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RING-SUBSTITUTED ARYLSULFONYLCYCLOPROPANES FROM γ,δ-EPOXYSULFONES. 1-ARYLSULFONYLBICYCLOBUTANES AND 1-ARYLSULFONYLSPIROBICYCLOBUTANES.

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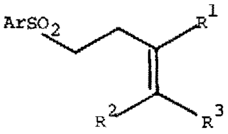
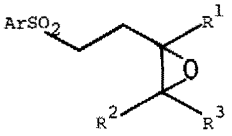
Intramolecular alkylations of α-sulfonylcarbanions are usually carried out with halogenated substrates which lead to unsubstituted or alkylsubstituted carbocyclic sulfones.[1] We report now that a similar alkylation-isomerization reaction takes place also with γ,δ-epoxysulfones (e.g. 2), affording 1-arylsulfonyl-2-(hydroxylalkyl)cyclopropanes (3) usually in high yields.[2] When the hydroxyl group is secondary or tertiary, compounds 3 can be dehydrated to yield (vinylcyclopropyl) sulfones (e.g. 5). The latter may then serve as useful synthetic intermediates, such as in the synthesis of condensed bicyclic systems through an aldol-type reaction at the 1-position and formation of cis-divinylcyclopropane derivatives.[5]

This communication describes the conversion of the epoxysulfones 2 into the cyclopropylsulfones 3 and the extension of the same reaction to epoxides derived from the dehydrated primary products to form bicyclobutanes and spirobicyclobutanes.

Aryl γ,δ-alkenyl sulfones (1)[6] were epoxidized with m-chloroperbenzoic acid. Treatment of epoxides 2 in tetrahydrofuran with n-butyl lithium in hexane at -15° yielded the trans-1-arylsulfonyl-2-(hydroxyalkyl)cyclopropanes 3 in 80-95% yields, except for 3a, where two isomers in a total 40% yield were obtained.



1



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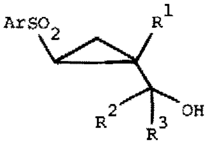


3

a, $R^1=CH_3$, $R^2=R^3=H$ (Ar=p-tolyl)

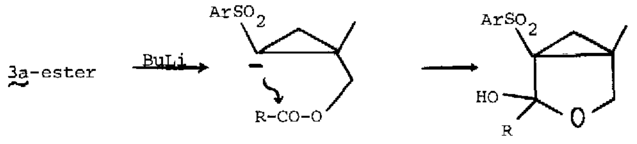
b, $R^1=R^2=H$, $R^3=CH(CH_3)_2$ (Ar=C_6H_5)

c, $R^1=H$, $R^2=R^3=CH_3$ (Ar=C_6H_5)

d, $R^1=H$, $R^2,R^3=(CH_2)_4$ (Ar=C_6H_5)

Configurations of the 3a isomers were assigned on the basis of the NMR chemical shifts. We have observed that a grouping cis to the arylsulfonyl on the cyclopropane ring is quite extensively deshielded relative to a trans grouping. This was demonstrated in the particular case of compound

4a, obtained by an ester condensation type reaction from either of the 3a-propionates.[8] The *cis*-methyl singlet of 4a appears at the relatively low field of δ 1.67 ppm. The 3a isomer with the methyl singlet at δ 1.47 was therefore assigned the *cis*-methyl configuration and the other (δ 1.27) the *trans* configuration (compound 4b, derived from 3a-acetate, showed two methyl singlets at δ 0.93 and 1.67 ppm).

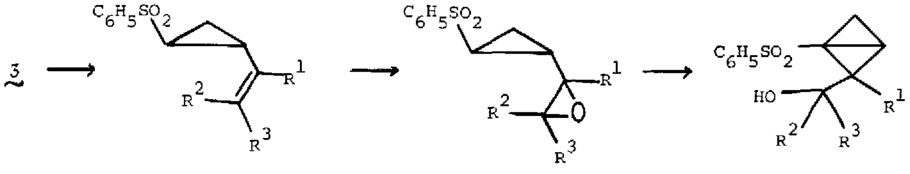


4

a, R=CH_2-CH_3

b, R=CH_3

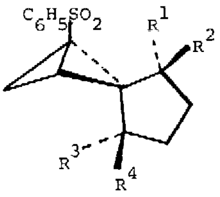
Compounds 3b-3d were dehydrated in high yields (*p*-TsOH in benzene) to the vinylcyclopropanes 5. These now are again γ,δ-unsaturated sulfones, on which the above sequence of reactions can be repeated. When the corresponding epoxides (6, diastereomeric mixture) were treated with *n*-BuLi, they yielded indeed the bicyclobutylsulfones 7, in varying yields. Thus, epoxide 6a afforded a 1:1 mixture of the *endo*- and *exo*-methyl isomers 7a in 25% yield. The diastereomeric epoxides 6b could be partially separated by chromatography and only one of them was found to be reactive, affording the *exo*-(hydroxyalkyl) derivative 7b in 60% yield. All four possible isomers 7c were obtained from epoxides 6c, in a total 43% yield.

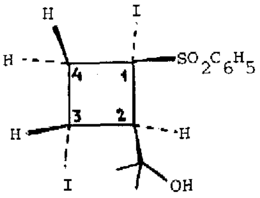


5 6 7

a, R^1=CH_3, R^2=R^3=H b, R^1=H, R^2=R^3=CH_3 c, R^2=H, R^1, R^3=$(CH_2)_3$

The structure of compounds 7 is given by their spectral properties (particularly NMR;[9] Table 1) and their property to readily absorb iodine in solution in spite of a lack of unsaturation. The lowest field proton in the NMR spectrum is the angular C-3 proton. It is totally replaced by deuterium when the reaction of 6b is quenched with D_2O[10] (and so is the C-1 proton of recovered 6b). The relative geometries of the 7a isomers were determined by analogy of the NMR spectra to those of the 3a isomers. Those of 7c by their similarity, two by two, to those of 7a, namely, an AMX-spectrum of the bicyclobutyl protons in the *exo*-CHOH isomers 7c-I and II and an ABX-spectrum for the *endo*-isomers III and IV (the polarity, or order of elution, of the 7c isomers on silica-gel also gives an indication as to their geometries: the sterically most hindered *exo*-*syn*-OH, 7c-I, is the least polar and it is followed by the *exo*-*anti* II, *endo*-*syn* III and *endo*-*anti* IV).





8

7c I, $R^2=R^3=R^4=H$, $R^1=OH$ III, $R^1=R^2=R^4=H$, $R^3=OH$

II, $R^1=R^3=R^4=H$, $R^2=OH$ IV, $R^1=R^2=R^3=H$, $R^4=OH$

All compounds 7 absorb iodine readily in solution.[9,11] The reaction of 7b with iodine could be followed in an NMR tube and was practically over in 20 minutes, in $CDCl_3$. Diiodide 8 was readily isolated from this reaction.[12]

Compounds 7 are quite stable and can be kept at room temperature for several weeks before deteriorating. Compounds 7c seem to be the first spirobicyclobutanes described. A spiro(cyclopropane-bicyclobutane) has been recently assumed as an intermediate in a reaction of dichlorocarbene with phenylallene,[13] but not actually isolated.

Table 1. NMR data of compounds 7[a]

Compound	H-3	H-4x	H-4n	R^1	R^2	R^3	$J_{3,4x}$	$J_{3,4n}$	$J_{4x,4n}$
7a,endo-Me[b]	3.07dd	2.37dd	1.80t	0.91s[c]	3.92[d]		4	2.5	2
7a,exo-Me[e]	2.77dd	2.57dd	1.92t	1.63[f]	3.77s		4	2.5	2.5
7b[g]	3.15quint	2.13d[h]	1.05d[h]		1.32s	1.44s	4	2	~ 0
7c-I[i]	2.84dd	2.33dd	1.67t	4.24br[j]	1.5-2.1m		4	2.5	2
7c-II[k]	3.21dd	2.44dd	l	4.47br[j]	1.2-2.2m		4	2.5	1.5
7c-III[m]	2.5-2.8m		l	3.73br[j]	1.5-2.1m				
7c-IV[n]	2.75dd	2.53dd	1.78dd	4.76br[j]	1.5-2.3m		4	2.5	1.5

[a] Solutions in $CDCl_3$; chemical shifts expressed in δ values; coupling constants, J, in Herz; n and x stand for endo and exo. [b] 3,5-Dinitrobenzoate (DNB), mp 163-164°. [c] n-methyl. [d] Close AB-pattern, $J \sim 14$. [e] DNB, mp 153-154°. [f] x-methyl. [g] Mp 57-58°, H-2n, δ 1.65d, $J_{2n,3}=2$. [h] Singlet when H-3 is exchanged with deuterium (the absence of a long-range exo-exo coupling indicates the endo configuration of the H-2 proton). [i] DNB, mp 178-179°. [j] CH-OH. [k] DNB, mp 183-184°. [l] Hidden H-4n. [m] DNB, mp 89-90°. [n] DNB, mp 172-173°.

References and Notes

1. H.O. House, "Modern Synthetic Reactions", Second Edition, W.A. Benjamin Inc., N.Y., 1972, pp 542, 729 and references therein.
2. The reaction is an extension of that of γ,δ-epoxyketones[3] or of epoxynitriles.[4]
3. Y. Gaoni, Isr.J.Chem., 63 (1971); Tetrahedron, 28, 5525, 5533 (1972).
4. G. Stork, L.D. Cama and D.R. Coulson, J.Am.Chem.Soc., 96, 5268 (1974); G. Stork and J.F. Cohen, ibid, 96, 5270 (1974).
5. See a forthcoming publication.
6. These were prepared by coupling of the Grignard derivative of aryl methyl sulfone[7] with an allylic halide, in the presence of cuprous chloride, in 60-70% yields. Satisfactory analyses have been obtained for all new compounds (solids or solid derivatives).
7. L. Field, J.Am.Chem.Soc., 74, 3919 (1952).
8. Inversion of the arylsulfonyl cyclopropylcarbanions seems to occur readily only when there are two substituents in the 2-position. When one of them is a hydrogen, both the formation of compounds **3** and their subsequent reactions show a high degree of stereoselectivity or total stereospecificity. See also ref. 1, p. 730 and references therein.
9. K.B. Wiberg in "Advances in Alicyclic Chemistry", Vol. 2, H. Hart and G.J. Karabatsos, Editors, Academic Press, 1968, p. 185.
10. G.L. Closs and L.E. Closs, J.Am.Chem.Soc., 85, 2022 (1963).
11. Compounds **7** are readily detected by thin layer chromatography when the plates are developed in iodine vapour: a white spot appears after a while, by absorption of the iodine.
12. Compound **8**, mp 158-159°, δ ($CDCl_3$): 1.37s and 1.42s (two methyls); 2.88dd and 3.56dd ($C\underline{H}_2$-4, ABX with H-3); 3.27d (H-2); 4.72q (H-3); 7.6-8.2m (aromatic protons).
13. E.V. Dehmlow, Tetrahedron Letters, 203 (1975).