PERKIN 2
COMMUNICATION

^{17}O NMR of benzamide derivatives: ground state torsion angle does not affect transmission of substituent effect by through-conjugation

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Through-conjugation is possible in the localized excited state and transmission of the resonance effect, as measured by σ^+, is not affected by ground state torsion angle.

Transmission of substituent effects in benzamide derivatives has been studied by ^{17}O NMR spectroscopy.[1] In these studies it was observed that the ^{17}O chemical shifts of the carbonyl oxygen correlated with σ^+. The σ^+ scale of substituent effects was defined by Brown from the rates of solvolysis of cumyl chloride derivatives.[2] This scale is used in those cases in which through-conjugation exists between the substituent and a cationic or incipient cationic center. Maximum through-conjugation occurs when the torsion angle between the p orbital on C-1 of the aromatic ring and the p orbital on the cationic center is zero (coplanar). Spychala and Boykin reported that the ^{17}O NMR chemical shifts of the carbonyl oxygen of 4-X-*N*,*N*-dimethylbenzamides correlated ($\rho = 2.2$, $R = 0.983$) with σ^+.[1c] Correlation with σ^+ was observed in spite of the fact that the torsion angle was estimated by them to be 51 ± 1° or 74 ± 2° by MM2 and AM1, respectively.[1c] An intriguing question, and the subject of this communication is, how is the resonance effect transmitted in 4-X-*N*,*N*-dimethylbenzamides derivatives when an appreciable torsion angle exists between the amide side chain and the aromatic ring bearing the substituent. The answer to this question will provide further insights into the nature of NMR substituent effects.

Results and discussion

The Yukawa–Tsuno equation can be used when through-conjugation is impeded by the existence of an appreciable torsion angle (steric inhibition of resonance).[3] This equation has the form given in eqn. (1) for NMR studies. Parameter *r* is

$$\delta_X = \rho(\sigma^\circ + r\Delta\sigma_R^+) \qquad (1)$$

characteristic of a given system and is a measure of the resonance interaction between the aromatic ring and the side chain, σ° is the substituent constant in the absence of through-conjugation and $\Delta\sigma_R^+ = \sigma^+ - \sigma^\circ$. When $r = 1$, eqn. (1) reduces to eqn. (2) and the torsion angle is assumed to be zero. Variation

$$\delta_X = \rho^+\sigma^+ \qquad (2)$$

of *r* with respect to the torsion angle θ has the dependency given in eqn. (3).[3b,4] In this equation, $r_{max} = 1$ when the system

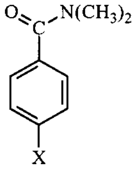
$$r = r_{max}\cos^2\theta \qquad (3)$$

is coplanar. The torsion angle in 4-substituted-benzamides, *N*-methylbenzamides and *N*-chlorobenzamides is approximately the same (28°).[5] When the torsion angle is 28° $r = 0.78$ and for values of *r* between 1 and 0.8 there is little difference noted in using eqn. (1) or eqn. (2) for carrying out correlations.[6] It might be expected then, that when the torsion angle is greater than 28°, the Yukawa–Tsuno equation would be required to get an acceptable correlation with σ^+. For this reason the Yukawa–Tsuno equation has only been applied to 4-X-*N*,*N*-dimethylbenzamides (**1**) ^{17}O chemical shifts (Table 1) where, given the torsion angle, the difference in the use of eqns. (1) and (2) is expected to be notable.

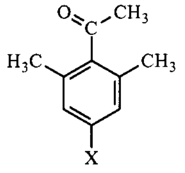
Table 1 ^{17}O NMR chemical shifts for 4-X-*N*,*N*-dimethylbenzamides (**1**)[a] and 2,6-dimethyl-4-X-acetophenones (**2**)[b]

X	**1**	**2**
H	347.9	592.5
Br	348.4	597.1
Cl	347.8	—
F	347.8	596.4
CH_3	347.1	593.7
OCH_3	346.5	592.4
NO_2	349.8	603.2
CF_3	348.7	—
CN	348.9	—
SCH_3	346.1	—
$N(CH_3)_2$	343.8	585.2
NH_2	—	588.8
$COCH_3$	—	597.4

[a] Data taken from ref. 1*c*. [b] Data taken from ref. 7.



1
X = H, Br, Cl, F, CH_3, OCH_3,
NO_2, CF_3, CN, SMe, NMe_2



2
X = H, Br, F, CH_3, OCH_3, NO_2,
NMe_2, NH_2, COMe

From eqn. (3) $r = 0.40$ when the torsion angle is 51° and 0.076 when it is 74°. These values were used in eqn. (1) to reanalyze substituent effects in 4-X-*N*,*N*-dimethylbenzamides (**1**) and the results in eqns. (4) and (5) were obtained for torsion angles of

$$\delta_X = 2.96(\sigma^\circ + 0.40\Delta\sigma_R^+) + 347.2 \quad R = 0.964 \qquad (4)$$

$$\delta_X = 0.23(\sigma^\circ + 0.076\Delta\sigma_R^+) + 78.0 \quad R = 0.921 \qquad (5)$$

51° and 74° respectively. Clearly, application of the Yukawa–Tsuno equation to 4-X-*N*,*N*-dimethylbenzamides (**1**) ^{17}O chemical shifts did not result in an improved correlation.

The torsion angle (52.5 ± 0.4°) in 2,6-dimethyl-4-X-acetophenones (**2**) is, as calculated by MM2, essentially the same as that calculated by the same method for *N*,*N*-dimethylbenzamides **1**.[7] These derivatives can serve as models for the expected effect of the torsion angle on the ^{17}O chemical shifts of *N*,*N*-dimethylbenzamides **1**. Dell'Erba, Spinelli and co-workers reported that the ^{17}O chemical shifts of 4-X-acetophenones correlated with σ^+ but in contrast 2,6-dimethyl-4-X-acetophenones (**2**) gave a better correlation ($\rho = 10.8$, $R = 0.961$) with σ_p.[7] The authors proposed, based on the NMR correlation and basicity constant measurements, that steric effects influenced through-conjugation in these derivatives.

The 2,6-dimethyl-4-X-acetophenones (**2**) ^{17}O chemical shift data (Table 1) were reanalyzed using the Yukawa–Tsuno equation with $r = 0.38$ for a torsion angle of 52°. In order to include the electron-withdrawing substituents NO_2 and $COCH_3$ the 'double' form of the Yukawa–Tsuno equation was used.[8] This method uses σ^- for the electron-withdrawing substituents and σ^+ for the electron-donating substituents.† Application of the Yukawa–Tsuno equation to 2,6-dimethyl-4-X-acetophenones (**2**) ^{17}O chemical shifts gave an improved correlation compared to using σ_p [eqn. (6)].

$$\delta_X = 8.57(\sigma^\circ + 0.38\Delta\bar{\sigma}_R^{\pm}) + 594.1 \quad R = 0.971 \qquad (6)$$

If the effect of the torsion angle on through-conjugation was the same in both systems comparable results would have been expected. The chemical shifts of 4-X-*N*,*N*-dimethylbenzamides (**1**) should correlate better with σ_p and the Yukawa–Tsuno equation should have given a better correlation than σ_p. Results of this study imply that there is a difference in how the torsion angle affects through-conjugation (as observed by ^{17}O NMR) in *N*,*N*-dimethylbenzamides **1** as compared to 2,6-dimethylacetophenones **2**.

Previous NMR studies have found that in benzamide derivatives ^{15}N and ^{17}O chemical shifts gave linear Hammett plots but the ^{13}C carbonyl correlation was not linear.[9] In a recent paper I proposed[1e] that this is because in the localized excited state[10] the mechanism of interaction of the substituent with the carbonyl carbon was different compared to the interaction with the carbonyl oxygen and amide nitrogen. Dahn and Carrupt have reported, that based on IGLO *ab initio* calculations, the differences in ^{13}C and ^{17}O behavior are determined mainly by how the energy of the n–π* transition is affected by substituents in the two systems.[11]

Several mechanisms through which the interaction between the substituent and the probe atom could change in the localized excited state were suggested.[1e] One possibility is that orbitals that are coplanar in the ground state could become orthogonal or twisted out of the plane in the localized excited state. The result would be equivalent to steric inhibition of resonance and a non-linear Hammett plot would be observed.

It was also suggested that the opposite effect could be observable — orbitals twisted out of the plane in the ground state could become coplanar in the localized excited state. As a result normal substituent effects would be observable by NMR (linear Hammett plot) in spite of the presence of a substantial torsion angle in the ground state.[1e,12] This is equivalent to the way in which substituents affect the solvolysis of benzyl halides. Through-conjugation is not possible in the reactant and only plays a role in the transition state leading to the carbocationic intermediate.

It is proposed that in the localized excited state of benzamides through-conjugation is possible between the substituent and the carbonyl oxygen. The net result is that transmission of the resonance effect, as measured by σ^+, is not affected by the ground state torsion angle.

The results of this study are further evidence that the effect of substituents on the localized excited state must be taken into account when studying NMR substituent effects.[1e]

Acknowledgements

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Notes and references

† Using the data in ref. 7, a $\rho = 6.37$ ($R = 0.950$) was obtained using σ^+ and $\rho = 5.26$ ($R = 0.952$) when σ^- constants for NO_2 and $COCH_3$ were used.

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