Directed Methylations of Unsymmetrical Stilbenes using Methylsulphinyl Anion

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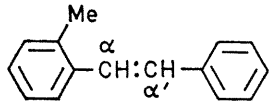
Summary Methylation of 2-methylstilbene with methylsulphinyl anion ($MeSOCH_2^-$) can be controlled to produce either the corresponding α- or α′-methylated stilbene: similar methylation of the more hindered 2,6-dimethylstilbene (**3a**) produced almost entirely the *Z*-form (**4**) of the α-methyl analogue, but the 2,2′,6,6′-tetramethylstilbene (**3d**) failed to react with $MeSOCH_2^-$.

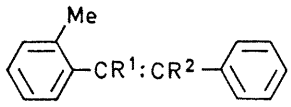
NUCLEOPHILIC addition of sulphur, sulphoxonium, and sulphinyl ylides to unsaturated linkages is well known, and has considerable use in synthesis.[1] The ylides $Me_2\overset{+}{S}-\overset{-}{C}H_2$, $Me_2\overset{+}{S}(O)\overset{-}{C}H_2$, and the methylsulphinyl anion, $MeSO\overset{-}{C}H_2$ derived from dimethyl sulphoxide, function as useful methylene transfer reagents in reaction with certain olefinic bonds, and they also add to some condensed aryl systems producing methylated compounds.[1a] These reactions bear certain similarities to the closely allied processes of biological methylation and cyclopropane ring formation from L-methionine.[2] The scope of this novel *C*-methylation procedure has not been fully investigated, and details of the processes involved are not known. We now describe some methylations of unsymmetrically substituted stilbenes by $MeSOCH_2^-$ which illustrate some synthetic uses of this reaction.

Methylation of either *Z*- or *E*-2-methylstilbene (**1**) with a 4 molar excess of $MeSOCH_2^-$ at 70° for 2 h, proceeded in a highly specific manner, and produced (*ca.* 70%) the α-methylstilbene (**2a**) (as a 2:1 *Z*–*E* mixture) containing negligible amounts (<3%) of the corresponding α′-methyl isomer (**2b**). Shorter periods of reaction or a diminished

excess of $MeSOCH_2^-$ proceeded with less selectivity, and led to varying proportions of α- and α′-methylated compounds. When the reaction between *E*-(**1**) and $MeSOCH_2^-$ was worked-up after only 2 min at 70°, >91% methylation had taken place at the α′-centre, and *E*-α′-methylstilbene



(1)



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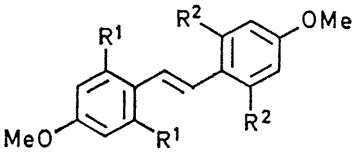

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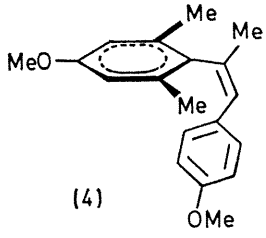

(4)

a; R^1 = Me, R^2 = H; **b**; R^1 = H, R^2 = Me; **c**; R^1 = R^2 = H; **d**; R^1 = R^2 = Me.

(**2b**), λ_{max} 263 nm, ε 13,300; τ 2·3—2·8 (9 ArH), 3·12 (C*H*), 7·72 (ArC*Me*), 7·88 (C*Me*), could be separated in 57% chemical yield. We did not detect the presence of the isomeric cyclopropane or the corresponding benzylstyrenes in these reaction products, but g.c.–m.s. data did indicate small amounts of bis-methylated material in some fractions.

Methylation of *Z*- and *E*-stilbene and 4,4′-dimethoxy-*E*-stilbene (**3c**) with $MeSOCH_2^-$ produced (*ca.* 80%) 1:9 *Z*–*E* mixtures of the corresponding α-methylstilbenes (*cf.* ref. 3). Treatment of the hindered stilbene (**3a**) with $MeSOCH_2^-$ at 70° for 3·5 h, gave almost entirely (>96%) the α-methylated analogue, from which the *Z*-form (**4**), b.p. 180°/0·1 mm, τ 3·26 (2H), 3·38 (2H), 3·46 (2H), 3·61 (1H), 6·26, 6·38 (2 O*Me*), 7·9 (2ArC*Me*), 8·0 (C*Me*), was separated in 61% chemical yield. Not more than a *ca.* 1% yield of the α′-methylated analogue of (**3a**) could be obtained from this reaction, and no α-methylation at all was detected from similar methylation studies with the more overcrowded stilbene (**3d**).

The overall methylation process is probably best rationalised in terms of a nucleophilic addition (of $MeSOCH_2^-$)–prototropic shift–β-elimination (of $MeSO^-$)–isomerisation sequence. We have established that cyclopropane intermediates are not involved by showing that such compounds are stable under these reaction conditions and we are currently investigating further details of the reaction mechanism.

Identification of methylated products was accomplished by comparison of retention times in g.l.c., and by spectral comparison of prep. g.l.c. separated materials with authentic samples prepared by independent routes. Satisfactory analytical and spectral data were obtained for all new compounds.

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[1] For recent reviews see (a) T. Durst, *Adv. Org. Chem.*, 1969, **6**, 285; (b) J. C. Bloch, *Ann. Chim.* (*France*), 1965, 419; (c) P. A. Lowr, *Chem. and Ind.*, 1970, 1070.

[2] See D. H. G. Crout, *Topics Carbocyclic Chem.*, 1969, **1**, 169; J. H. Law, *Accounts Chem. Res.*, 1971, **4**, 199.

[3] M. Feldman, S. Danishefsky, and R. Levine, *J. Org. Chem.*, 1966, **31**, 4322.