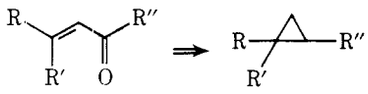
Preparation of Cyclopropanes from α,β-Unsaturated Aldehydes, Esters, and Ketones

Summary: α,β-Unsaturated carbonyl compounds are efficiently transformed into the corresponding cyclopropanes by a sulfone-mediated bond formation.

Sir: In connection with natural product synthesis, we have been concerned with the problem of converting α,β-unsaturated compounds into cyclopropanes (eq 1) and recently de-



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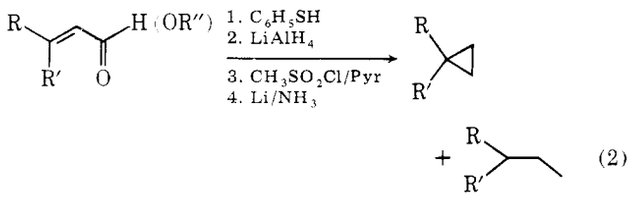
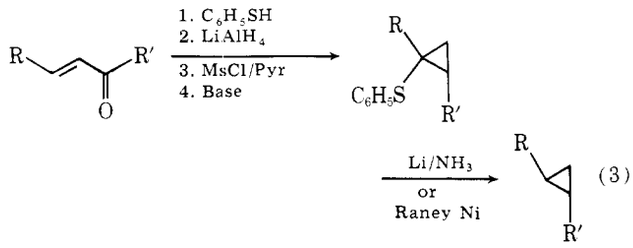
veloped a method to accomplish this; however, the open chain hydrocarbon was also formed (eq 2).[1] We now report another



(2)

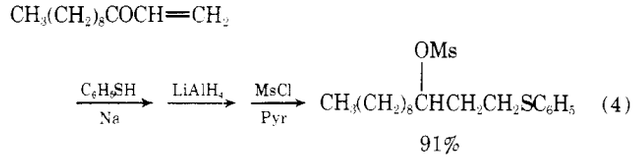
approach which cleanly gives the desired goal.

The new strategy is summarized in eq 3. It was hoped that



(3)

the thiophenyl moiety would stabilize an adjacent carbanion and thus promote cyclopropane formation. In fact, the first three steps in the sequence work well. The conversion of 1-dodecen-3-one into the methanesulfonate ester is accomplished in 91% yield (eq 4). It is therefore very disappointing



(4)

that stirring this ester with lithium diisopropylamide (LDA) in THF between −78 °C and room temperature gives only recovered starting material. The corresponding tosylate also fails to react.[2]

Because a sulfone group is better than a lone sulfur at stabilizing an adjacent carbanion, we decided to explore sulfones.[3,4] Indeed, methyl vinyl ketone is converted into phenyl 3-tosyloxybutyl sulfone in 65% yield and then successfully cyclized with LDA in THF between −78 °C and room temperature to 2-methylcyclopropyl phenyl sulfone in 99% yield (eq 5).[5-7] Table I summarizes the cyclopropyl sulfones pre-

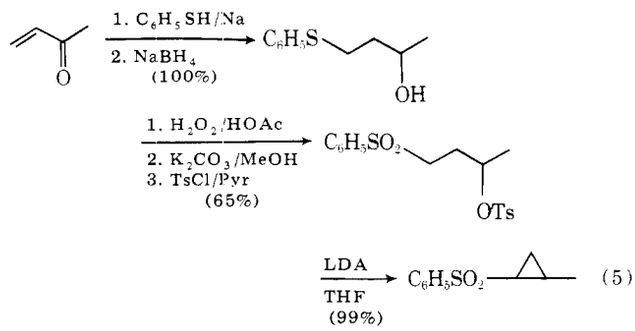


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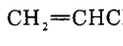
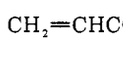
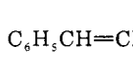
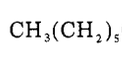
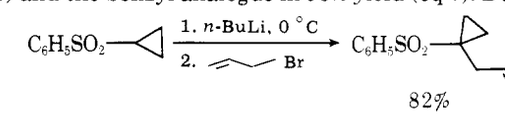
Table I. Cyclopropyl Sulfones from α, β-Unsaturated Carbonyl Compounds

Carbonyl compd	Sulfone tosylate,[a] % yield	Cyclopropyl sulfone (% yield)
CH_2=CHCHO	78	 (100)
CH_2=CHCOCH$_3$	65	 (99)
C_6H_5CH=CHCHO	84[b]	 (100)
$CH_3(CH_2)_5$CH=CHCO$_2$Et	86[b]	 (100)
	75	(100)

[a] Includes addition of thiophenol, reduction of carbonyl, oxidation of sulfide, and tosylate formation. [b] Mesylate ester used instead of tosylate.

pared in this way. Desulfurization yields the desired cyclopropanes. This was carried out for representative systems with 6% sodium amalgam[8] in refluxing ethanol. For example, cyclopropylbenzene is obtained in 83% yield.

The utility of cyclopropyl sulfones containing an acidic α hydrogen can be extended. For example, cyclopropyl phenyl sulfone can be alkylated to give the allyl derivative in 82% yield (eq 6) and the benzyl analogue in 96% yield (eq 7). Desulfur-



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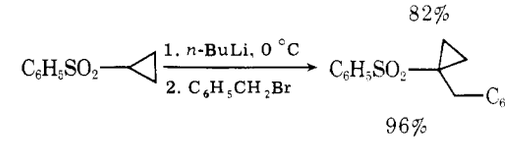

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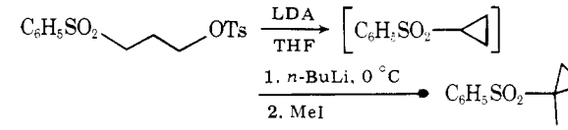
ization of the latter compound with 6% Na(Hg) in refluxing ethanol gives benzylcyclopropane in 75% yield.

For added convenience, cyclopropyl phenyl sulfone need not be isolated. A one-pot conversion of phenyl 3-tosyloxypropyl sulfone to 1-methylcyclopropyl phenyl sulfone proceeds in 90% overall yield (eq 8).



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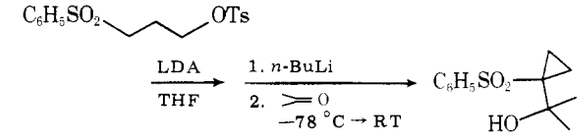
The sulfone anion can be quenched with carbonyl compounds as well. For example, the one-pot sequence of eq 9 gives the tertiary alcohol in 92% overall yield. Hexanal gives the secondary alcohol of eq 10 in 91% yield. Desulfurization



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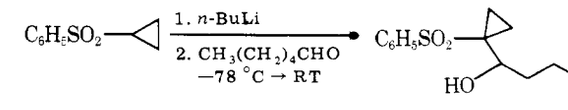

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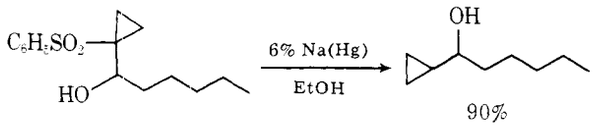
of the latter compound in the usual way gives the cyclopropylcarbinol in 90% yield (eq 11). These compounds can be



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converted stereospecifically into homoallylic bromides by the elegant method developed by Julia[9a] and Johnson.[9b] In addition, cyclopropyl ketones are available by oxidation of the carbinols.

In conclusion, this method allows the synthesis of a wide variety of functionalized cyclopropanes derived from readily available α,β-unsaturated aldehydes, esters, and ketones.

A typical experimental procedure for the conversion of cinnamaldehyde into phenylcyclopropane is described.

Cinnamaldehyde (26.4 g, 200 mmol) in 80 mL of 95% EtOH was added dropwise over 20 min to 0.6 g of sodium in 200 mL of 95% EtOH containing 30.8 g (280 mmol) of thiophenol at room temperature. After 20 h, 3.80 g (100 mmol) of $NaBH_4$ was added and the reaction mixture was stirred for 2 h. Workup gave 48.3 g (100%) of 3-phenyl-3-thiophenylpropanol as a thick oil which solidified upon standing: NMR (CCl_4) δ 2.2 (br s, 1 H), 3.6 (m, 2 H), 4.3 (t, J = 7 Hz, 1 H), 7.2 (m, 10 H). This alcohol (24.2 g, 100 mmol) was dissolved in 32 mL of glacial acetic acid and 32 mL of 30% H_2O_2 was added dropwise over 30 min such that the temperature did not exceed 70 °C (exothermic). When the addition was complete, the reaction mixture was refluxed for 1 h, cooled, and worked up with 10% NaOH. This crude product was stirred with K_2CO_3 in aqueous MeOH overnight to give 24.1 g (88%) of solid sulfone. This sulfone (5.08 g, 18.5 mmol) was dissolved in 20 mL of pyridine and 3.10 g (25.9 mmol) of mesyl chloride was added dropwise over 20 min. After 5 h, the reaction mixture was poured into cold 5% HCl and extracted with CH_2Cl_2 to give 6.2 g (95%) of sulfone mesylate as a white solid: NMR ($CDCl_3$) δ 2.5–2.8 (m, 2 H), 2.9 (s, 3 H), 4.0–4.5 (m, 3 H), 7.1–7.6 (m, 10 H). Diisopropylamine (3.73 g, 37.0 mmol) was dissolved in 130 mL of dry THF (distilled from potassium) at 0 °C and 34 mmol of n-BuLi/hexane was added. After 30 min, the reaction mixture was cooled to −78 °C and 9.30 g (26.4 mmol) of the sulfone mesylate in 200 mL of THF was added dropwise over 40 min. After an additional 90 min at −78 °C, the reaction mixture was allowed to warm to room temperature and stir for 2 h more. The reaction was quenched with water and extracted with CH_2Cl_2 to give 6.8 g (100%) of phenyl 1-phenylcyclopropyl sulfone as a yellow solid: NMR ($CDCl_3$) δ 1.25 (dt, J_d = 2 Hz, J_t = 5 Hz, 2 H), 2.0 (dt, J_d = 2 Hz, J_t = 5 Hz, 2 H), 7.1–7.6 (m, 10 H). This sulfone (5.16 g, 20.0 mmol) was dissolved in 50 mL of absolute EtOH and refluxed with 30 g of 6% Na(Hg) for 12 h. The reaction mixture was poured into 5% HCl and extracted with ether. Careful removal of the solvent and distillation of the residue at atmospheric pressure gave phenylcyclopropane as a colorless liquid (1.95 g, 83%): bp 153–154 °C; NMR (CCl_4) δ 0.6–1.0 (m, 4 H), 1.7–2.1 (m, 1 H), 6.9–7.2 (m, 5 H).

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References and Notes

(1) Y.-H. Chang, D. E. Campbell, and H. W. Pinnick, *Tetrahedron Lett.*, 3337 (1977). The only earlier report of a conversion such as that of eq 1 is that of C. P. Casey, L. D. Albin, and T. J. Burkhardt (*J. Am. Chem. Soc.*, **99**, 2533 (1977)), who prepared 1-methyl-2,3-diphenylcyclopropane from 1,3-diphenyl-2-buten-1-one. The two cyclopropanes synthesized in this paper each contain two aromatic rings so the method may be severely limited.

(2) (a) This is surprising since Johnson has reported[2b] without experimental detail that 3-chloropropyl phenyl sulfide yields cyclopropyl phenyl sulfide when treated with potassium amide in ether. (b) C. R. Johnson and E. R. Janiga, *J. Am. Chem. Soc.*, **95**, 7692 (1973).

(3) In fact, phenyl cyclopropyl sulfone has been prepared from the open-chain sulfone by several groups: H. E. Zimmerman and B. S. Thyagarajan, *J. Am. Chem. Soc.*, **82**, 2505 (1960); W. E. Truce and L. B. Lindy, *J. Org. Chem.*, **26**, 1463 (1961); R. Bird and C. J. M. Stirling, *J. Chem. Soc. B*, 111 (1968).

(4) (a) A possible alternative solution to this problem is suggested by the recent work of Bryson,[4b] who has found that alkyl phenyl sulfides can be metalated with *tert*-butyllithium in the presence of hexamethylphosphoramide. This paper appeared as our study was almost complete so we did not investigate bases stronger than LDA. (b) T. M. Dolak and T. A. Bryson, *Tetrahedron Lett.*, 1961 (1977).

(5) The methine adjacent to the sulfone group (2.1–2.4 ppm, multiplet) disappears when the sulfone is treated with LDA and then quenched with D_2O.

(6) The required sulfones could also be prepared by Michael-type addition of a sulfinic acid. For example, 3-oxobutyl *p*-tolyl sulfone has been prepared recently from methyl vinyl ketone and sodium *p*-tolylsulfinate: J. Fayos, J. Clardy, L. J. Dolby, and T. Farnham, *J. Org. Chem.*, **42**, 1349 (1977).

(7) Cyclopropyl sulfones have been prepared by a similar intramolecular epoxide opening: Y. Gaoni, *Tetrahedron Lett.*, 503 (1976).

(8) G. H. Posner and D. J. Brunelle, *Tetrahedron Lett.*, 935 (1973). We thank Dr. Posner for providing experimental details for the preparation of 6% Na(Hg) powder.

(9) (a) M. Julia, S. Julia, and R. Guegan, *Bull. Soc. Chim. Fr.*, 1072 (1960); (b) S. F. Brady, M. A. Ilton and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968).

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Reduction of Aldehydes and Ketones to Alcohols and Hydrocarbons through Use of the Organosilane–Boron Trifluoride System

Summary: Ketones and many aldehydes are converted directly and rapidly to hydrocarbons by the action of gaseous boron trifluoride and organosilicon hydrides in dichloromethane solution.

Sir: Deoxygenation of aldehydes and ketones to alkanes is a step frequently encountered in organic synthesis. Of the relatively few direct methods available, none appears to be of universal applicability;[1] many require harsh reaction conditions incompatible with the requirements of high selectivity needed when dealing with polyfunctional compounds.[2] We report here a convenient alternative to previously existing methods.

Aldehydes and ketones are reduced by organosilicon hydrides[3] upon addition of Brønsted acids[4] or certain Lewis acids.[5] In general, only aryl ketones and aryl aldehydes with electron-donating ring substituents give synthetically useful yields of completely deoxygenated products.[6] Reductions of other aldehydes and ketones normally stop after 1 equiv of hydride has been transferred, to give a variety of products (e.g., alcohols, esters, silyl ethers, ethers, olefins, or Friedel–Crafts dimers) whose nature depends upon substrate and reaction conditions. Doyle and co-workers have reported similar results using boron trifluoride etherate to promote the reductions.[7]

Recently we reported the unique ability of a system consisting of an organosilicon hydride and gaseous boron trifluoride to effect rapid direct reductions of alcohols to hydrocarbons.[8] With this system, reductions of even simple secondary aliphatic alcohols to hydrocarbons take place in minutes at room temperature or below. We now report that use of this system on aldehydes and ketones results in facile reductions to alcohols and hydrocarbons in synthetically useful yields (Table I). Under the reaction conditions, the organosilicon hydride is converted into an organosilicon fluoride.

The best reaction results were obtained by a method (A) which consisted of initial formation of the carbonyl–boron

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