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A NOVEL SYNTHESIS OF CARBOCYCLIC SPIRO-TYPE METHYLENECYCLOPROPANE DERIVATIVES[1]

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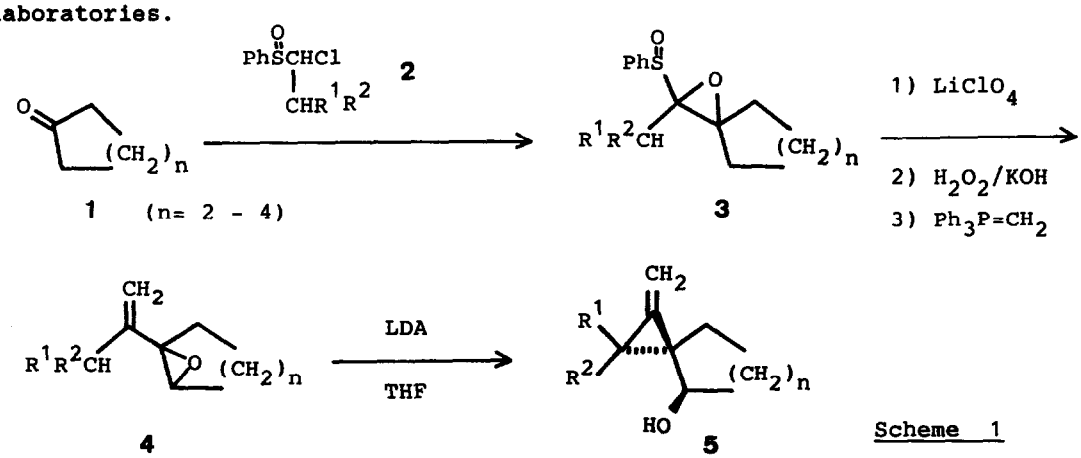
Abstract: A novel method is described for the synthesis of carbocyclic spiro-type methylenecyclopropane derivatives via the cyclization of allyl-epoxides, which are readily available from ketones and 1-chloroalkyl phenyl sulfoxides.

Methylenecyclopropanes are quite interesting compounds from physicochemical and synthetic organic chemical point of view.[2] A few methods for the synthesis of methylenecyclopropanes and its use in organic synthesis have been reported;[3] however, to our best knowledge no report has been published for the synthesis of carbocyclic spiro-type methylenecyclopropanes.[4] In this paper we report the new and facile method for the synthesis of carbocyclic spiro-type methylenecyclopropanes 5 from ketones 1 and 1-chloroalkyl phenyl sulfoxides 2 through the α,β-epoxy sulfoxides 3 and allyl epoxides 4 (Scheme 1).

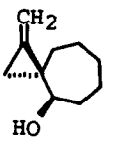
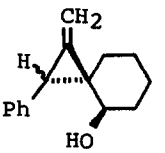
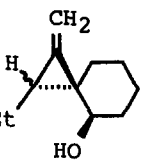
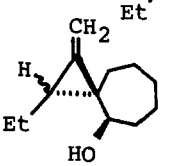
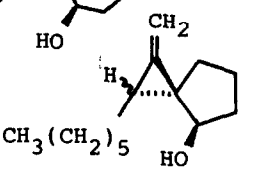
α,β-Epoxy sulfoxides 3 were easily prepared from cyclic ketones 1 and sulfoxides 2 in nearly quantitative yields.[5] Treatment of 3 with $LiClO_4$ and $n\text{-}Bu_3PO$ in refluxing toluene gave α,β-unsaturated ketones,[5] which were epoxidized and then treated with Wittig reagent to afford allyl epoxides 4 in good overall yields. Cyclization of 4 to methylenecyclopropanes 5 took place with excess LDA in THF at -60 to 0 °C.[6] Representative results of this method are listed in Table 1.

The results in Table 1 indicate that this procedure is useful for a preparation of non- or monosubstituted spiro-cyclic methylenecyclopropanes. When R^1=Ph, the cyclization took place quite smoothly in quantitative yield (entry 2). Disubstituted spiro-cyclic methylenecyclopropane was not obtained (entry 3). Scope and limitation of this method and further extension of this procedure to novel synthetic method is underway in these laboratories.



Scheme 1

Table 1. Preparation of Carbocyclic Spiro-Type Methylenecyclopropane Derivatives from Cyclic Ketones 1 through Allyl Epoxides 4

Entry	n	R^1	R^2	4 (Yield/%)[a]	5 (Yield/%)[b]
1	4	H	H	(70)	 (88)
2	3	Ph	H	(43)	 (99)[c]
3	3	—— $(CH_2)_5$ ——		(57)	(0)[d]
4	3	Et	H	(57)	 (83)[c]
5	4	Et	H	(74)	 (89)[c]
6	2	$CH_3(CH_2)_5$	H	(70)	 (91)[e]

a) The overall yield from the α,β-epoxy sulfoxide 3. Isolated yield. b) The yield in the cyclization step. Isolated yield. c) Inseparable diastereomeric mixture. d) No reaction was observed. e) Separable diastereomeric mixture (ratio about 2:1).

References and Notes

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6. Typical experimental procedure: A solution of 4 (R^1=R^2=H, n=4; 76 mg; 0.5 mmol) in 2 ml of THF was added to a solution of LDA (3 mmol) in 5 ml of THF under N_2 at -60 °C with stirring. The reaction mixture was stirred at -60 °C for 10 min, then at 0 °C for 4 h. The reaction was quenched with sat. aq. NH_4Cl and the whole was extracted with ether. The usual workup gave 5 (67 mg; 88%) as a colorless oil.

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