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Electronic properties of the nitrone substituent. Stabilization of benzylic carbocations

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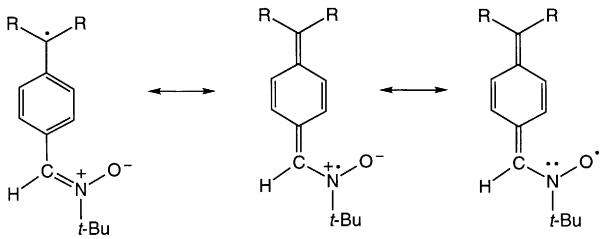
ABSTRACT: The nitrone substituent CH═N(O) *t*-Bu is electron-withdrawing with a Taft σ_I value of 0.20. It also retards the solvolysis rate of a cumyl chloride when placed in the *meta*-position ($\sigma^+ = 0.20$). However, CH═N(O) *t*-Bu becomes weakly cation stabilizing when placed in the *para*-position of a cumyl cation ($\sigma^+ = -0.04$). This weak cation stabilization is a result of a conjugative interaction which delocalizes charge and offsets the inductive effect of the nitrone. When the nitrone is placed in the *para*-position, but then twisted out of conjugation with the aromatic ring by incorporation of flanking 3,5-dimethyl groups, it again retards solvolysis rates. Computational studies (B3LYP/6–31G*) show that the nitrone substituent stabilizes a *para*-substituted benzyl cation relative to the *meta*-substituted analog by a conjugative interaction. However, the calculated stabilization greatly overestimates the cation stabilization seen in solvolytic reactions. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: nitrone substitution; benzylic carbocations; stabilization; electronic properties

INTRODUCTION

Nitrones are useful synthetic intermediates and also effective spin traps and are therefore of interest to both synthetic and mechanistic organic chemists.[1] We recently reported on the radical-stabilizing ability of the nitrone substituent CH═N(O)-*t*-Bu and related nitrogen-containing groups on benzylic radicals.[2] The nitrone is a potent radical stabilizer by a spin delocalization mechanism which can be described in valence bond terms as involving nitroxyl radical forms **1a** and **1b**. This led to



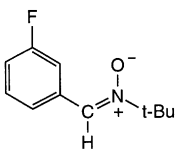
1 **1a** **1b**

the classification of the nitrone functional group as a 'super radical stabilizer'. We further suggested that the large radical-stabilizing effects of this and related groups made them specifically suited for free radical substituent effect studies. Since the nitrone is a potent radical stabilizer of potential use in correlating radical reactions, it becomes important to know the effect of this group on carbocation forming reactions. Can this group be cation stabilizing? Reported here are the results of studies designed to evaluate the electronic effect of the nitrone functional group on benzylic carbocations.

RESULTS AND DISCUSSION

Taft σ_I value for CH═N(O)-*t*-Bu

Polar substituent constants have not been reported for the nitrone group. The ^{19}F NMR method developed by Taft *et al.*[3] has therefore been used to determine the σ_I value for CH═N(O)-*t*-Bu. The nitrone **2** was prepared and the ^{19}F signal appears 0.829 ppm downfield from that of fluorobenzene. This shift corresponds to a σ_I value of 0.20 and indicates that inductively, the nitrone is a moderately electron-withdrawing group.



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Solvolytic studies

We next wanted to determine the electronic effect of the

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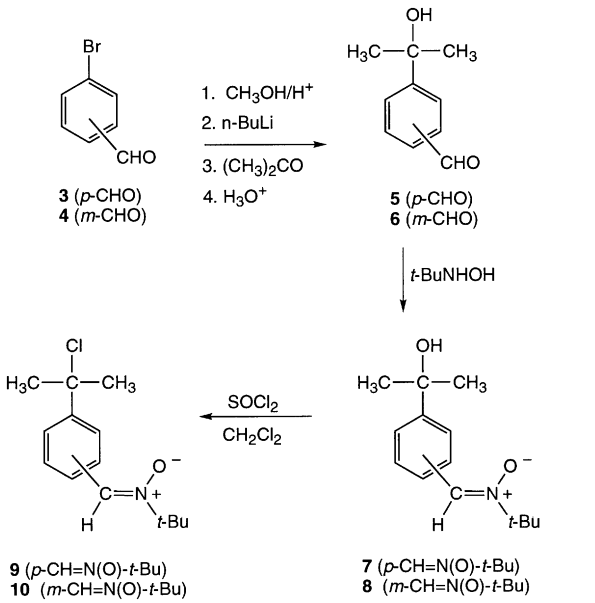
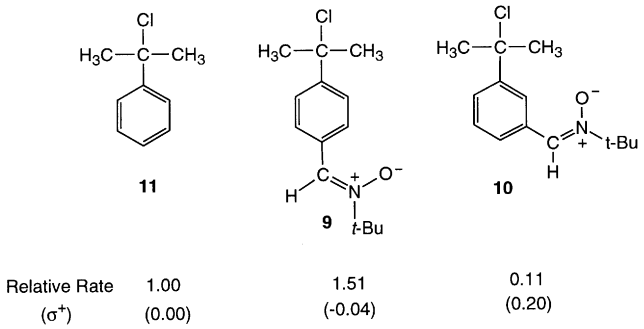
nitrone under conditions of high electron demand, i.e. the σ^+ values of both *meta* and *para* nitrone substituents.[4] The requisite cumyl chlorides **9** and **10** were prepared from aldehydes **5** and **6**, which we had previously synthesized.[5] Conversion to nitrones **7** and **8** using *N*-*t*-butylhydroxylamine hydrochloride in pyridine was straightforward. These alcohols were then reacted with thionyl chloride which gave the *O*-protonated forms of chlorides **9** and **10**. The neutral nitrones were regenerated on addition of bases such as 2,6-lutidine or pyridine.



Solvolyses of chlorides **9** and **10** in methanol containing 2,6-lutidine as a buffering base gave the simple methyl ether substitution product along with smaller amounts of the corresponding α-methylstyrene elimination product. Rates of reaction (Table 1) of **9** and **10**, and also the unsubstituted cumyl chloride **11**, were monitored

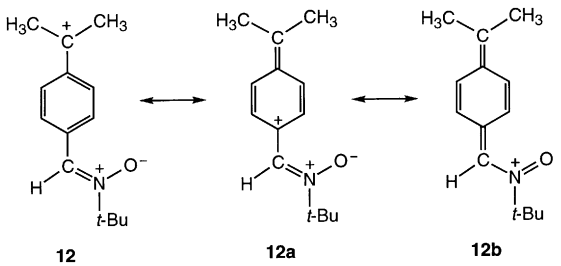


by UV spectrophotometry. These data were used to determine σ^+ values using the expression $\sigma^+ = \log (k/k_H)/\rho$, where $\rho = -4.82$ in methanol.[6] The rate retardation seen in the *meta*-derivative **10** corresponds to a σ^+ value of 0.20 for *m*-CH═N(O)-*t*-Bu (which is identical with the σ^I value). The more interesting rate behavior is seen in the *p*-CH═N(O)-*t*-Bu derivative **9**, which is actually more reactive than the unsubstituted cumyl chloride **11**.

Table 1. Solvolysis rates of substrates at 25.0 °C

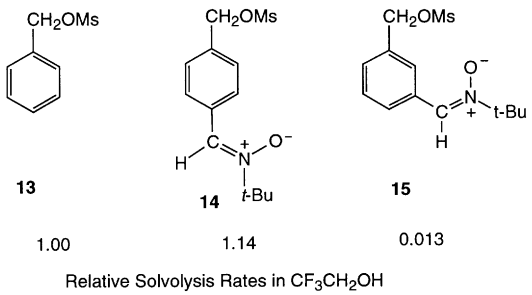
Substrate	Solvent	k (s^{-1})
9	CH_3OH	7.68×10^{-3}
10	CH_3OH	5.75×10^{-4}
11	CH_3OH	5.09×10^{-3}
13	CF_3CH_2OH	2.81×10^{-4}
14	CF_3CH_2OH	3.19×10^{-4}
15	CF_3CH_2OH	3.76×10^{-6}
17	CH_3OH	6.00×10^{-3}
18	CH_3OH	2.94×10^{-2}

The σ^+ value of −0.04 suggests that the cation-destabilizing inductive effect of the nitrone is being offset by a cation stabilizing resonance interaction as represented by **12a** and **12b**. Hence the nitrone



substituent becomes a weak cation stabilizer under conditions of increased electron demand.

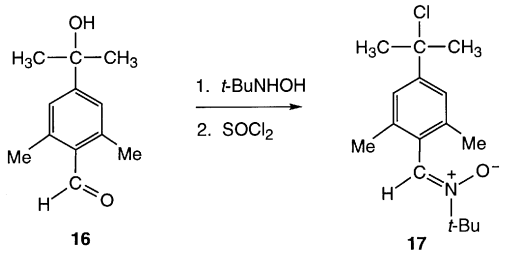
A further demonstration of the differing stabilities of *para*- and *meta*-nitrone-substituted carbocations is seen in the solvolyses of the benzylic mesylates **13**–**15** in



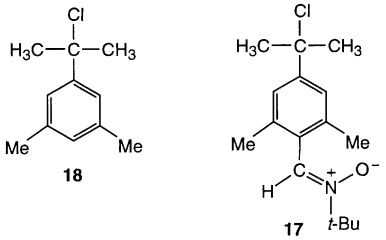
trifluoroethanol. The *meta*-derivative **15** is substantially less reactive than either the unsubstituted benzyl mesylate **13** or the *para*-derivative **14**. The transition state for solvolyses of these benzylic systems in the highly ionizing, non-nucleophilic trifluoroethanol solvent[7] is highly cationic in nature. The reduced rate of **15** reflects the inductive effect of the nitrone substituent, while the faster rate of the *para*-isomer **14** presumably reflects the offsetting cation stabilizing resonance effect of the nitrone substituent.

In order to support further the notion of a cation-stabilizing resonance effect of the inductively electron-withdrawing nitrone substituent, the 3,5-dimethyl-sub-

stituted analog **17** was prepared from aldehyde **16** in a



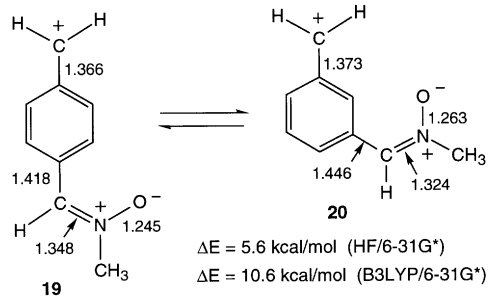
straightforward manner. This *p*-CH=N(O)-*t*-Bu derivative undergoes methanolysis at a rate which is *slower* than that of the model compound **18**. This rate retardation

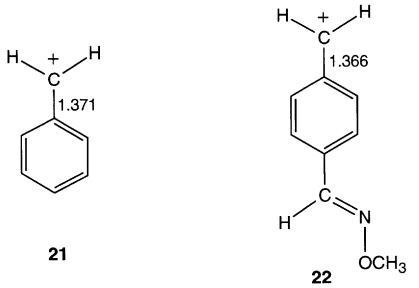


is attributed to steric inhibition of the potential cation stabilizing conjugative effect by the *ortho*-dimethyl substituents.[8] The cation derived from **17** prefers to have the nitrone twisted out of conjugation with the benzylic cation. Hence solvolysis rates of **17** manifest mainly the inductive effect of the *p*-CH=N(O)-*t*-Bu substituent.

Computational studies

Ab initio molecular orbital calculations[9] were also carried out on a variety of cationic systems in an attempt to demonstrate further that the nitrone substituent can interact in a conjugative fashion with benzylic-type cations. Studies were carried out on benzylic cations **19** and **20** at both the HF/6–31G* and B3LYP/6–31G* levels. Methyl groups were used instead of *t*-butyl in order to simplify the calculations. Both of these calculations show the *para*-isomer to be the more stable of the two cations. Calculated bond lengths (B3LYL/6–31G* level) are also informative. The shorter Ar—CH_2 bond (1.366 Å) in **19**, relative to the *meta*-isomer **20** or the parent benzyl cation **21**, suggests increased conjugation in **19**. Indeed, this bond length in **19** is identical with that in the cation **22**, which has a cation-stabilizing *p*-CH=$NOCH_3$ (oxime) functional group.[10] Comparison of bond lengths in the nitrone functional group of the *meta*-isomer **20** with those of **19** shows a shortening of the C—C bond from 1.446 to 1.418 Å, and a corresponding increase in C=N from 1.324 to 1.348 Å. The N—O bond also contracts from 1.263 to 1.245 Å. These bond length changes are all consistent with a conjugative interaction of the nitrone in **19** with the cationic center (as represented in **12b**).

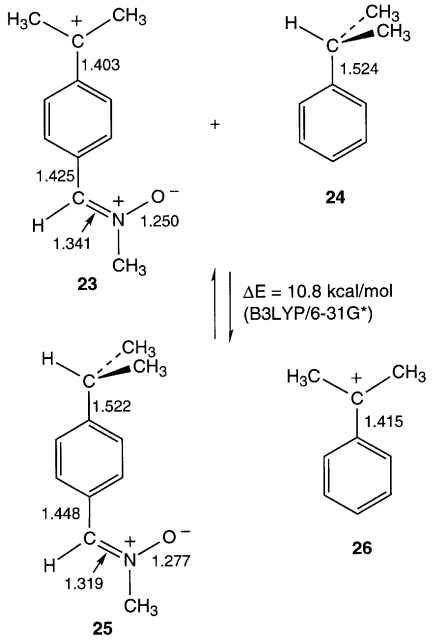




An alternative computational approach which allows an evaluation of the conjugative properties of the nitrone functional group is the isodesmic reaction of the tertiary *p*-CH=N(O)CH_3-substituted cation **23** with cumene as shown. The ΔE value of 10.8 kcal mol^{-1} (B3LYP/6–31G*) indicates extensive stabilization of **23** relative to the unsubstituted cumyl cation **26**. As before, bond length data are also consistent with conjugation effects as the origin of this stabilization. Comparison of the tertiary cation **23** with the neutral substrate **25** shows analogous bond contractions and bond lengthening seen in the primary cation **19**. As noted previously, these bond lengths in **23** are consistent with nitrone conjugation as a cation-stabilizing feature.

Although all of these computational data are consistent with conjugative nitrone stabilization of cations, they probably overestimate the importance of this stabilization in the solvolytically generated cations. The calculated 10.8 kcal mol^{-1} gas-phase stabilization of cation **23** (relative to the unsubstituted cumyl cation **26**) is not reflected in the very slight solvolytic rate enhancement (a factor of 1.51) of chloride **9**. Indeed, the B3LYP/6–31G*-calculated stabilization of cation **19** relative to the *meta*-analog **20** (10.6 kcal mol^{-1}) is greater than the calculated *p*-CH_3 stabilization of a benzylic cation (3.9 kcal mol^{-1}) but less than *p*-OCH_3 stabilization (14.9 kcal mol^{-1}). However, solvolytic studies on mesylates **14** show no great stabilization of the cationic intermediate. We therefore conclude that although the *p*-CH=N(O)-*t*-Bu substituent can indeed impart some conjugative stabilization to solvolytically generated benzylic carbocations, computational studies overestimate this stabilization. The

'gas-phase' nature of these calculations undoubtedly contributes to this overestimation.



Conclusions

The behavior of the nitrone substituent CH=N(O)-*t*-Bu is reminiscent of the oxime group $CH{=}NOCH_3$.[10] Both groups are inductively electron-withdrawing ($\sigma_I = 0.20$ and 0.14), but both become weakly stabilizing when placed in the *para*-position of cumyl cations ($\sigma^+ = -0.04$ and -0.03). Computationally, both groups stabilize *para*-substituted benzyl cations $ArCH_2^+$ relative to *meta*-substituted benzyl cations. Both *p*-$CH{=}N(O)CH_3$- and *p*-$CH{=}NOCH_3$-substituted benzyl cations are 10.6 kcal mol^{-1} more stable than the *meta*-isomers at the B3LYP/6-31G* level. We conclude that both groups can interact with *para*-substituted benzylic cations by a stabilizing conjugative interaction, but this cation stabilization in solvolytic reactions is overestimated by computational studies. In contrast to the 'super radical-stabilizing' effect of the nitrone group, actual rate effects indicate that the nitrone is a minimal benzylic cation stabilizer.

EXPERIMENTAL

Preparation of nitrone 2. A solution containing 112 mg of *m*-flurobenzaldehyde (0.502 mmol) in 1 ml of pyridine was stirred as 228 mg (1.815 mmol) of *N*-*t*-butylhydroxylamine hydrochloride were added in one portion. The mixture was stirred at room temperature for 36 h and then most of the pyridine was removed by distillation at 15 mmHg pressure. The mixture was then taken up into diethyl ether and the solution was washed with water. The ether phase was dried over a mixture of Na_2SO_4 and $MgSO_4$. Filtration and removal of solvent by rotary evaporation gave the crude nitrone **2**, which was slurried with cold hexanes to remove the last traces of pyridine. The yield of nitrone **2**, m.p. 63–64 °C, was 156 mg (89%). ^{1}H NMR ($CDCl_3$), δ 8.38 (m, 1 H), 7.76 (d, J = 7.7 Hz, 1 H), 7.56 (s, 1 H), 7.36 (d of t, J = 8.1, 6.1 Hz, 1 H), 7.09 (d of d of t, J = 1.0, 2.7, 8.4 Hz, 1 H), 1.612 (s, 9 H). ^{13}C NMR ($CDCl_3$), δ 162.6 (d, J = 245 Hz), 132.9.6 (d, J = 9 Hz), 129.6.6 (d, J = 9 Hz), 128.8, 124.7 (d, J = 3 Hz), 116.9 (d, J = 21 Hz), 115.0 (d, J = 25 Hz), 71.3, 28.3. Exact mass (EI), calculated for $C_{11}H_{14}FNO$ 195.1059, found 195.1055. Anal., calculated for $C_{11}H_{14}FNO$, C 67.67, H 7.23; found C 67.47, H 7.12%.

Preparation of nitrone 7. A solution containing 114 mg of *p*-formylcumyl alcohol[5] (0.694 mmol) in 1 ml of pyridine was stirred as 181 mg (1.441 mmol) of *N*-*t*-butylhydroxylamine hydrochloride were added in one portion. The mixture was stirred at room temperature for 22 h and then most of the pyridine was removed by distillation at 15 mmHg pressure. The nitrone **7** was very water soluble and care must be taken when using extraction procedures. Accordingly, the mixture was then taken up into 25 ml of diethyl ether and the ether solution was washed with 3 ml of water which contained a small amount of $KHSO_4$. The ether phase was dried over a mixture of Na_2SO_4 and $MgSO_4$. Filtration and removal of solvent by rotary evaporation gave the crude nitrone **7**, which contained a trace of pyridine. The last traces of pyridine were removed by evacuation of the residue at 0.1 mmHg for 7 h, which left 128 mg (78%) of nitrone **7** as a white solid, m.p. 125–127 °C. ^{1}H NMR ($CDCl_3$), δ 8.26 and 7.53 (AA 'BB' quartet, 4 H), 7.54 (s, 1 H), 1.617 (s, 9 H), 1.589 (s, 6 H). ^{13}C NMR ($CDCl_3$), δ 151.2, 129.6, 129.4, 128.8, 124.5, 72.6, 70.6, 31.6, 28.3. Exact mass (EI), calculated for $C_{14}H_{21}NO_2$ 235.1572, found 235.1557.

Preparation of nitrone 8. Using a procedure analogous to that used in preparation of **7**, reaction of 232 mg of *m*-formylcumyl alcohol[5] in 2 ml of pyridine with 355 mg of *N*-*t*-butylhydroxylamine hydrochloride gave 293 mg (88%) of crude nitrone **8**. Purification of **8** was accomplished by chromatography on silica gel. The pure nitrone **8** m.p. 88–89 °C, eluted with 90% diethyl ether–10% hexanes. ^{1}H NMR ($CDCl_3$), δ 8.45 (t, J = 1.6 Hz, 1 H), 8.16 (m, 1 H), 7.56 (m, 1 H), 7.40 (t, J = 7.8 Hz, 1 H), 7.58 (s, 1 H), 1.80 (br, 1 H), 1.620 (s, 9 H), 1.609 (s, 6 H). ^{13}C NMR ($CDCl_3$), δ 149.3, 130.9, 130.1, 128.4, 127.3, 126.4, 124.8, 72.6, 70.8, 31.8, 28.4. Exact mass (EI), calculated for $C_{14}H_{21}NO_2$ 235.1572, found 235.1548. Anal., calculated for $C_{14}H_{21}NO_2$, C 71.46, H 8.99; found, C 71.57, H 8.96%.

Reaction of 3,5-dimethyl-4-formylcumyl alcohol (16) with N-t-butyl hydroxylamine hydrochloride. Using a

procedure analogous to that used in preparation of **7**, reaction of 155 mg of 3,5-dimethyl-4-formylcumyl alcohol (**16**)[10] in 1.5 ml of pyridine with 205 mg of *N*-*t*-butylhydroxylamine hydrochloride for 23 h at 50 °C gave the crude nitrone derivative. This nitrone, m.p. 134–136 °C, was purified by slurrying with 6 ml of 30% diethyl ether in hexanes. The yield was 140 mg (66%). ^{1}H NMR ($CDCl_3$, δ 7.74 (s, 1 H), 7.17 (s, 2 H), 2.275 (s, 6 H), 1.65 (br, 1 H), 1.638 (s, 9 H), 1.550 (s, 6 H). ^{13}C NMR ($CDCl_3$), δ 149.7, 137.3, 129.6, 127.5, 123.6, 72.4, 70.4, 31.6, 28.4, 20.0. Exact mass (EI) calculated for $C_{16}H_{25}NO_2$ 263.1885, found 263.1889. Anal. calculated for $C_{16}H_{25}NO_2$, C 72.97, H 9.57; found C 72.74, H 9.47%.

Reaction of alcohols with thionyl chloride. The chlorides **9**, **10**, **11**, **17** and **18** were all prepared by reaction of the corresponding alcohols with $SOCl_2$ in CH_2Cl_2. In a typical procedure, 48.9 mg of alcohol **7** [*p*-CH=N(O)-*t*-Bu] was dissolved in 1.0 ml of CH_2Cl_2 and 32 mg of $SOCl_2$ in a small amount of CH_2Cl_2 was added at 0 °C. The mixture was then stirred at room temperature for 30 min. The solvent was removed using a rotary evaporator and the crude residue was analyzed directly by NMR spectroscopy. ^{1}H NMR of **9** (protonated form) ($CDCl_3$), δ 8.499 (s, 1 H), 8.44 (d, J = 8.7 Hz, 2 H), 7.75 (d, J = 8.7 Hz, 2H) 1.978 (s, 6 H), 1.684 (s, 9 H). ^{13}C NMR of **9** (protonated form) ($CDCl_3$), δ 154.2, 151.3, 134.7, 134.4, 126.5, 72.3, 68.4, 33.9, 27.7. All chlorides were all stored in CH_2Cl_2 solution at −20 °C and used as soon as possible for kinetic studies.

Preparation of p-hydroxymethylbenzaldehyde. A solution of 5.998 g of *p*-carboxybenzaldehyde in 25 ml of methanol containing 11.02 g of trimethyl orthoformate and six drops of H_2SO_4 was refluxed for 12h. A slight excess of 1.0 M $NaOCH_3$ in methanol was then added to neutralize the H_2SO_4. Most of the methanol was removed using a rotary evaporator. The residue was taken up into diethyl ether and washed with dilute $NaHCO_3$ solution and saturated NaCl solution, and dried over a mixture of Na_2SO_4 and $MgSO_4$. After filtration, the solvent was removed using a rotary evaporator to give 7.861 g (94%) of crude *p*-carbomethoxybenzaldehyde dimethylacetal.

A solution of 7.851 g of *p*-carbomethoxybenzaldehyde dimethylacetal in 10 ml of diethyl ether was added dropwise to a stirred suspension of 1.06 g of $LiAlH_4$ in 25 ml of diethyl ether under nitrogen. Upon completion of the addition, the mixture was refluxed for an additional 10 min and then a solution of 4.48 ml of 10% NaOH in water was added carefully dropwise. Stirring was continued for an additional 2 h and $MgSO_4$ was added to the mixture. The mixture was filtered and the salts were washed thoroughly with diethyl ether. The ether solvent was removed using a rotary evaporator, leaving, 5.792 g (85%) of crude *p*-hydroxymethylbenzaldehyde dimethylacetal.

A solution of 5.683 g of *p*-hydroxymethylbenzaldehyde dimethylacetal in 10 ml of THF was stirred as 10 ml of 2% H_2SO_4 in water were added. After 3 h the H_2SO_4 was neutralized by the addition of solid Na_2CO_3. The mixture was then taken up into diethyl ether and the aqueous phase was separated. The ether extract was washed with saturated NaCl solution and dried over a mixture of Na_2SO_4 and $MgSO_4$. After filtration, the solvent was removed using a rotary evaporator and the residue was chromatographed on 25 g of silica gel. The *p*-hydroxymethylbenzaldehyde[11] (3.229 g; 76%) was eluted with 70% diethyl ether–30% hexanes. ^{1}H NMR of *p*-hydroxymethylbenzaldehyde ($CDCl_3$), δ 10.005 (s, 1 H), 7.88 and 7.53 (AA 'BB' quartet, 4 H), 4.810 (s, 2 H), 2.02 (br, 1 H). ^{13}C NMR ($CDCl_3$), δ 192.0, 147.8, 135.7, 130.1, 127.0, 64.6.

Preparation of mesylate 14. A solution containing 187 mg of *p*-hydroxymethylbenzaldehyde (1.373 mmole) in 3 ml of pyridine was stirred as 345 mg (2.747 mmol) of *N*-*t*-butylhydroxylamine hydrochloride were added in one portion. The mixture was stirred at room temperature for 12 h and then most of the pyridine was removed by distillation at 15 mmHg pressure. The mixture was then taken up into 5 ml of CH_2Cl_2 and extracted with 1 ml of water and the CH_2Cl_2 phase was dried over $MgSO_4$. The mixture was filtered and the solvent was removed by rotary evaporation. The residual pyridine was removed by evacuation at 0.1 mmHg pressure and a small amount diethyl ether was added to the solid which formed. The mixture was cooled in ice and the ether was carefully decanted from the solid nitrone. The last traces of ether were removed at 15 mmHg, leaving 220 mg (77%) of the crude nitrone, m.p. 84–85 °C, which was converted to the mesylate **14** without further purification. ^{1}H NMR of *p*-hydroxymethylbenzaldehyde *N*-*t*-butyl nitrone ($CDCl_3$), δ 8.24 and 7.37 (AA'BB' quartet, 4 H), 7.537 (s, 1 H), 4.703 (s, 2 H), 2.45 (br, 1 H), 1.612 (s, 9 H). ^{13}C NMR ($CDCl_3$), δ 143.4, 130.1, 130.0, 129.0, 126.7, 70.8, 64.8, 28.3.

A solution of 86 mg of *p*-hydroxymethylbenzaldehyde *N*-*t*-butyl nitrone (0.415 mmol) and 53 mg of mesyl chloride (0.463 mmol) in 1.5 ml of CH_2Cl_2 was stirred at −15 °C as 52 mg (0.515 mmol) of triethylamine in 0.3 ml of CH_2Cl_2 were added dropwise. The mixture was warmed to 0 °C and 4 ml of diethyl ether were added to the stirred mixture followed by 3 ml of water. The water phase was separated and the organic extract was rapidly washed with dilute HCl solution and saturated NaCl solution. The solution was dried over $MgSO_4$ and cooled in a freezer at −20 °C. The mesylate **14** (74 mg; 63%) crystallized from the diethyl ether–CH_2Cl_2 solvent mixture. The mesylate **14**, m.p. 102 °C (decomp) was stored at −20 °C. ^{1}H NMR of **14** ($CDCl_3$), δ 8.34 and 7.47 (AA 'BB' quartet, 4 H), 7.580 (s, 1H), 5.261 (s, 2 H), 2.910 (s, 3 H), 1.624 (s, 9 H). ^{13}C NMR of **14** ($CDCl_3$), δ 134.9, 132.0, 129.1, 129.0, 128.7, 71.3, 71.0, 38.5, 28.3.

Anal., calculated for $C_{13}H_{19}NO_4S$, C 54.72, H 6.71; found, C 55.12, H 7.07%.

Preparation of mesylate 15. The preparation of mesylate **15** from *m*-hydroxymethylbenzaldehyde[12] [from $NaBH_4$ reduction of the mono(dimethylacetal) of isophthalaldehyde followed by hydrolysis] was completely analogous to the preparation of **14**. ^{1}H NMR of *m*-hydroxymethylbenzaldehyde *N*-*t*-butyl nitrone ($CDCl_3$), δ 8.48 (br, 1 H), 8.05 (m, 1 H), 7.572 (s, 1 H), 7.43 (m, 2 H), 4.737, (s, 2 H), 1.85 (br, 1 H), 1.622 (s, 9 H). ^{13}C NMR ($CDCl_3$), δ 141.5, 131.3, 130.2, 128.9, 128.8, 128.4, 127.2, 71.1, 65.3, 28.5. ^{1}H NMR of **15** ($CDCl_3$), δ 8.53 (br, 1 H), 8.18 (m, 1 H), 7.60 (s, 1 H), 7.48 (m, 2 H), 5.267 (s, 2 H), 2.964 (s, 3H), 1.631 (s, 9 H). ^{13}C NMR of **15** ($CDCl_3$) δ 134.0, 131.8, 130.5, 129.9, 129.7, 129.2, 129.0, 71.5, 71.4, 38.5, 28.5.

Solvolysis of chloride 9 in methanol. Chloride **9** was prepared as described above from 54 mg of alcohol **7** and 33 mg of $SOCl_2$. After removal of the CH_2Cl_2, the crude residue was dissolved in 4 ml of methanol containing 74 mg of 2,6-lutidine. After 1 h the methanol was removed using a rotary evaporator and the residue was taken up into diethyl ether. The ether extract was washed with a small amount of dilute HCl solution and saturated NaCl solution and then and dried over $MgSO_4$. After solvent removal using a rotary evaporator, the crude residue was chromatographed on 7.5 g of silica gel and eluted with increasing amounts of diethyl ether in hexanes. The methyl ether product, $(CH_3)_2CH_3OCC_6H_4$-*p*-CH=N(O)-*t*-Bu m.p. 112–114 °C, (38 mg; 66%) was eluted with 50% diethyl ether in hexanes. ^{1}H NMR ($CDCl_3$), δ 8.27 (d, J = 8.4 Hz, 2 H), 7.55 (s, 1 H), 7.46 (d, J = 8.4 Hz, 2 H), 3.067 (s, 3 H), 1.618 (s, 9 H), 1.533 (s, 6 H). ^{13}C NMR ($CDCl_3$), δ 148.2, 129.6, 129.5, 128.7, 125.9, 76.7, 70.7, 50.7, 28.3, 27.8. Exact mass (EI), calculated for $C_{15}H_{23}NO_2$ 249.1729, found 249.1722. Anal., calculated for $C_{15}H_{23}NO_2$, C 72.25, H 9.30; found C 72.38, H 9.35%.

Kinetic studies. Rates of solvolyses of chlorides **9**, **10**, **11**, **17** and **18** in methanol (2.5×10^{-4} M in 2,6-lutidine) were monitored by UV spectrophotometry at 245 nm using the previously described method.[13] A solution of about 10 mg of the appropriate chloride in 1 ml of anhydrous diethyl ether was prepared and a 5 µl aliquot of this solution was injected into a cuvette containing 3 ml of 2.5×10^{-4} M 2,6-lutidine in methanol at 25.0 °C. This initiated the kinetic run. Absorbance changes were monitored for two half-lives and infinity readings were taken after 10 half-lives. Solvolyses of mesylates **13**, **14** and **15** in trifluoroethanol were monitored by ^{1}H NMR spectroscopy using our previously described kinetic method.[14] The mesylates were dissolved in a 0.05 M solution of 2,6-lutidine in trifluoroethanol and the solutions were sealed in NMR tubes, which were then placed in a constant-temperature bath. At periodic time intervals the shift of the methyl signal of the 2,6-lutidine was determined by 300 MHz NMR spectroscopy. First-order rate constants were determined by standard least-squares methods. All kinetic runs were performed in duplicate (maximum error ±2%) and the rate constants given in Table 1 represent average values.

Computational studies. Ab initio molecular orbital calculations were performed using the Gaussian 94 and Gaussian 98 series of programs.[9] Structures were characterized as minima via frequency calculations which showed no negative frequencies.

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