REACTIONS OF ALKYL HETARYL KETONES WITH CARBON TETRACHLORIDE UNDER LIQUID/SOLID PHASE-TRANSFER CATALYSIS CONDITIONS


Reactions of methyl and ethyl hetaryl ketones in the CCl₄/solid KOH system in the presence of 18 crown-6 at room temperature yield the corresponding 2-hetaryl-2-trichloromethyloxiranes in 8-22% yields. Reactions of sterically hindered ketones of the type (hetaryl)COCHR₂ (R = Me, Et) with CCl₄/OH⁻ form the corresponding α-hydroxy ketones of the type (hetaryl)COC(OH)R₂ in 28-44% yields.

Perhalo alkanes (in particular, carbon tetrachloride) are strong electrophiles that react with carbanions. The chief reaction of a carbanion, generated by the action of a strong base, with CCl₄ is the chlorination reaction [1-8]. Apparently, a Cl⁺ ion becomes detached from CCl₄ and adds to a carbanion as a result of a series of successive steps [7]. The process of chlorination of a carbanion is often accompanied by transformations of the chlorinated products, i.e., dimerization (phenyl- and diphenylacetonitrile [5]), formation of compounds containing a trichloromethyl group [1, 6, 8], and other reactions. The possibility of generation of carbanions from CH acids in two-phase catalytic systems considerably simplifies the reactions of these CH acids with CCl₄ and opens up new possibilities of synthesis [5-11].

A study of phase-transfer catalytic (PTC) reactions of aromatic ketones with CCl₄ has shown that benzyl methyl ketone in the system CCl₄ - 50% aqueous NaOH/Bu₄NBr at room temperature forms PhCHCl₂, PhCCl₃ and 2-methyl-2-trichloromethyl-3-phenyloxirane [9]. Acetophenone under analogous conditions yields a mixture of two epoxides, i.e., 2-phenyl-2-trichloromethyloxirane (9% yield) and 2-phenyl-2-trichloromethyl-3-chlorooxirane (10%), as well as benzoic acid. Formation of the indicated oxiranes involves the step of halogenation of the ketone [10]. A detailed study of reactions of ketones of the type PhCOCH₂R (R = H, C₁...C₄-alkyl, PhCH₂) with CCl₄ in presence of 50% aqueous NaOH and Bu₄NBr [11] has generally confirmed the above conclusions. Use of liquid/solid type PTC (CCl₄/solid KOH/dibenzo-18-crown-6) makes it possible to obtain from acetophenone only one product, 2-phenyl-2-trichloromethyloxirane (10.5%) [12]. Reactions of hetaryl ketones with carbon tetrachloride under PTC conditions have not been studied.

We studied reactions of a series of alkyl hetaryl ketones with carbon tetrachloride under phase-transfer catalysis conditions. Use of 50% aqueous alkali as the base was found to be ineffective, since it resulted in the formation of a complex mixture of products in very low yields. Use of the liquid/solid (CCl₄/KOH) system in the presence of 18-crown-6 as phase transfer agent at room temperature made it possible to carry out the reaction of ketones I-IV with carbon tetrachloride and to show that the reaction of ketones I-IV with CCl₄ takes place selectively and results in the formation of the corresponding 2-hetaryl-2-trichloromethyloxiranes (V-VIII) (scheme 1).

Compounds V-VIII were isolated from the reaction mixture by vacuum distillation in 8-22% yields. All the oxiranes obtained are very unstable and resinify quickly on contact with air. As a result, from 5-bromo-2-acetylthiophene, 5-methyl-2-acetyltiophene and 2-acetylpuridine we were unable to obtain hetaryl-substituted 2-trichloromethyloxiranes in pure form, which were recorded only chromatograph-mass-spectrometrically, i.e., 2-(5-bromo-2-thienyl)-2-trichloromethyloxirane, m/z 321 (M⁺); 2-(5-methyl-2-thienyl)-2-trichloromethyloxirane, m/z 256 (M⁺); 2-(2-pyridyl)-2-trichloromethyloxirane, m/z 237 (M⁺) (for the ion containing 35Cl, respectively). In the reaction of 4-acetylpuridine with CCl₄/OH⁻, not even trace amounts of any product could be obtained.
The identification of oxiranes V-VIII obtained was carried out with $^1$H and $^{13}$C NMR (VI and VII) and mass-spectrometrically. In the $^1$H-NMR spectrum of oxirane V, a multiplet $\Delta$ of type $MX$ was observed, characteristic of the furan ring with a substituent in the 2 position, and two doublets of AB type nonequivalent protons of the oxirane ring (3.35 and 3.73 ppm). A 5.1-Hz splitting is characteristic of the geminal interaction of the protons of the oxirane ring. The assignment of signals in the $^{13}$C-NMR spectra of compounds VI and VII was based on the coupling constant of $^{13}$C–$^1$H.

Thus, methyl and ethyl hetaryl ketones I-IV as a whole react with CCl$_4$/OH$^-$ similarly to acetophenone. Products V-VIII obviously also are formed as a result of chlorination of the carbanion with the subsequent addition of CCl$_3$ anion and intramolecular cyclization.

Sterically hindered ketones, i.e., 2-methyl-1-(2-thienyl)-1-propanone (IX), 1-(2-thienyl)-2-ethyl-1-butanone (X), and 2-methyl-1-(2-furyl)-1-propanone (XI) in the CCl$_4$/KOH system in the presence of 18-crown-6 at room temperature do not undergo any transformations. Stirring of the reaction mixture at an elevated temperature leads to the formation of $\alpha$-hydroxy ketones XII-XIV (scheme 2):

The formation of compounds XII-XIV apparently takes place via the intermediate chlorination products XV-XVII [for compound XVI m/z 216 (M$^+$)], which disappear completely from the mixture toward the end of the reaction. These data are consistent with the work of Meyers and Kolb [3, 13], who obtained the corresponding $\alpha$-hydroxy ketone by reacting isopropyl phenyl ketone with CCl$_4$ in the presence of alkali. However, in the case of reaction of ketones IX and XI with CCl$_4$/OH$^-$, the intermediate $\alpha$-chloro ketones XV and XVII were not recorded mass-spectrometrically because of fast transformations.

The method of synthesis of compounds XII and XIV, based on the reaction of bromination of ketones IX and XI by bromine followed by treatment of the intermediate with sodium ethoxide (or potassium hydroxide) and hydrolysis [14-16], is less convenient and less safe.

Thus, methyl and ethyl hetaryl ketones I-IV react with CCl$_4$/OH$^-$ to form hetaryl-substituted 2-trichloromethyloxiranes V-VIII. In the case of ketones IX-XI, analogous products cannot be obtained, obviously because of steric hindrances. The corresponding $\alpha$-hydroxy ketones XII-XIV were isolated as the main products in this case.

**EXPERIMENTAL**

The $^1$H- and $^{13}$C-NMR spectra were recorded for solutions in CDCl$_3$ with a Bruker WH-90/DS spectrometer at 90 and 22.63 MHz, respectively. The internal standard used was TMS. The mass spectra were obtained with a Kratos MS-25 chromatograph-mass spectrometer with 70-eV ionizing electrons. The GLC analysis was carried out with a Chrom-5 chromatograph.