Acid-catalysed Conversion of Sulphinamides into Sulphinates: A New Synthesis of Optically Active Sulphinates

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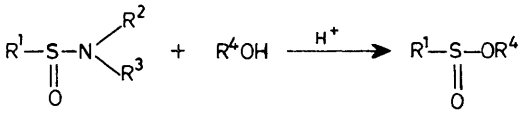
Summary Treatment of sulphinamides with alcohols in the presence of strong acids results in the formation of sulphinates in good yields; this reaction has been shown to proceed with inversion of configuration at the sulphinyl centre and high stereospecificity which is dependent on the structure of the alcohol used.

OUR continuing interest[1] in the synthesis and stereochemistry of sulphinates led us to investigate the alcoholysis of sulphinamides in the hope of devising a new and general synthetic approach to optically active sulphinates with sulphur as the sole chirality centre. To our knowledge this reaction has not been reported in the literature and it seemed promising in view of the easy accessibility of optically active sulphinamides[2] and also that the analogous reaction with optically active phosphorus amides has been found recently to proceed stereospecifically with predominant inversion of configuration at phosphorus.[3] It is also interesting to note that the opposite reaction, *i.e.*, ester–amide interchange, takes place with high stereospecificity and with inversion of the configuration at sulphur.[2a,b]

In the first part of this study we have demonstrated that the reaction of the sulphinamides (**1**) with an excess of alcohol carried out at 0 °C or at room temperature in the presence of strong acids used in 2 mol. equiv. with respect to (**1**) affords the sulphinates (**2**) in excellent yields.

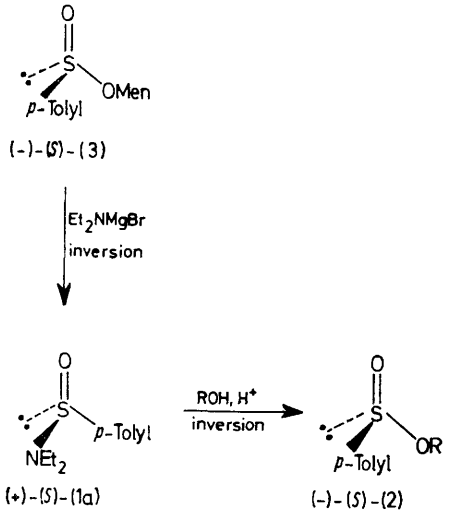
Since the nucleophilic substitution at sulphur may be considered to proceed by a direct back-side attack involving



(1) (2)

(1a), R^1 = *p*-Tolyl, R^2=R^3=Et — (2a), R^1=*p*-Tolyl, R^4=Me (88%)
(1b), R^1 = *p*-Tolyl, R^2=H, R^3=Pr^i — (2b), R^1=*p*-Tolyl, R^4=Et (87%)
(1c), R^1=Me, R^2=R^3=Et — (2c), R^1=Me, R^4=Pr^n (88%)
(2d), R =Me, R^4=Pr^i (91%)

a transition state (S_N2–*S* mechanism) or by an addition–elimination mechanism (*A*–*E*) involving a sulphuran intermediate, possibly allowing racemization or retention *via* pseudorotation or a front-side attack, it was desirable to probe the stereochemical course of this new sulphinate synthesis. With this end in mind we synthesized (+)-(*S*)-*NN*-diethyl toluene-*p*-sulphinamide (**1a**)† *via* the (−)-menthol ester (**3**)[2b] as outlined in the Scheme and it was then subjected to an acid-catalysed alcoholysis. A series of



SCHEME. Men = menthyl.

specificity of the acid-catalysed conversion of the sulphinamide (**1a**) into the sulphinates (**2**) has been found to be markedly dependent on the structure of the alcohol used and also to some extent on the nature of the acidic catalyst. In the case of primary alcohols the conversion took place with complete or almost complete inversion. When Pr^{i}OH was used, the stereospecificity of the reaction varied from 58 to 84% depending on the nature of the catalyst. The best result has been obtained with the mixture of CF_3CO_2H and $AgClO_4$. A low degree of stereospecificity was observed with Bu^{t}OH.

Since it has been found that the optically active sulphinamide (**1a**) undergoes fast racemization with simultaneous decomposition in the presence of strong acids, the lowering of the degree of stereospecificity of the reaction of [(+)-(**1a**)] with secondary and tertiary alcohols is, in our opinion, caused by the concurrent racemization process of optically active (**1a**) when the nucleophilic attack at sulphur by an alcohol molecule is retarded by steric hindrance, and is not due to a competition with the retention mechanism.

Although the detailed mechanism of the acid-catalysed interconversion of a sulphinamide into a sulphinate needs further studies, we suppose at present that the *N*-protonated sulphinamide is involved as an intermediate which is then subjected to nucleophilic attack by an alcohol. A transition state or short-lived intermediate in this displacement which accounts for the inversion of configuration at the sulphur is most likely a bipyramidal structure with the entering alkoxy group and departing protonated amino group occupying apical positions.

TABLE

Stereospecific synthesis of (−)-(*S*)-alkyl toluene-*p*-sulphinates (**2**), $MeC_6H_4S(O)OR$

Sulphinamide (**1a**) $[\alpha]_{589}$ (Me_2CO)	E.e.	Catalyst	Yield (%)	R	Sulphinate (**2**) $[\alpha]_{589}$ (EtOH)	E.e.[a]	Stereospecificity of (**1a**) → (**2**)	% of inversion
+107°	88	CF_3CO_2H	94	Me	−192·6°	88	100	100
+105°	86	$PhSO_3H$	76·5	Et	−179·2°	86	100	100
+107°	88	CF_3CO_2H	90	Et	−137·5°	66	75·5	87·7
+105°	86	$PhSO_3H$	80	Pr^n	−161·2°	84	98·2	99·1
+106°	87	$PhSO_3H$	95	Allyl	−106·5°	73	84	92
+105°	86	CF_3CO_2H	84	HC ≡ CCH_2	− 85·9°	77	89·5	94·7
+ 96°	78·5	CF_3CO_2H	87	Pr^i	−109·3°	54	69·5	84·7
+105°	86	$PhSO_3H$	53	Pr^i	−100·7°	50	58	79
+104·7°	86	CF_3SO_3H	86	Pr^i	−107·9°	54	62·7	81·5
+105°	86	$HSbF_6$	61	Pr^i	−134·2°	67	77	88·5
+100°	82	CF_3CO_2H + $AgClO_4$	62	Pr^i	−140·9°	70·5	84	92
+104·7°	86	CF_3SO_3H	55	Bu^t	− 29·85°	23	27·4	63·7

[a] Enantiomeric excess (E.e.) and absolute configuration of the sulphinates (**2**) obtained have been estimated from data from ref. 1 and on the results of their stereospecific conversion into methyl *p*-tolyl sulphoxide.

simple primary, secondary, and tertiary alcohols was tested for their ability to give optically active sulphinates.

The results obtained (Table) indicate that the optically active sulphinates (**2**) are formed with inversion of configuration at the sulphinyl centre. However, the stereo-

Added in proof: The kinetic resolution of sulphinates in the reaction with optically active Grignard reagents has been reported recently.[4]

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† The sulphinamide (+)-(*S*)-(**1a**) was prepared by treating the menthyl ester, (−)-(*S*)-(**3**), with *NN*-diethylaminomagnesium bromide in ether solution at 0 °C. After 7 h work-up gave the crude amide (**1a**) which was purified by column chromatography on silica gel 200—300 mesh (Koch-Light) using n-hexane–ether (2 : 1) as eluant.

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