

ARYL CYCLOBUTYL SULFONES BY REDUCTION OF 1-ARYLSULFONYLBICYCLOBUTANES
 WITH LITHIUM ALUMINIUM HYDRIDE SYNTHESIS OF RACEMIC JUNIONONE

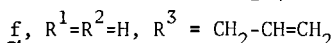
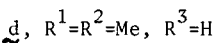
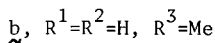
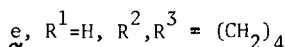
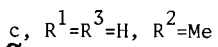
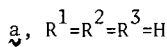
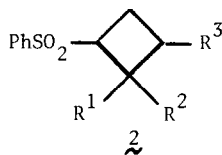
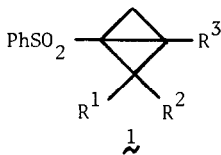
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Cyclobutyl sulfones are obtained by reduction of bicyclobutyl sulfones with lithium aluminium hydride and these may be used in further synthetic transformations, as illustrated by the synthesis of rac-junionone

The similarity of the central bond of bicyclobutanes to a double bond in its chemical behaviour makes 1-arylsulfonylbicyclo[1.1.0]butanes (1)¹ behave like α,β -unsaturated sulfones. In particular, these compounds undergo conjugate addition with organocopper reagents² or they may be reduced with lithium aluminium hydride (LAH)³ to cyclobutane derivatives.

Reduction of sulfones 1 were carried out with excess LAH (ca. 4 molar equiv) in tetrahydrofuran (THF) at 0 °C, and were usually complete in 30 minutes. Addition of ether and then careful addition of a saturated sodium sulfate solution until a well-formed precipitate had formed, followed by filtration, drying, and evaporation of the solvent, usually provided a crude solid product that could be recrystallized or passed on a plug of silica gel for final purification. Cyclobutyl sulfones 2 were thus obtained in over 80% yields^{4,5} (melting points 2a, 45-6, 2b, 113-4, 2c, 62-3, 2d, 57-8, 2e, 128-9 °C).

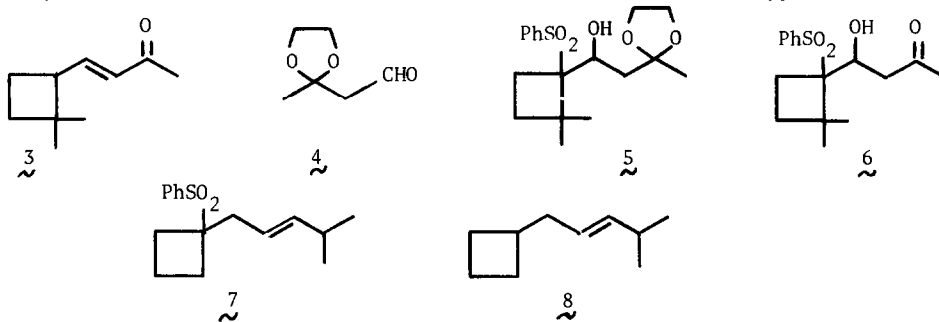


Still other cyclobutyl sulfones could be obtained from 1 (R³=H) by prior alkylation at the 3-position, followed by reduction. Thus, deprotonation of 1a with lithium diisopropyl amide in THF, followed by alkylation with allyl bromide, provided 1f, mp 78-9 °C, in 53% yield (75% relative to unrecovered starting material). Reduction of 1f in the usual way then furnished 2f as a liquid, in 73% yield.

The merit of compounds 2 is in that they can be further modified by reaction of their α -sulfonyl carbanion with various electrophiles and then by reductive elimination of the aryl-sulfonyl grouping, to provide sulfur-free cyclobutane derivatives. Various isoprenoid non-natural compounds and the non-isoprenoid natural compound junionone⁶ could thus be synthesized.

Synthesis of rac-junionone (3) involved reaction of the anion of 2d (n-BuLi, THF) with

aldehyde 4⁷ at -15 °C to provide two diastereomeric addition products 5, mps 143-4 and 116-7 °C,

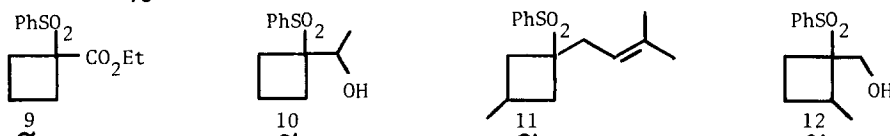


in a ca 1:1 ratio and in a total 53% yield (82% relative to unrecovered starting material) a mixture of the 5 isomers was deketalized with pyridinium tosylate in wet acetone⁸ to furnish a mixture of two diastereomeric ketones 6 (¹H NMR) in practically quantitative yield. This ketone mixture was desulfonated with 6% sodium amalgam (4 equivalents of sodium, stirring in ethanol at room temperature for 2 h), whereby junionone 3 was directly produced, besides unrecovered starting material and other minor products (¹H NMR).⁹ Longer treatment of 6 with sodium amalgam or the use of larger excess of the reagent brought about a decrease in the yield of 3.

Pure junionone was obtained from the above mixture by preparative gas chromatography (15% Carbowax on Chromosorb W, 20 feet x 1/2 inch column, 190 °C) and found to have a proton NMR spectrum identical with that published for the natural compound.⁶

An example for the synthesis of a non-natural isoprenoid compound is provided by alkylation of 2a with 1-bromo-4-methyl-2-pentene to give sulfone 7 in 85% yield, followed by desulfonation (6% sodium amalgam in refluxing ethanol) to furnish hydrocarbon 8 in 60% yield.

A few other synthesized compounds illustrate the potential use of sulfones 2: ester 9, mp 9-80 °C (from 2a and ethyl chloroformate, 41% yield), alcohol 10, mp 52-3 °C (from 2a and acetaldehyde, 36% yield), sulfone 11 (from 2b and prenyl bromide, 86% yield), alcohol 12, mp 1-3 °C (from 2c and formaldehyde, 78% yield).



References and Notes

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- See G. A. Russel, E. Sabourin, and G. J. Mikol, *J. Org. Chem.* 31, 2854 (1966). Correct analytical and/or spectral data have been obtained for all new compounds. Reported yields refer to recrystallized or chromatographically separated, spectroscopically pure compounds.
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- T. Oishi, M. Nagai, and Y. Ban, *Tetrahedron Lett.* 1968, 491.
- R. Sterzycki, *Synthesis*, 1979, 724.
- The ratio of starting material to product was ca 1:1 and the estimated yield of 3 was 25-30%.

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