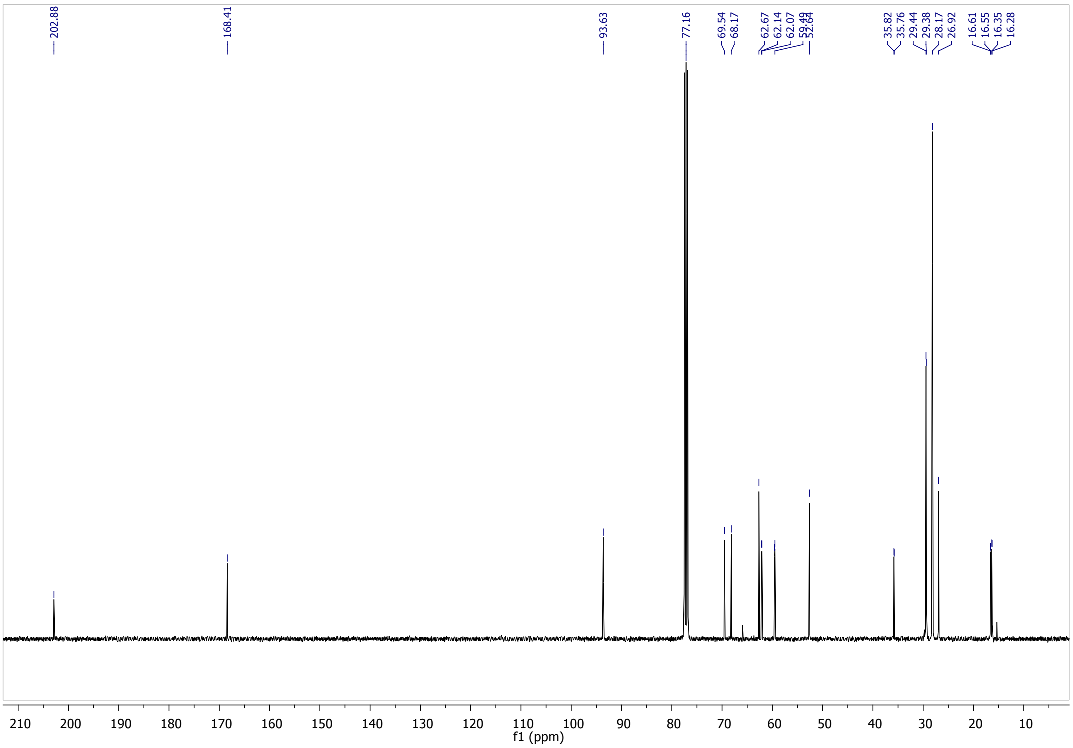




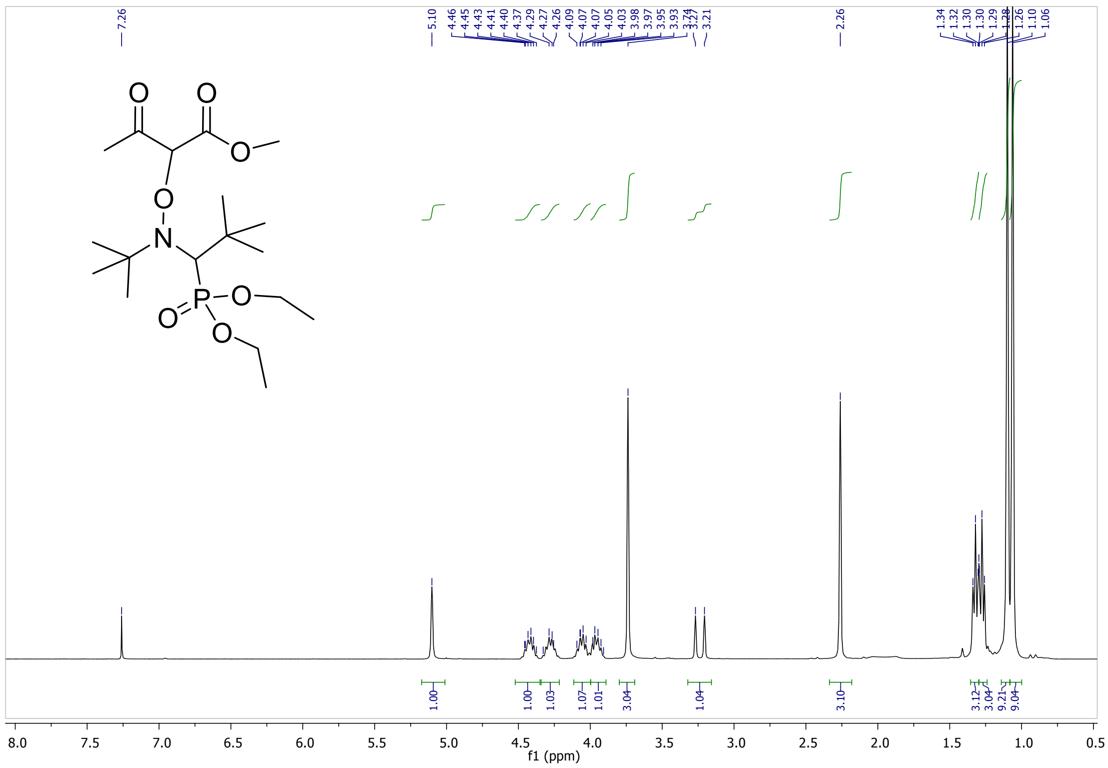
Methyl 2-((*tert*-butyl(1-(diethoxyphosphoryl)-2,2-dimethylpropyl)amino)oxy)-3-oxobutanoate 2c.

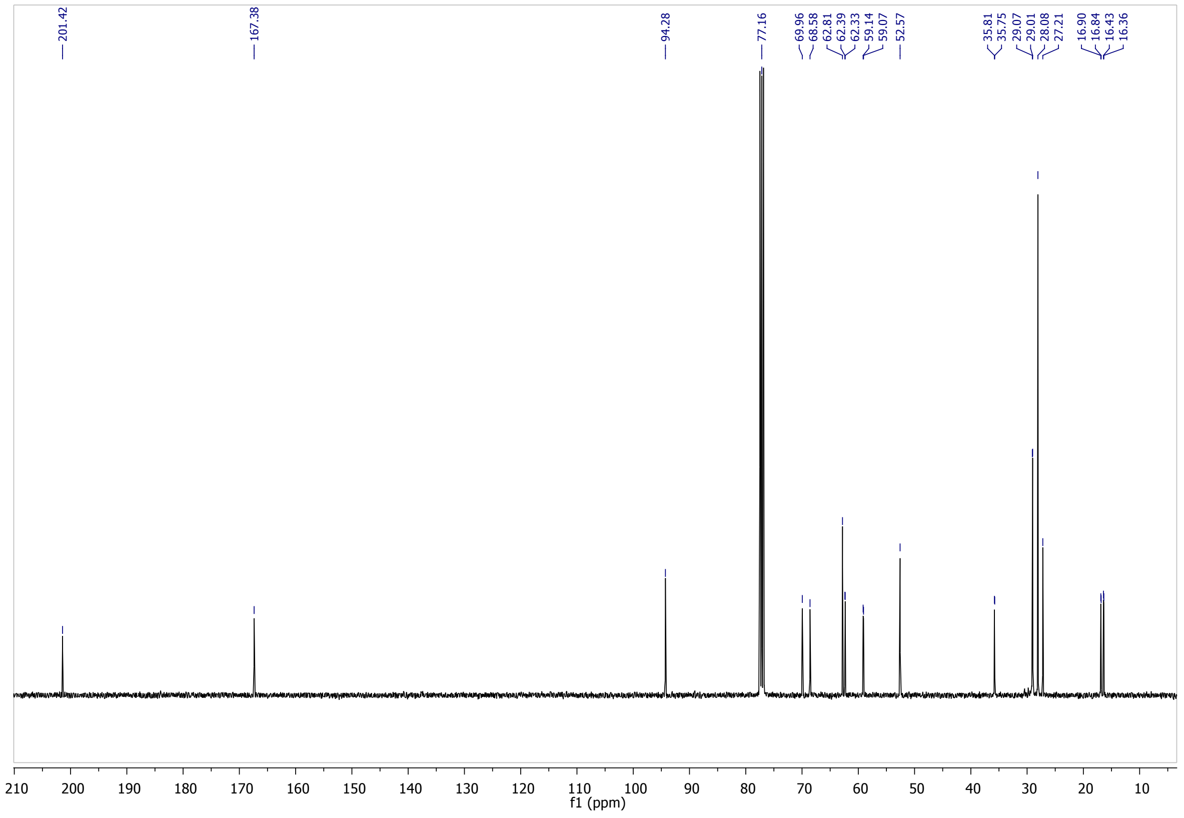
Minor isomer





Major isomer



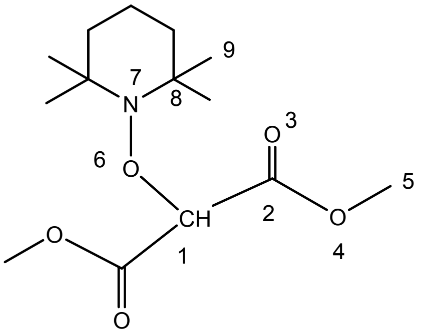


DFT calculations on 1a and 2a

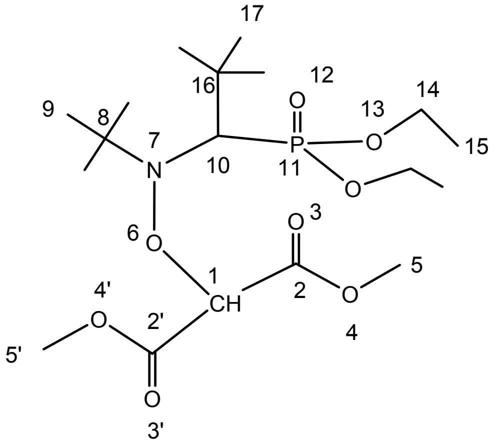
All calculations were performed using Gaussian package 09, revision A02.[13]

The geometry of the species were optimized at the M062X/6-31+G(d,p) level of theory. Vibrational frequencies were calculated at M062X/6-31+G(d,p) level to insure that the obtained geometries are minima (no imaginary frequency). The vibrational frequencies were scaled by a usual factor of 0.967. PCM standart calculations method has been used for calculations in solvents.[14] The corresponding thermal corrections were included to obtain the enthalpy and Gibbs free energy values under the standard conditions (p = 1 atm and T = 298.15 K). Values are given in u.a.

1a



2a



Despite sharp contrast in differences $\Delta E_\mathrm{a} - \Delta E_\mathrm{a}$ = -6.7 kJ/mol from **1a** to **2a** in water:MeOH, ΔE_a = -22.0 kJ/mol from **1a** to **2a** in *t*-BuPh, ΔE_a = -20.0 kJ/mol from *t*-BuPh to water:MeOH for **1a**, and ΔE_a = -4.7 kJ/mol from *t*-BuPh to water:MeOH for **2a** – and $\Delta\Delta H_\mathrm{r}$ (see Table 1SI) – calculated $\Delta\Delta H_\mathrm{r}$ = 0 kJ/mol from **1a** to **2a** in water, $\Delta\Delta H_\mathrm{r}$ = -3.0 kJ/mol from **1a** to **2a** in *t*-BuPh, $\Delta\Delta H_\mathrm{r}$ = -9.2 kJ/mol from *t*-BuPh to water for **1a**, and $\Delta\Delta H_\mathrm{r}$ = -6.2 kJ/mol from *t*-BuPh to water for **2a** – are observed, the trends are the same.

Table 2SI. Selected calculated geometrical parameters (bond length *l*, distance *d*, valence angle α, and torsion angle θ) by DFT at M062X/6-31+G(d,p) level

	1a		**2a**	
	Water	**Toluene**	**Water**	**Toluene**
bond length l (Å)				
O6–C1	1.403	1.404	1.405	1.405
N7–O6	1.447	1.445	1.424	1.427
C8–P9	------	------	1.855	1.856
P9–O10	------	------	1.488	1.485
distance d (Å)				
N7••••C1	2.344	2.345	2.315	2.332
O12••••C1	------	-----	4.285	4.464
valence angle α (º)				
<N7O6C1>	110.58	110.72	109.78	110.82
<C8N7O6>	105.14	104.96	108.79	111.07
torsion angle θ (º)				
<O6C1C2O3>	113.99	113.75	-14.27	52.09
<O6C1C2'O3'>	174.03	172.78	125.60	13.97
<N7O6C1C2>	-90.351	-90.89	-74.36	79.52
<N7O6C1C2'>	149.11	148.52	164.24	-160.74
*<C1O6N7*$n_{\sigma,N7}$*>*^{a}	-11.16	-10.65	-4.6	-9.18
<O12P11C10 N7>	------	------	8.83	18.52
$\Delta_r H$ *(kJ/mol)*	144.6	153.8	144.6	150.8

^{a}*<nNOC>= <*$C_8N_7O_6C_1$*>-120°*

Conformation changes are mainly ruled by 4 effects: *i*) stabilizing hyperconjugation, *ii*) destabilizing steric strain which has to be minimized, *iii*) dipole moment which has to be minimized in non-polar solvent, and *iv*) H-bonding.

Noteworthily, the most stable conformation of **1a** is the same in toluene and water, as highlighted by the same geometrical parameters both in the nitroxyl (Table 2SI) and the alkyl (Table 2SI and geometrical parameters for IHB and hyperconjugation in Table 3SI) fragments. This conformation is stabilized both by 3 hyperconjugation interactions – two strong ones $\sigma_{C—H} \rightarrow \sigma^*_{C—O}$ and $\sigma_{C—H} \rightarrow \pi^*_{C=O}$ and a weak one $\sigma_{C—H} \rightarrow \sigma^*_{C—O}$ (Table 3SI) – and two IHB – between the proton of the methyne group with the *N* atom of the nitroxyl moiety and with an *O* atom from one carbonyl moiety (Table 3 and Figure 8 in manuscript).[15,16-17] The only difference between toluene and water is the increase of the dipole moment μ (Table 3SI and figure 9 in manuscript). This means that there are no other conformations providing less steric strains or better hyperconjugation interactions which overbalance the increase in dipole moment.

In sharp contrast to **1a**, from toluene to water, the change in conformation of the alkyl fragment in **2a**, is more striking as the <NOCH> angle changes from -43° to 4° (see Table 1SI), respectively. Moreover, conformation of **2a** in water (Figure 9 in manuscript) exhibits larger dipole moment ($\mu = 6.0$ D) and larger steric strain (shortest distances between carbonyl moieties and methyl groups are 3.11 Å and 3.17 Å, Figure 8 in manuscript) than the conformation in toluene ($\mu = 4.0$ D, and 3.30 Å and 3.54 Å, Figure 8 in manuscript). These changes are governed by both the occurrence of hyperconjugation interactions and IHB in toluene – 3 hyperconjugation interactions (two strong interactions $\sigma_{C—H}\rightarrow\sigma^*_{C=O}$ and $\sigma_{C—H}\rightarrow\pi^*_{C=O}$ and a weak interaction $\sigma_{C—H}\rightarrow\pi^*_{C=O}$, (Table 3SI)) and 2 IHB (bidentate interaction between the proton of the methyne group and the *N* and *O* atoms of the nitroxyl and ester moieties (Table 3SI and Figure 8 in manuscript)) – and in water – 4 hyperconjugation interactions (two strong interactions $\sigma_{C—H}\rightarrow\sigma^*_{C=O}$ and two weak interactions $\sigma_{C—H}\rightarrow\pi^*_{C=O}$, (Table 3)) and 3 IHB (tridentate interaction between the proton of the methyne and the *N* and *O* atoms of the nitroxyl and two ester moieties (Table 3 and Figure 8 in manuscript)).

Thus, dipole moment, IHB and hyperconjugation are the interactions ruling the conformation of **2a**. That is, the dispersion of coulomb forces in polar solvent such as water affords a decrease in dipole moment large enough so that hyperconjugation and IHB occurring in water are strong enough to overbalance larger the steric strain in water (water/MeOH) than in toluene (*t*-BuPh).

These changes in conformations in **1a** and **2a** depending on the solvent account partly for the changes in E_a reported above (vide supra).

Table 3SI. Dipole moment μ charges δ and energies *E* for hyperconjugation interactions for **1a** and **2a**. Geometrical parameters for IHB (distances *d* and valence angles) and for hyperconjugation interactions (dihedral angles) for **1a** and **2a** calculated by DFT at M062X/6-31+G(d,p) level of theory.

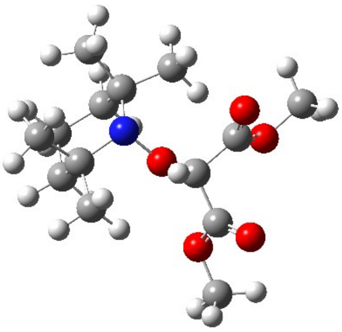
	1a		**2a**	
	toluene	water	toluene	water
μ (D)	4.1	4.9	4.0	6.0
δ	0.29	0.29	0.27	0.29
$d_{H\cdots N}$ (Å)	2.40	2.40	2.48	2.36
$d_{H\cdots O=C}$ (Å)	2.52	2.53	-[a]	-[a]
$d_{H\cdots O=C}$ (Å)	2.73[b]	2.73[b]	-[a]	-[a]
$d_{H\cdots OMe}$ (Å)	-[a]	-[a]	2.36	2.45
$d_{H\cdots OMe}$ (Å)	-[a]	-[a]	2.68[b]	2.45
<NHC> (°)	74	74	69	76
$\langle CHO_{=C}\rangle$ (°)	72	72	-[a]	-[a]
$\langle CHO_{=C}\rangle$ (°)	60[b]	61[b]	-[a]	-[a]
$\langle CHO_{Me}\rangle$ (°)	-[a]	-[a]	77	72
$\langle CHO_{Me}\rangle$ (°)	-[a]	-[a]	60[b]	71
$E\sigma_{C-H}\rightarrow\sigma^{*}_{C-O}$ (kJ/mol)	20	20	-[c]	-[c]
$E\sigma_{C-H}\rightarrow\sigma^{*}_{C-O}$ (kJ/mol)	6	6	-[c]	-[c]
$E\sigma_{C-H}\rightarrow\sigma^{*}_{C=O}$ (kJ/mol)	-[c]	-[c]	23	21
$E\sigma_{C-H}\rightarrow\sigma^{*}_{C=O}$ (kJ/mol)	-[c]	-[c]	20	20
$E\sigma_{C-H}\rightarrow\pi^{*}_{C=O}$ (kJ/mol)	23	23	7	7

$E\sigma_{C-H}\rightarrow\pi^*_{C=O}$ (kJ/mol)	-[c]	-[c]	-[c]	5
<HCCO> (°)	173	173	-[a]	-[a]
<HCCO> (°)	114	116	-[a]	-[a]
<HCC=O> (°)	66	64	176	147[d,e]
<HCC=O> (°)	-[a]	-[a]	106[d,f]	154[d,g]

[a] Not measured. [b] The distance larger than the sum of the van der Waals radii and the closed angle preclude the occurrence of IHB. [c] Energies below 2 kJ/mol are not reported. [d] <HCCπ*> = 180 - <HCC=O>. [e] <HCCπ*> = 36°. [f] <HCCπ*> = 74°. [g] <HCCπ*> = 41°.

Calculations in water

1a



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C	2.496062	0.014442	-0.046600
C	1.235362	0.690252	-0.584122

H	-0.066008	-1.009473	-0.351263
H	-0.919501	0.536456	-0.327890
H	3.397311	0.514000	-0.421343
H	2.526733	-1.021874	-0.406807
H	1.245775	1.762070	-0.352748
H	1.211389	0.613769	-1.676024
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C	1.067728	-2.798246	2.787817
H	0.480738	-2.289823	3.557316
C	0.318362	-4.071012	2.397288
C	2.383398	-3.225534	3.447832
O	2.723687	-2.896175	4.560147
O	0.144112	-4.960420	3.202038
O	3.102735	-3.990342	2.631373
O	-0.106581	-4.088950	1.146100
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H	5.013169	-3.494232	3.275008
H	4.297325	-4.939728	4.044281
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H	-0.208910	-6.147108	0.863242
H	-1.733589	-5.365075	1.368483
H	-1.102475	-5.104085	-0.289811
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H	0.312050	2.197364	1.597962
C	2.812301	1.392507	2.067380

H	2.598565	1.411226	3.140026
H	3.870552	1.629333	1.926731
H	2.243091	2.183470	1.582681
C	3.731100	-0.882493	1.936998
H	3.783954	-0.933680	3.030288
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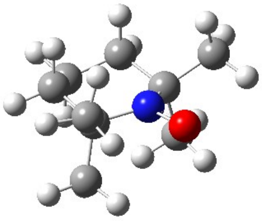
1$^{\bullet}$



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H	3.898309	-0.987295	2.879755
H	3.349801	-2.043024	1.558976
C	3.051843	1.382750	1.930901
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C	-0.365680	1.382938	2.100920
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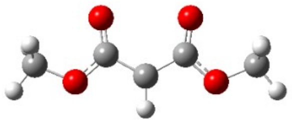

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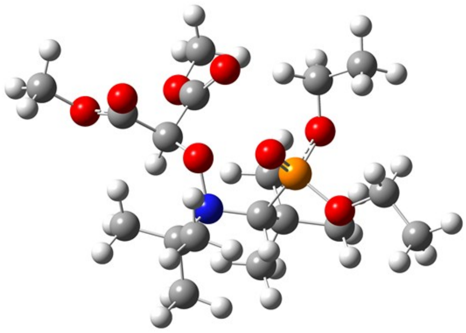

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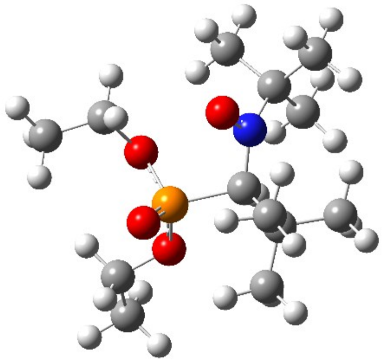

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C	-0.875387	-2.152879	1.801925
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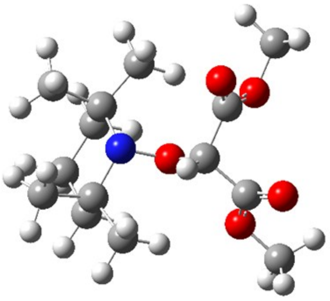
Calculations in toluene

1a



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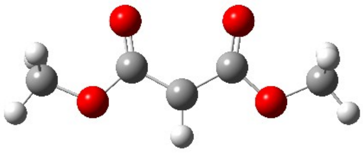

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O	-1.469580	0.021186	-1.897338
O	1.455650	0.143105	-1.880234
O	-2.306179	0.086287	0.195727
O	2.278189	-0.165459	0.196619
C	-3.620914	0.140578	-0.367506
H	-4.301130	0.187281	0.480144
H	-3.724470	1.026497	-0.997230
H	-3.809907	-0.752496	-0.966648
C	3.596742	-0.154785	-0.360332
H	3.704567	-0.961562	-1.088065
H	3.789595	0.801771	-0.850295
H	4.271194	-0.300170	0.480707

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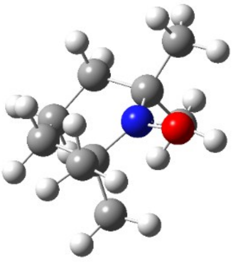

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E = -483.258648

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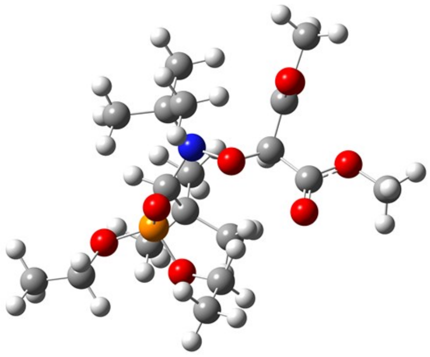
$\langle S^2 \rangle = 0.75489$

C	0.000501	0.000346	0.001956
C	-0.000679	-0.000115	1.536361
C	2.632451	-0.000259	1.405370
C	2.478987	0.000216	-0.121343
C	1.212887	0.701742	-0.600290
H	-0.013740	-1.040383	-0.348705
H	-0.934251	0.464241	-0.333081
H	3.375921	0.464016	-0.547500
H	2.458245	-1.040514	-0.471678
H	1.226716	1.762716	-0.323404
H	1.158531	0.666720	-1.692910
N	1.344373	-0.401918	2.043968
O	1.406183	-0.682884	3.286878
C	3.685023	-1.033054	1.811971
H	4.615538	-0.822236	1.275857
H	3.876626	-0.995485	2.885337
H	3.350972	-2.041676	1.551563
C	3.049274	1.382140	1.930573
H	3.001805	1.388658	3.022964
H	4.078416	1.592323	1.622777
H	2.411998	2.182416	1.547252
C	-1.007807	-1.032794	2.045442
H	-1.091876	-0.995244	3.132530
H	-1.986930	-0.821835	1.604381
H	-0.701393	-2.041447	1.753124
C	-0.363155	1.382329	2.100329
H	-1.417724	1.592657	1.896131
H	-0.207565	1.388826	3.182624

H	0.233065	2.182522	1.655684

2a



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E = -1704.397316

H = -1704.396372

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C	0.335156	-2.314972	-0.929102
C	1.471818	-3.243873	-0.476939
H	1.498611	-4.139864	-1.106069
C	0.583966	-1.840809	-2.365462
H	-0.200389	-1.152584	-2.682888
H	0.579175	-2.721753	-3.015643
H	1.552736	-1.350217	-2.464235
C	-0.965296	-3.131987	-0.905557
H	-1.161168	-3.576662	0.075910
H	-0.850629	-3.955786	-1.614889
H	-1.829614	-2.542434	-1.223264
C	-1.652288	2.704649	-0.586285
H	-1.316604	3.409659	0.179374
H	-0.770934	2.322902	-1.107664
C	-2.644591	3.337322	-1.539305

H	-2.956592	2.609904	-2.293435
H	-2.182450	4.188934	-2.047083
H	-3.526347	3.691184	-0.997111
C	-4.751498	-0.055108	-0.471217
H	-4.876492	1.001136	-0.207766
H	-4.672095	-0.140752	-1.559924
C	-5.884904	-0.898638	0.070080
H	-5.738982	-1.949028	-0.193618
H	-6.834441	-0.560503	-0.353459
H	-5.938555	-0.814385	1.158535
N	0.298635	-1.165975	0.060746
O	0.872719	0.014994	-0.501954
O	-1.906563	0.016504	-1.846699
O	-2.291292	1.628672	0.142060
O	-3.526262	-0.531514	0.122137
P	-2.140812	0.116404	-0.383772
H	-1.480748	-1.746902	0.881837
C	-0.781502	-0.206975	2.147696
C	0.148722	-1.154748	2.923377
C	-0.236951	1.244646	2.184533
C	-2.145499	-0.224112	2.860184
H	-0.239951	-2.180287	2.903757
H	1.158637	-1.183794	2.508592
H	0.207798	-0.833693	3.968455
H	-1.036489	1.949721	2.426404
H	0.539828	1.344738	2.950862
H	-2.007930	0.098098	3.897921
H	-2.857499	0.457771	2.388636
H	-2.583576	-1.228620	2.867840
C	2.074029	0.344192	0.147192
H	1.983887	0.232984	1.232347
C	3.271592	-0.485573	-0.320928
C	2.371241	1.815179	-0.144312

O	3.595241	-0.621202	-1.475339
O	1.587815	2.604589	-0.603665
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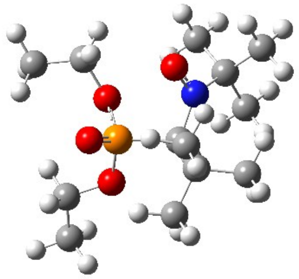
O	3.919654	-1.018499	0.714804
C	5.098402	-1.766857	0.387475
H	5.809341	-1.128177	-0.139976
H	5.506431	-2.102701	1.338042
H	4.836758	-2.618965	-0.243714
C	4.019589	3.473334	0.034542
H	5.050271	3.525491	0.377569
H	3.947914	3.735012	-1.022246
H	3.380788	4.134815	0.622130
H	2.444601	-2.755129	-0.563053
H	1.325494	-3.547875	0.564756
H	0.175496	1.572563	1.229193

2$^\bullet$



ZPE = 0.409698

E = -1209.053841

H = -1209.052897

G = -1209.133316

$\langle S^2 \rangle$ = 0.754661

C	0.012556	-0.001485	-0.008772
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C	1.505845	-0.023580	-0.461126
C	1.650564	-0.192015	-1.978018
H	2.713365	-0.128868	-2.236864
H	1.108710	0.588636	-2.517262
H	1.272506	-1.163329	-2.307278
C	2.199270	-1.195170	0.244778
H	1.716781	-2.147329	0.000292
H	2.193566	-1.066466	1.333474
H	3.242426	-1.256253	-0.081760
C	2.180887	1.283831	-0.019876
H	2.032979	1.471651	1.049361
H	1.798869	2.143123	-0.579270
H	3.256693	1.211793	-0.209390
C	-1.380125	-2.212938	0.364669
C	-0.907731	-2.119670	1.813297
H	0.181260	-2.177909	1.894464
H	-1.328834	-2.965917	2.362982
H	-1.258792	-1.204290	2.299340
C	-0.983446	-3.564406	-0.236975
H	-1.258948	-3.601022	-1.293092
H	-1.503582	-4.367939	0.292473
H	0.094306	-3.731965	-0.146971
C	-2.900147	-2.026810	0.298441
H	-3.182244	-1.046832	0.693784
H	-3.389382	-2.805174	0.891499
H	-3.241970	-2.102927	-0.736605
C	-1.078453	3.783021	0.815682
H	-0.614637	4.290240	-0.035818
H	-2.167079	3.799388	0.685863

C	-0.671501	4.411138	2.130139
H	-1.135974	3.885287	2.967885
H	-0.989074	5.456916	2.154830
H	0.414161	4.373763	2.250067
C	-3.314760	1.081216	-1.496054
H	-4.028520	0.283567	-1.276276
H	-2.717693	0.789018	-2.362596
C	-4.004725	2.412268	-1.711347
H	-4.566218	2.703670	-0.819082
H	-4.701077	2.340404	-2.551970
H	-3.266415	3.186255	-1.939414
N	-0.750944	-1.154436	-0.487065
O	-1.132304	-1.106772	-1.704909
O	-0.570727	2.197352	-1.773127
O	-0.638598	2.408822	0.828161
O	-2.459777	1.153774	-0.331857
P	-0.905660	1.528554	-0.491140

References

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[1] Bertin, D.; Gigmes, D.; Marque, S. R. A.; Tordo, P.; *Macromolecules* **2005**, *38*, 2638–2650.

[2] Bertin, D.; Dufils, P.–E.; Durand, I.; Gigmes, D.; Giovanetti, B.; Guillaneuf, Y.; Marque, S. R. A.; Phan, T.; Tordo, P. *Macromol. Chem. Phys*. **2008**, *209*, 220-224.

[3] $a_{\mathrm{H}\beta} = 16.6$ G for PhMeC•COOMe is used to estimate the lower limit of RSE for **g•** and **k•**. Thus, as PhMeCH• and MeCOMeCH• radicals exhibit very similar RSE, meaning that the stabilization effect of Ph and MeCO groups are very similar, one can assume that the upper limit of stabilization is given by the RSE of the Ph_2CH•, i.e., $a_{\mathrm{H}\alpha} = 14.7$ G, as PhMeHC• and MeCOMeHC• radicals exhibit very similar RSE.

[4] $a_{\mathrm{H}\alpha} = 21.5$ G for both •CH_2COOMe and •CH_2NH_2, meaning that the stabilization of the odd electron is the same for these two groups. It is assumed that the stabilization should be very similar for the CONMeOMe group.

[5] Brocks, J. J.; Beckhaus, H. D.; Beckwith, A. *J. Org. Chem.* **1998**, *63*, 1935–1943.

[6] To be on the correlation lines, outliers need to be shifted leftward, meaning that bulkiness must be lower than estimated, i.e., to assume the bulkiness of COOMe or other group close to the bulkiness of H atom.

[7] Charton, M. *Topics Curr, Chem.* **1983**, 58–91.

[8] $R^2 = 0.98$, $s = 0.51$, $N = 16$, $F_{99.99\%} = 202$, $t = 99.99\%$ for all coefficients.

[9] Bertin, D.; Gigmes, D.; Marque, S. R. A.; Tordo, P.; *Macromolecules* **2005**, *38*, 2638–2650.

[10] Bertin, D.; Dufils, P.–E.; Durand, I.; Gigmes, D.; Giovanetti, B.; Guillaneuf, Y.; Marque, S. R. A.; Phan, T.; Tordo, P. *Macromol. Chem. Phys*. **2008**, *209*, 220-224.

[11] Krężel, A.; Bal, W. J. Inorg. Biochem. 2004, 98, 161-6.

[12] Henderson, J. J. *Am. J. Physiol.* **1908**, *21*, 173–179

[13] Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E;.

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

[14] Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.*, **2005**, *105*, 2999-3093.

[15] Intramolecular H-bonding is observed between H-acceptor and H-donor for distances smaller than the sum of the Van der Waals radii of the atoms involved in IHB: r_H = 1.09 Å, r_N = 1.50 Å, and r_O = 1.52 Å. IHB depends also on the valence angle α, that is, strong IHB are expected for α larger than 150°, weak IHB for α smaller than 120°. IHB for α lower than 90° requires strained conformations. See refs. 19 and 20.

[16] R. S. Rowland, R. Taylor, *J. Phys. Chem.* **1996**, *100*, 7384–7391.

[17] G. A. Jeffrey, W. Saenger *Hydrogen Bonding in Biological Structures*, Springer, Berlin, Heidelberg, **1994**.