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STEREOSELECTIVE SYNTHESIS OF α,β-EPOXYPHENYLKETONES FROM α,α-DIBROMOPHENYLKETONES AND ALDEHYDES USING STANNOUS FLUORIDE

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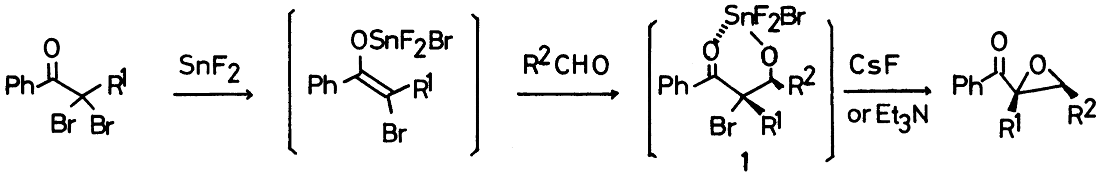
trans-α,β-Epoxyphenylketones are stereoselectively synthesized via aldol type intermediates under mild conditions starting from α,α-dibromophenylketones and aldehydes using stannous fluoride.

Stereoselective formation of carbon-carbon single bond is an important problem in synthetic organic chemistry. Recently, much effort has been devoted to find effective metal enolates to utilize in the stereoselective Aldol-type reactions.[1]

On the other hand, in the previous paper[2], we have described that organotin(IV) compound, readily prepared from allyl iodide and stannous fluoride, reacts with aldehydes or ketones to afford the corresponding γ,δ-unsaturated alcohols in good yields. During our continuous investigation on the exploration of new synthetic reactions using stannous fluoride, we now found a novel method for the stereoselective synthesis of α,β-epoxyphenylketones by the Aldol type reaction using α,α-dibromophenylketones and aldehydes as starting materials.



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Organotin(IV) compounds[3], formed by the reductive insertion of stannous fluoride into the α,α-dibromophenylketones, reacted with aldehydes at -45 °C to afford adduct 1.[4] This adduct was then converted into the corresponding α,β-epoxyphenylketone by the internal nucleophilic attack of oxygen atom on α-carbon atom by the assistance of bases. For example, by the addition of cesium fluoride or triethylamine, this step was successfully promoted probably by effective scavenge of stannic halide liberated.

The following is a typical procedure for the preparation of 1,5-diphenyl-2-methyl-2,3-epoxypentan-1-one: A suspension of stannous fluoride[5] (118 mg, 0.75 mmol), α,α-dibromopropiophenone (219 mg, 0.75 mmol) and 3-phenylpropanal (67 mg, 0.5 mmol) in DMF (2 ml) was stirred at -45~ -55 °C for 15 h. Cesium fluoride (484 mg, 3.2 mmol) was then added and the reaction mixture was stirred at 80 °C for 2 h. The reaction mixture was quenched with water and the product was extracted with ether. The ether extract was washed with brine, and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was separated by silica gel thin layer chromatography to afford 1,5-diphenyl-2-methyl-trans-2,3-epoxypentan-1-one in 81% yield.

Table. Synthesis of α,β-Epoxyketones [a]

R^1	R^2	Yield (%)
Me	$C_6H_5CH_2CH_2$	81
Me	C_6H_5	77
Me	n-C_8H_{17}	70
Me	p-ClC_6H_4	75
Et	C_6H_5	52[b]
Et	$C_6H_5CH_2CH_2$	58[b]

a) These compounds were spectroscopically identical (NMR,IR) with the authentic samples prepared from α,β-unsaturated ketones with hydrogen peroxide in the presence of NaOH.[6]

b) Triethylamine was used as a base.

As shown in Table, α,β-epoxyphenylketones are prepared in good yields from the corresponding α,α-dibromophenylketones and aldehydes by one pot procedure.

Concerning the preparation of α,β-epoxyketones, there are several general methods, namely, 1) the reaction of hydrogen peroxide and α,β-unsaturated ketones in the presence of sodium hydroxide,[7] and 2) the Darzens reactions.[8] However, in both of these methods, reactions are carried out under rather strongly basic conditions. The present reaction enables a stereoselective preparation of trans-α,β-epoxyphenylketones in good yields under essentially neutral conditions.

References and Notes

1) W. A. Kleschick, C. T. Buse, and C. H. Heathcock, J. Am. Chem. Soc., 99, 247 (1977); T. Mukaiyama and T. Inoue, Chem. Lett., 1976, 559; D. A. Evans, E. Vogel, and J. V. Nelson, J. Am. Chem. Soc., 101, 6120 (1979); M. Hirama, D. S. Garvey, L. D. Lu, and S. Masamune, Tetrahedron Lett., 1979, 3937 and references cited therein.

2) T. Mukaiyama, T. Harada, and S. Shoda, Chem. Lett., 1980, 1507.

3) The configuration of this intermediate is not clear, however, E-enolate is assumed to be formed judging from the configuration of the final product.

4) When the reaction mixture was quenched with water at this stage, α-bromo-β-hydroxyketone was obtained as a major product.

5) Good stereoselectivity could not be realized when zinc or stannous chloride was employed in place of stannous fluoride.

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