

CONJUGATE ADDITION OF ORGANOCOPPER REAGENTS TO 1-ARYLSULFONYLBICYCLOBUTANES SYNTHESIS OF THE
 RACEMIC FORM OF THE SEX PHEROMONE OF THE CITRUS MEALYBUG, *PLANOCOCCUS CITRI* (RISSO)

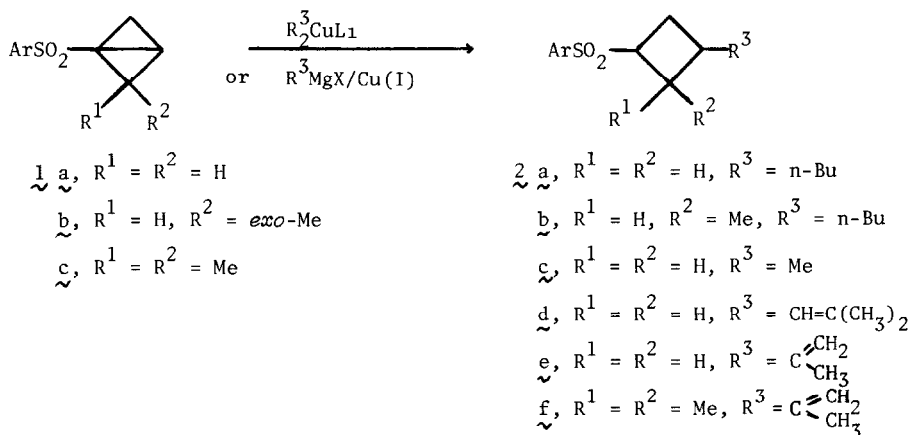
Yehiel Gaoni

Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel

Conjugate addition of organocopper reagents to 1-arylsulfonylbicyclobutanes yields 3-alkyl or alkenyl 1-arylsulfonylcyclobutanes, a synthesis of the sex pheromone of *Planococcus citri* is based on this reaction

The central bond of the bicyclo[1.1.0]butane system is known to possess a high degree of π -character and to exhibit olefinic properties¹ When an electron withdrawing group is located at C₁, this bond becomes even more activated and it can add various nucleophiles by stabilization of a negative charge α to the electronegative group²

It has now been found that 1-arylsulfonylbicyclobutanes (1), readily obtainable from γ, δ -epoxy sulfones,³ exhibit some chemical properties characteristic of α, β -unsaturated sulfones. In particular, they can be reduced with lithium aluminium hydride to cyclobutyl-sulfones,⁴ or undergo conjugate addition of organocopper reagents⁵



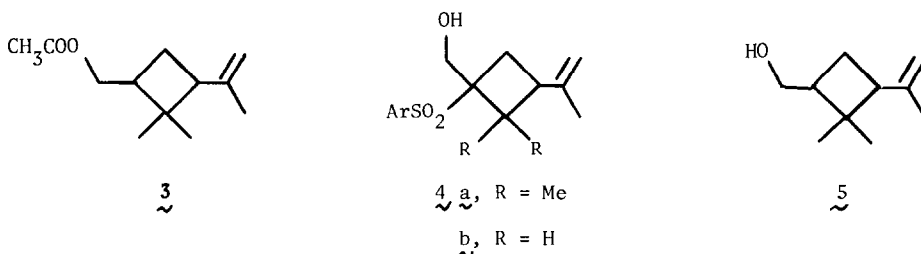
Addition of lithium dibutylcuprate (from n-butyllithium and $\text{Me}_2\text{S CuBr}$ in hexane-ether-dimethyl sulfide⁶) to 1a (Ar=p-tolyl), mp 91-2 °C,⁷ or 1b (Ar=Ph), mp 44-5 °C, provided 2a (Ar=p-tolyl) or 2b (Ar=Ph) in 87 and 73% yield, respectively.⁸ One sole isomer, of a yet undetermined geometry, was obtained in both cases

Addition of methyl magnesium iodide in ether to 1a (Ar=Ph),³ in the presence of 6 mole percent of a cuprous salt (added as $\text{Me}_2\text{S CuBr}$ or as CuCl) provided 2c (Ar=Ph), again as one sole isomer, in 85% yield. This product, mp 113-4 °C, was identical with the lithium aluminium hydride reduction product of the corresponding bicyclobutane.⁴

Addition of vinylic reagents to 1 was not specific, but showed some selectivity. Thus, addition of isobutenyl magnesium bromide in tetrahydrofuran (with 6 mole % of $\text{Me}_2\text{S CuBr}$) to 1a (Ar=p-tolyl) furnished two 2d (Ar=p-tolyl) isomers, in a ratio of ca 1:2 by order of elution from silica gel, and in a total 77% yield.

A similar ratio of 1:2 of two 2e (Ar=p-tolyl) isomers was obtained from 1a (Ar=p-tolyl) and isopropenyl magnesium bromide (CuBr catalysis), in a total 61% yield. Addition of lithium diisopropenyl cuprate (prepared from the bromide, with lithium and then cuprous iodide) to the same substrate, furnished a similar mixture of the 2e isomers, but in a low, 28% yield.

A synthesis of the racemic form of the sex pheromone of the citrus mealybug *Planococcus citri* (Risso), *cis*-3,⁹ was based on the addition of isopropenyl magnesium bromide to 1c (Ar=Ph).^{3,10} Only one 2f isomer could be isolated in pure form from the complex reaction mixture, in 22-31% yield. The low yield results here probably from steric hindrance and from the relative instability of both substrate and reagent.



Treatment of the α -sulfonyl carbanion of 2f (n-BuLi in THF, 0 °C) with monomeric formaldehyde produced two 4a (Ar=Ph) isomers, mps 122-3 and 98-9 °C, in a ratio of 1.7 and in 73% total yield. When carried out on 2e, this reaction gave the same mixture of two 4b isomers from each 2e isomer, in a ratio of ca. 1.2 and in a total 50-55% yield.

Desulfonylation of the major, lower-melting 4a isomer with 6% sodium amalgam in methanol produced a mixture of two alcohols 5, which were acetylated directly with acetic anhydride in pyridine to yield a mixture of *cis*- and *trans*-3 in a ratio of 2:1, respectively. Gas chromatography coupled with mass spectrum measurement established the ratio of products and showed for both the characteristic fragmentation reported for the natural pheromone.⁹ The ¹H NMR showed two sets of *gem*-dimethyl signals and of side chain methylene multiplets in the indicated ratio.

Separation of the two isomers was achieved by preparative gas chromatography (15% Carbowax on Chromosorb W, 20 feet x 1/2 inch column, 195 °C). Pure *cis*- and *trans*-3 were thus obtained, with ¹H NMR spectra, matching exactly those published⁹ (except for the lower field signal of the *gem*-dimethyl in *cis*-3, which appears at δ 1.19 instead of 1.12, this value is in accordance with the value obtained by extrapolation from the reproduced spectrum in ref. 9).

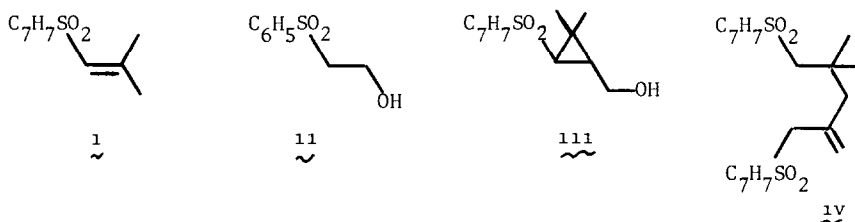
The biological activity of the racemic pheromone is now being tested in the field.

A synthesis of grandisol, the boll weevil sex pheromone, is now in progress along similar lines.

References and Notes

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- 7 Correct analytical and/or spectral data have been obtained for all new compounds
- 8 Reported yields refer to chromatographically separated, spectroscopically pure compounds
- 9 B A Bierl-Leonhardt, D S Moreno, M Schwarz, J Fargelund, and J R Plimmer, *Tetrahedron Lett* 22, 389 (1981)
- 10 The *p*-tolyl homologue of 1c, mp 73-4 °C, could be alternatively prepared via 111, mp 104-5 °C, obtained by addition of the dianion of 11 to 1 (n-BuLi, THF) ¹¹ The optimal conditions for this reaction have, however, still to be worked out, the major product in several instances being dimer 1v



- 11 See R V M Campbell, L Crombie, D A R Findley, R W King, G Pattenden, and D A Whiting, *J. Chem Soc Perkin Trans 1*, 1975, 897 for the addition of α -sulfonyl carbanion to α,β -unsaturated esters, and references cited therein

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