Reverse Orientation in the 1,3-Dipolar Cycloaddition of Some Pyridinium Betaines to Unsymmetrical Alkenes
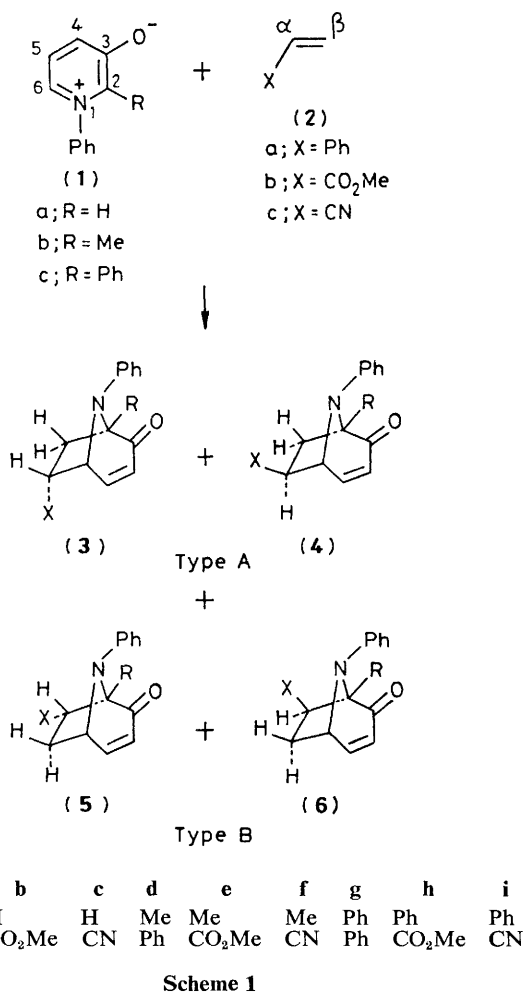
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Analysis of the products formed by the addition of N-phenylpyridinium betaines to some unsymmetrical alkenes revealed that the 2-methyl- or 2-phenyl-N-phenylpyridinium betaine tends to form the reverse orientation products, whereas the unsubstituted N-phenylpyridinium betaine gives the expected orientation.

Although the question of orientation in 1,3-dipolar cyclo-addition had been unsolved for a long time,[1] it has recently been rationalised in terms of a frontier molecular orbital (F.M.O.) interaction between the reactants.[2] According to the frontier orbital treatment, the orientation should be decided by the sizes of the coefficients at the reaction centre

Scheme 1

Table 1. Product distributions in the reactions of pyridinium betaines with alkenes.

Com- pound	R	X	Type A %[endo-(3): exo-(4)]	Type B %[endo- (5):exo-(6)]
a	H[3b]	Ph	100 (100: 0)	0 (——)
b	H[3b]	CO₂Me	100 (63:37)	0 (——)
c	H[3b]	CN	100 (44:56)	0 (——)
d	Me	Ph	100 (100: 0)	0 (——)
e	Me	CO₂Me	79 (64:36)	21 (100: 0)
f	Me	CN	6 (100: 0)	94 (40:60)
g	Ph	Ph	0 (——)	100 (100: 0)
h	Ph	CO₂Me	0 (——)	100 (61:39)
i	Ph	CN	0 (——)	100 (68:32)

atoms of the reactant F.M.O.s. When one reaction centre of the 1,3-dipole is substituted by a particular group, there may be a change in the size of the coefficient of its F.M.O. resulting in the reverse orientation for the addition.

We show one example in which a substituent at a reaction centre causes the orientation of cycloaddition to be reversed. Katritzky and his co-workers[3] have investigated the 1,3-dipolar cycloadditions of pyridinium betaines and found that the non-substituted N-phenylpyridinium betaine (1a) (with carbon atoms at both reaction centres) undergoes a 1,3-dipolar cycloaddition with mono-substituted ethylenes to give products of type A only (Scheme 1). When we treated the 2-methyl-N-phenylpyridinium betaine (1b) with methyl acrylate at 75 °C for 48 h, a mixture of the type A *endo*-adduct (3e), the type A *exo*-adduct (4e), and the type B *endo*-adduct (5e), separated by column chromatography, was formed in a ratio of 51:28:21. In contrast, (1b) and styrene reacted to form only the expected adduct (3d).† The

reaction of (1b) with acrylonitrile gave three isomeric adducts: (3f), (5f), and (6f) in a ratio of 6:38:56, type B predominating over type A adducts. Furthermore, the reactions of the 2-phenyl derivative (1c) of the pyridinium betaine with several mono-substituted ethylenes gave no adducts of type A, but afforded only type B adducts.

These results, shown in Table 1, indicate that 2-substituted pyridinium betaines show a tendency to form the reverse orientation regioisomer, and that a 2-phenyl group has a greater effect than a 2-methyl group. The observation that the regioselectivity of addition varies with the substituent at the 2-position of the pyridinium betaine cannot be explained by consideration of effects such as steric, dipole-dipole, or π-π interactions. An explanation may be found using the F.M.O. method. According to Katritzky's calculation[4] for non-substituted pyridinium betaine, the atomic coefficient c_2 at C-2 is larger than c_6 at C-6 in both the H.O.M.O. and the L.U.M.O. The 2-substituent should change the shape of the H.O.M.O. and the L.U.M.O. of the betaine. Interaction between the betaine and the 2-substituent results in partial mixing of the H.O.M.O. and the L.U.M.O. of the betaine to give a new H.O.M.O. with a decreased c_2 and an increased c_6. In some cases, the relationship between the sizes of the coefficients c_2 and c_6 may be reversed, because the same sign of the coefficient with respect to the C-2 and C-6 carbon atoms of the L.U.M.O. makes the c_2 of the H.O.M.O. (with different signs at C-2 and C-6) smaller, and the c_6 coefficient larger. Similarly, the L.U.M.O. of the betaine also partially mixes with the H.O.M.O. to give a new L.U.M.O. where c_2 has decreased and c_6 increased. In acrylonitrile, methyl acrylate, and styrene, the c_β coefficient of the H.O.M.O. and the L.U.M.O. is larger than c_α coefficient. Thus a substituent at the 2-position of the betaine allows both H.O.M.O.-(betaine)–L.U.M.O.(olefin) and H.O.M.O.(olefin)–L.U.M.O.-(betaine) interactions leading to an increase in the tendency to form type B orientation products.

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† N.m.r. data: (3e): δ 1.55 (s, 3H), 2.34 (dd, 1H, J 7.8, 13.9 Hz), 2.42 (dd, 1H, J 9.3, 13.9 Hz), 3.70 (s, 3H), 3.73 (ddd, 1H, J 6.0, 7.8, 9.3 Hz), 4.83 (dd, 1H, J 4.8, 6.0 Hz), 6.05 (d, 1H, J 9.8 Hz), and 6.7—7.3 (m, 6H); (4e): δ 1.55 (s, 3H), 2.23 (dd, 1H, J 9.3, 14.1 Hz), 2.68 (dd, 1H, J 3.3, 14.1 Hz), 2.88 (dd, 1H, J 3.3, 9.3 Hz), 3.82 (s, 3H), 4.93 (d, 1H, J 4.8 Hz), 6.00 (d, 1H, J 9.8 Hz), and 6.7—7.3 (m, 6H); (5e): δ 1.68 (s, 3H), 2.22 (dd, 1H, J 4.8, 12.0 Hz), 2.62 (ddd, 1H, J 6.4, 10.0, 12.0 Hz), 3.37 (dd, 1H, J 4.8, 10.0 Hz), 3.65 (s, 3H), 4.53 (dd, 1H, J 5.2, 6.4 Hz), 6.03 (d, 1H, J 10.0 Hz), and 6.7–7.4 (m, 6H).

References

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