Tetrahedron Letters No. 27, pp 2469 - 2470, 1973. Pergamon Press. Printed in Great Britain.

A STEREOCHEMICAL STUDY ON THE ADDITION OF AN ALKOXIDE ANION TO AN α,β-UNSATURATED SULFOXIDE

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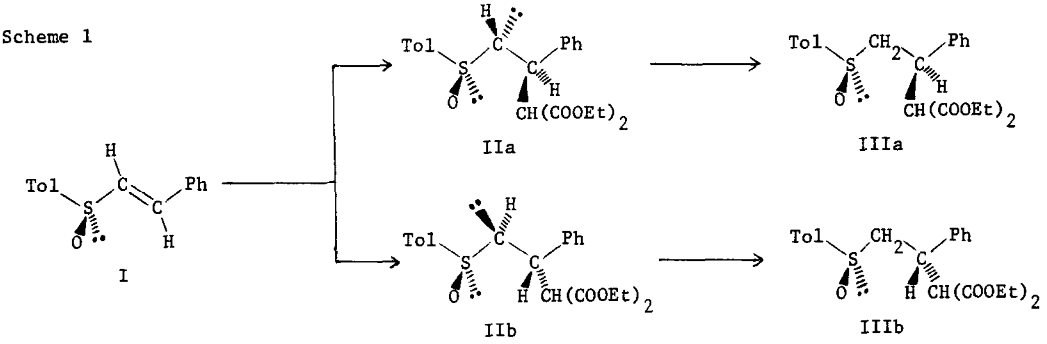
(Received in Japan 10 May 1973; received in UK for publication 25 May 1973)

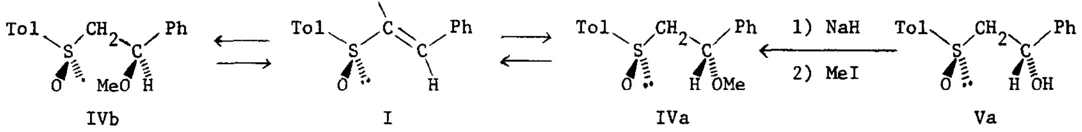
Recently, we reported a highly selective Michael addition of diethyl malonate to trans-β-styryl p-tolyl sulfoxide (I)$^{1)}$ This selectivity$^{2)}$ may be accounted for by the proposal that the carbanion IIa is preferentially formed with respect to IIb, as a result of electronic demand of the adjacent chiral sulfinyl group.$^{3)}$ This kind of selectivity would also be expected for related anionic additions$^{4)}$, for this reason the present study was undertaken$^{5,\ 6)}$

Scheme 1



A solution containing methanol (5.5 ml), I (1.5 mmol), and sodium methoxide (1.0 mmol) was refluxed for 6 days. A usual workup gave an oily residue which, when subjected to column chromatography (silica gel, dichloromethane), afforded two diastereomers of 2-methoxy-2-phenylethyl p-tolyl sulfoxide, IVa (184 mg) and IVb (117 mg), while 84 mg of I was recovered. Based on unrecovered I, the total yield of IVa and IVb was 93%, the respective ratio being 61:39.

Scheme 2



IVa$^{7)}$ mp 95-7°, ν^{KBr}. 1040 cm^{-1}, δ^{CDCl_3} 2.34(s, 3H), 2.7-3.2(m, 2H), 3.32(s, 3H), 4.75(d of d, 1H, J=4.0, 9.0 Hz), 7.1-7.6(m, 9H). IVb an oil, ν^{neat} 1050 cm^{-1}, δ^{CDCl_3}: 2.49(s, 3H), 2.86(d of d, 1H, J=6.0, 13.0 Hz), 3.08(s, 3H), 3.43(d of d, 1H, J=8.0, 13.0 Hz), 4.27(d of d, 1H, J=6.0, 8.0 Hz), 7.2-7.6(m, 9H)

The configurations of IVa and IVb were determined unequivocally by the following chemical transformations: From a mixture of both diastereomers of 2-hydroxy-2-phenylethyl p-tolyl sulfoxide (V),[8] isomer Va was easily separated and also purified by recrystallization from methanol-water: mp 138-140°, δ^{CDCl_3} 2.41(s, 3H), 2.84(d of d, 1H, J=3.0, 13.5 Hz), 3 23(d of d, 1H, J=9.7, 13.5 Hz), 4.05(broad s, 1H), 5.30(d of d, 1H, J=3.0, 9.7 Hz), 7.2-7.6(m, 9H), the ir and nmr spectra of the isomer Va were in every respect identical with those of (+)-(R)s-(S)c-V.[8] Methylation of Va (methyl iodide, 1 equiv. of sodium hydride) afforded IVa quantitatively, a fact firmly establishing the configuration of racemic IVa as (R)s-(S)c and (S)s-(R)c.

It should be noted that the major isomers from the addition reactions, *i.e.*, IIIa and IVa, have opposite configurations at their respective β-sulfinyl-carbon atoms (see Schemes 1 and 2). This unexpected result was experimentally associated with the reversible (thermodynamically controlled) addition of the alkoxide in contrast to the irreversible (kinetically controlled) addition of diethyl malonate.[10] That is, a methanolic solution containing equimolar amounts of I and sodium methoxide refluxed for 37 hr provided I, IVa, and IVb in a ratio of 26 : 46 : 28, determined by nmr analysis. Under the same conditions, IVa provided almost identical results. It is concluded that this ratio reflects the relative thermodynamic stabilities of I, IVa, and IVb in this equilibration reaction and shows that isomer IVa is thermodynamically more stable than IVb.

We have established that two types of results may be observed in anionic additions to α,β-unsaturated sulfoxides, arising from either kinetic or thermodynamic control The electronic effect of the chiral sulfinyl group determines the most stable transition state of a newly formed carbanion which in turn determines the ratio of initially formed isomers. When the reaction is reversible and equilibration is attained, the ratio of the isomeric products becomes thermodynamically controlled and is thereby dependent on the relative isomer stabilities.

The asymmetric induction by the chiral sulfinyl group is expected to be highly effective in other kinetically controlled additions of anions to α,β-unsaturated sulfoxides. Synthesis of chiral molecules by this means is now being investigated

REMARKS AND REFERENCES

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2) The ratio of IIIa and IIIb was 8 : 2, see reference 1.
3) The maximum stability of β-sulfinyl carbanion is attained when the carbanion-electron lobe is trans to the sulfinyl oxygen, R. R Fraser, F J Schuber and Y. Y Wigfield, J. Amer. Chem. Soc., 94, 8795 (1972)
4) The stereochemical course of the addition of an amine to an α,β-unsaturated sulfoxide was reported by D. J. Abbott, S. Colonna and C. J. M Stirling, Chem. Comm., 471 (1971).
5) The anionic addition of an alcohol to an α,β-unsaturated sulfoxide was studied by Shostakovskii and his coworkers, but the steric course of the reaction was not revealed, M. F. Shostakovskii, E N. Prilezhaeva, L. V Tsymbal, R. Ya Tolchinskaya and N. G Starova, J. Gen Chem USSR, 31, 2326 (1961) and references cited therein.
6) The photochemical non-stereoselective addition of an alcohol to methyl β-styryl sulfoxide was reported by N Miyamoto, K Utimoto and H. Nozaki, Tetrahedron Lett , 2895 (1972).
7) Satisfactory elemental analyses were obtained for IVa and IVb.
8) Compound V was obtained by the reaction of p-tolylsulfinyl carbanion with benzaldehyde, see reference 9
9) G. Tsuchihashi, S. Iriuchijima and M. Ishibashi, Tetrahedron Lett , 4605 (1972)
10) We previously demonstrated that the reaction of I with diethyl malonate is kinetically controlled, see reference 1