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THE EQUILIBRIUM BETWEEN SYN AND ANTI 2-SUBSTITUTED 1,4-BENZOQUINONE-4-OXIME ACETATES

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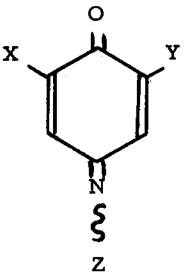
In connection with our investigations[1,2] of the syn-anti equilibria in 2-substituted 1,4-benzoquinone-4-oximes we have prepared the quinone monoxime acetates listed in table 1, as well as those corresponding to the parent compound and the 2,6-dimethyl and 2,6-di-tert.butyl derivatives. The identities of the syn and anti isomers were assigned by NMR in a manner analogous to that employed with the corresponding quinone monoximes[1,3]. With the exception of the syn 2-methoxy[4], the syn and anti 2-methyl[5] and the syn and anti 2-chloro[6] derivatives, the compounds listed in table 1 have not been previously reported and satisfactory analytical and spectroscopic data were obtained for them. Crystallographic data[6] reported for the syn and anti 2-chloro derivatives confirm our NMR assignments.

It was found (by NMR) that both stereoisomers retained their identity when heated for up to 15 minutes in acetic anhydride or tetrachloroethylene at 100°, but that rapid equilibration took place at room temperature in acetic anhydride containing approximately 3% concentrated sulphuric acid. Equilibration also took place in dimethyl sulphoxide at 100°, but was accompanied by the hydrolysis of the acetates unless rigorous exclusion of moisture was maintained.

TABLE 1

SYN-ANTI ISOMER DISTRIBUTION AT EQUILIBRIUM



X	Y	% Syn to X[a] [ΔG^{o} K cal/mole]		
		Z = $OCOCH_3$[b]	Z = OH[c]	X = O^-[d]
OCH_3	H	80 ± 2(80°)[0.97]	86 (40°) [1.13]	90 ± 2 [1.32]
F	H	75 ± 2 [0.66]	76[e] (30°) [0.70]	78 ± 2 [0.76]
CH_3	H	61 ± 1 [0.27]	62 [0.30]	60 ± 2 [0.24]
Cl	H	60 ± 2 [0.24]	60 (40°) [0.25]	57 ± 4 [0.17]
$CONMe_2$	H	38 ± 2 [-0.30]	f	43 ± 2(10°)[-0.16]
CN	H	36 ± 2 [-0.35]	f	f
CF_3	H	34 ± 2 [-0.40]	28[g] (40°) [-0.59]	34 ± 2 [-0.40]
CN	OCH_3	9 ± 1 [-1.40]	<30 [<-0.51]	≤10 [≤-1.32]

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a) At 29° unless otherwise stated

b) In acetic anhydride containing 3% sulphuric acid

c) In dioxan and accurate to ± 2% unless otherwise stated

d) In D_2O/K_2CO_3

e) In ether

f) Data not available due to fast exchange

g) May be in error due to appreciable content of the nitroso form (14%)

The relative proportions of *syn* and *anti* isomers in the acetic anhydride-sulphuric acid mixtures are listed in table 1 and compared with the values[2] for the corresponding quinone monoximes in dioxan and in D_2O/K_2CO_3 (i.e. the anion). It can be seen that, not only is the order of substituent effects the same for the three columns, but that the *syn*/*anti* ratios at equilibrium are (within the experimental limits) virtually identical for the oximes, the anions and the oxime acetates.

For this and other[2] reasons we conclude that the substituent effects in all three series are electronic in nature. It is important to note that (a) the property affected by electronic substituent effects (*syn*/*anti* ratio) is of a rather different type than those usually studied in connection with linear free energy relationships[7]; (b) conversely, and not unexpectedly, there is no obvious correspondence between the order of substituent effects shown in table 1 and Hammet type constants; (c) the *syn*-*anti* ratio is a ground-state property, easily estimated by NMR; (d) the effect of common substiuents appears to correspond to the range of equilibrium constants which can be estimated by a single experimental method (NMR); (e) it should be possible to obtain the enthalpy and entropy data through variable temperature NMR studies of the equilibrium, although results from these laboratories[2] and some data reported by Uffman[3] indicate that experimental difficulties (particularly those associated with fast exchange conditions for oximes and their anions) may be encountered.

Clearly there is general interest in the study of this novel type of substituent effect. Obvious extensions include the study of analogous equilibria in other *p*-benzoquinone derivatives with the $C_4 = N - Z$ function, in particular the oxime ethers ($Z = OR$) which we are presently investigating.

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REFERENCES

1 R.K. Norris and S. Sternhell, Aust. J. Chem., 19, 841 (1966).

2 R.K. Norris and S. Sternhell, Tetrahedron letters, 97 (1967) and unpublished data from these laboratories.

3 H. Uffmann, Z. Naturforsch., 22b, 491 (1967).

4 A. Pfob, Monatsh., 18, 467 (1897).

5 J. L. Bridge and W. C. Morgan, Am. Chem. J., 20, 766 (1898).

6 F. Kehrmann, Ann., 303, 5 (1898); E. Fischmann, C. H. MacGillavry and C. Romers, Acta Crystallogr., 14, 753 and 759 (1961).

7 K. B. Wiberg, "Physical Organic Chemistry", John Wiley, New York (1964), Ch. 2 - 8 and 3 - 7.