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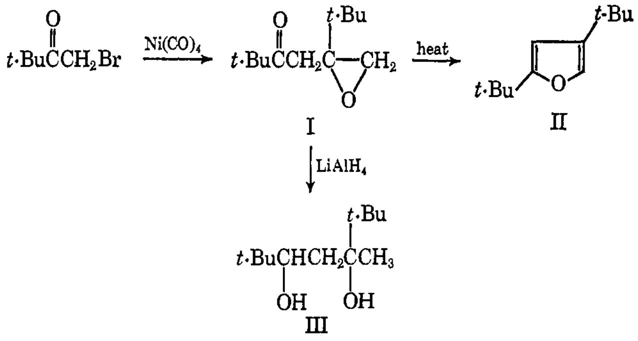
Direct Synthesis of β-Epoxy Ketones from α-Bromo Ketones and Nickel Carbonyl

Sir:

In general β-epoxy ketones can be prepared by epoxidation of β,γ-unsaturated ketones with perbenzoic acid.[1] However difficulty arises in the synthesis of β,γ-unsaturated ketones owing to easy rearrangement to the more stable α,β-unsaturated ketones. In the course of our studies on the reaction mechanism of furan formation between α-bromo ketones and nickel carbonyl in N,N-dimethylformamide (DMF)[2] we isolated β-epoxy ketones in good yield and find that this is a convenient method for the synthesis of β-epoxy ketones from α-bromo ketones using nickel carbonyl as a homogeneous reagent.

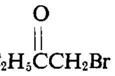
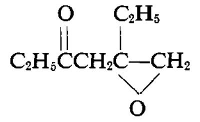
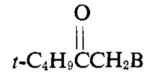
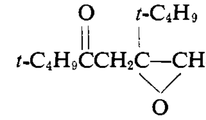
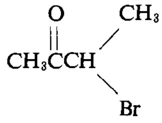
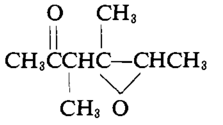
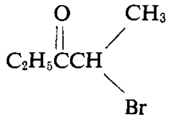
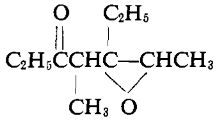
The reaction of 0.1 mol of an α-bromo ketone and 0.06 mol of nickel carbonyl in 30 ml of DMF was carried out under argon at 30° for 5 hr. The reaction mixture was then poured into dilute HCl aqueous solution and extracted with ether. The ether extract was washed with water and dilute sodium bicarbonate solution and then dried over anhydrous sodium sulfate. After removal of ether the residue was distilled and the product was characterized by infrared and nmr spectra, analysis, and chemical reactions. For example, the reaction of bromomethyl *t*-butyl ketone and nickel carbonyl gave a compound (I), bp 94° (9 mm), which showed a carbonyl band at 1735 cm^{-1} in its infrared spectrum. The nmr spectrum showed two singlet bands (9 H) for protons on two *t*-butyl groups at τ 9.10 and 8.89, and complex bands (4 H) for protons on two methylene groups at 7.1∼7.7. *Anal.* Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.70; H, 11.15. This compound gave a negative ferric chloride test, showing the absence of enolizable protons, but gave a positive test with sodium thiosulfate solution, indicating the presence of an epoxide ring. When this compound is heated above 130°, dehydration occurred to give 2,4-di-*t*-butylfuran[3] (II), bp 184°. It has been reported that cyclohexenylacetone was converted into 2,3-tetramethylene-5-methylfuran by the dehydration of the epoxide intermediate with *p*-toluenesulfonic acid.[1] In our experiments it was found that the β-epoxy ketones can be used as unique starting materials for synthesizing furans. The formation of unsymmetrical furans by the reaction of α-bromo ketones and magnesium[3] or zinc[4] has recently been reported by two groups, but no attempts have been made to isolate epoxides in either case.

Upon reduction of I with lithium aluminum hydride in ether at 35° for 3 hr, a glycol (III), mp 84∼86°, was obtained. The nmr spectrum showed two singlet bands (9 H) at τ 9.11 and 9.06, a singlet (3 H) at 8.80, two doublets (1 H) for methylene protons at 8.46 and 8.50, two doublets (1 H) for a tertiary proton, and a singlet (2 H) for alcoholic protons at 6.73 which disappeared by addition of D_2O. *Anal.* Calcd for $C_{12}H_{26}O_2$: C, 71.23; H, 12.95. Found: C, 71.37; H, 12.90. Formation of III by lithium aluminum hydride reduction of I is consistent with the general mode of rupture of primary linkage observed in substituted epoxide.[5]



The results of formation of β-epoxy ketones are given in Table I.

Table I. Formation of β-Epoxy Ketones from α-Bromo Ketones and Nickel Carbonyl

α-Bromo ketone	Product	% yield[a]
 $C_2H_5\overset{\overset{O}{\|}}{C}CH_2Br$	 $C_2H_5\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{C_2H_5}{|}}{C}\underset{O}{\text{—}}CH_2$	52
 $t\text{-}C_4H_9\overset{\overset{O}{\|}}{C}CH_2Br$	 $t\text{-}C_4H_9\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{t\text{-}C_4H_9}{|}}{C}\underset{O}{\text{—}}CH_2$	61
 $CH_3\overset{\overset{O}{\|}}{C}CH\genfrac{}{}{0pt}{}{CH_3}{Br}$	 $CH_3\overset{\overset{O}{\|}}{C}\overset{\overset{CH_3}{|}}{CH}\underset{\underset{CH_3}{|}}{C}\underset{O}{\text{—}}CHCH_3$	70
 $C_2H_5\overset{\overset{O}{\|}}{C}CH\genfrac{}{}{0pt}{}{CH_3}{Br}$	 $C_2H_5\overset{\overset{O}{\|}}{C}\overset{\overset{C_2H_5}{|}}{CH}\underset{\underset{CH_3}{|}}{C}\underset{O}{\text{—}}CHCH_3$	84

[a] Based on halide used.

These β-epoxy ketones are considered to be formed *via* aldol-type condensation between the nickel enolate and the α-bromo ketone, followed by elimination of $NiBr_2$, but a more detailed discussion of the mechanism will be given in a forthcoming paper.

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(1) For example, see H. Freitel and P. Baranger, *Compt. Rend.*, 241 674 (1955).
(2) E. Yoshisato and S. Tsutsumi, *Chem. Commum.*, 33 (1968).
(3) J. E. Dubois and J. Itzkowitch, *Tetrahedron Letters*, 2839 (1965).
(4) T. A.Spencer, R. W. Britton, and D. S. Watt, *J. Am. Chem. Soc.*, **89**, 5727 (1967).
(5) W. G. Brown, *Org. Reactions*, 6, 472 (1951).

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