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REACTION OF α,β-EPOXYSULFONES WITH $MgBr_2$. PREPARATION OF α-BROMO ALDEHYDES AND KETONES.

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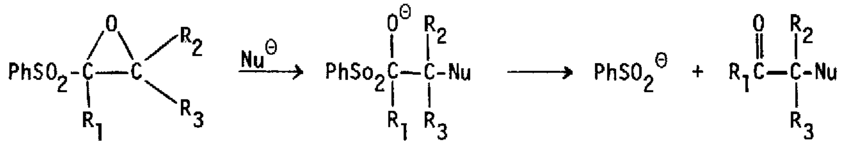
Several years ago we reported the preparation of α,β-epoxysulfones and studied their *thermal and acid-catalysed rearrangement. (1) We have now investigated the possibility that* these compounds might serve as useful intermediates in the preparation of α-substituted aldehydes and ketones according to the equation 1.

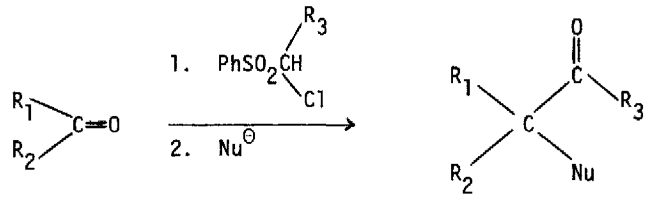
(1)



1 2 3

It was expected that any nucleophilic or electrophilic ring opening of the epoxide should occur with complete regioselectivity as shown since S_N2 reactions α to a sulfonyl group are known to be extremely slow (2) and α-sulfonyl carbocations would be expected to be very unstable. Since the epoxysulfones are now conveniently available in good to excellent yields from α-chlorosulfones and ketones or aldehydes under phase transfer conditions (3) the overall synthetic transformation represented by equation 2 involves the introduction of both an acyl and a nucleophilic group at the original carbonyl carbon. The carbon α to the sulfone group functions as a masked nucleophilic acyl carbon.

(2)



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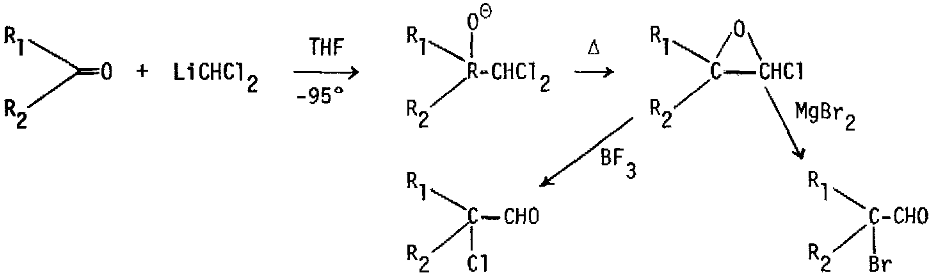
We have briefly investigated a number of possible examples based on equation 2 (4) and would like to report the successful preparation of α-bromoaldehydes and ketones. Reaction of eight different epoxysulfones of the type 1 with excess $MgBr_2$ in ether at room temperature or below gave, in almost quantitative yield, the expected α-bromocarbonyl compounds 4 (Nu = Br). The reaction is exceptionally clean and n.m.r. spectra of the crude products were essentially identical with those of the purified materials.

The following procedure is representative: a solution of $MgBr_2$ was prepared in ether by reacting Mg with 1,2-dibromoethane. It was cooled to about 5° and the epoxysulfone was added as an ether or CH_2Cl_2 solution. After approximately 15 - 30 min., t.l.c. indicated the absence of starting material and the formation of a more polar product. The reaction mixture was carefully quenched with ice-water and the product isolated. Residual dibromoethane, if present, was most easily removed by simple column chromatography using a short silica gel column; the dibromoethane being eluted with hexane and desired material with 1 : 1 CH_2Cl_2-hexane.

α-Brominated ketones and aldehydes are usually prepared from the corresponding carbonyl compound and a variety of brominating agents. (5) In the case of ketones such reactions sometimes lack high regioselectivity. The present method involves a variable chain extension and complete regioselectivity and thus should prove a useful addition to the synthetic methodology for these compounds.

The overall interconversion (Nu = Br or Cl) outlined in reaction 2 in which α-chloroepoxides, (prepared from dichloromethyllithium and ketones or aldehydes) are the key intermediates, has been known for some time, reaction 3. (6) We feel that the epoxysulfone route

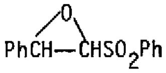
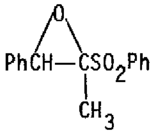
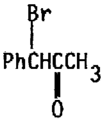
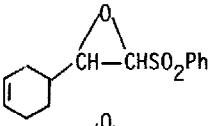
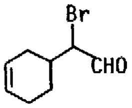
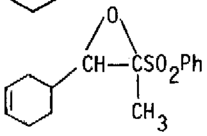
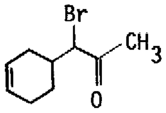
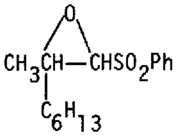
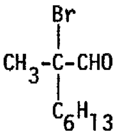
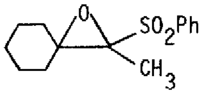
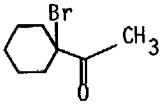
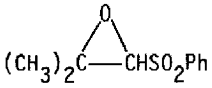
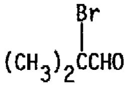
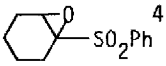
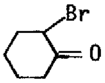
(3)



has a number of important advantages over the α-chloroepoxide route: (i) the condensation between α-chlorosulfones (8) and ketones or aldehydes can be carried out conveniently, and in generally good to excellent yield, under phase-transfer conditions, whereas the synthesis of the α-chloroepoxides requires the generation of dichloromethyllithium in THF at -95°, (ii) the epoxysulfones are generally stable, easily purified crystalline substances, while many of the chloroepoxides are not stable enough to be purified by distillation (iii) the epoxysulfone route is more general, being applicable by the synthesis of α-bromoketones as well as aldehydes.

TABLE

PREPARATION OF α-BROMOALDEHYDES AND KETONES VIA α,β-EPOXYSULFONES AND $MgBr_2$

$R_1\text{-}\overset{O}{\overset{\|}{C}}\text{-}R_2$			Epoxysulfone (%)[1,2]	M.p. °C.	α-Bromo Deriv. (%)[1]
1.	Ph	H		(92)	 $\mathrm{Ph\overset{Br}{C}HCHO}$ (> 78)
2.	Ph	H		(85)	 $\mathrm{Ph\overset{Br}{C}H\underset{O}{\overset{\|}{C}}CH_3}$ (> 95)
3.		H		(95)	 (80)
4.		H		(72)	 (90)
5.	CH_3	C_6H_{13}		(78)	 $\mathrm{CH_3\text{-}\underset{C_6H_{13}}{\overset{Br}{C}}\text{-}CHO}$ (80)
6.	$-C_5H_{10}-$			(60)	 (89)
7.	CH_3	CH_3		(94)	 $\mathrm{(CH_3)_2\overset{Br}{C}CHO}$ (85)[3]
8.	-		 [4]		 (80)

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1. Yields refer to isolated yields after chromatography or recrystallization.
2. All epoxysulfones, except entry 8, were prepared under phase transfer conditions, ref. 3.
3. Not determined accurately. Estimated yield > 85%.
4. Prepared by epoxidation (MCPBA in refluxing CCl_4) of the corresponding alkene.

The substituted α-chloroalkyl phenyl sulfones required for the ketone synthesis are readily prepared by several routes. (7)

α-Nitroepoxides also react with $MgBr_2$ in the same manner as the α-chloro and α-sulfonyl-epoxides and thus, when easily prepared, could be considered as possible precursors of α-bromo carbonyl compounds. For example, 1-phenyl-2-nitro-1,2-epoxypropane (8) and $MgBr_2$ in ether gave exclusively 1-bromo-1-phenyl-2-propanone (85 - 90%). In contrast, initial investigations suggest that α-epoxynitriles are opened by $MgBr_2$ in the opposite sense, i.e., to give stable α-bromo-β-hydroxynitriles. (4)

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4. For example, RS^-, $H^-(LiAlH_4)$, N_3^-, CN^- and RMgx. Up to the present, the reaction has been successful according to equation 2 only for RS^-, H^- and RMgx. For the latter two reagents, the resultant carbonyl compound reacts further with the reagent to give alcohols, (J. Decesare, unpublished observations).
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7. Among the possible routes are: (i) $PhSCH_2R$ + chlorinating agents, followed by oxidation [F.G. Bordwell and B.M. Pitt, J. Amer. Chem. Soc., 77, 572 (1955); D.L. Tuleen and T.B. Stephens, J. Org. Chem., 34, 31 (1969); (ii) PhSH + RCHO + HCl (H. Bohme, H. Fischer and R. Frank, Ann., 563, 54 (1949).
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