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

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Reactions of methyl and ethyl hetaryl ketones in the CCl_4/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)$COCHR_2$ (R = Me, Et) with CCl_4/OH^- form the corresponding α-hydroxy ketones of the type (hetaryl)$COC(OH)R_2$ 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 CCl_4 is the chlorination reaction [1-8]. Apparently, a Cl^+ ion becomes detached from CCl_4 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 CCl_4 and opens up new possibilities of synthesis [5-11].

A study of phase-transfer catalytic (PTC) reactions of aromatic ketones with CCl_4 has shown that benzyl methyl ketone in the system CCl_4 – 50% aqueous NaOH/Bu_4NBr at room temperature forms $PhCHCl_2$, $PhCCl_3$ 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 $PhCOCH_2R$ (R = H, $C_1...C_4$-alkyl, $PhCH_2$) with CCl_4 in presence of 50% aqueous NaOH and Bu_4NBr [11] has generally confirmed the above conclusions. Use of liquid/solid type PTC (CCl_4/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 (CCl_4/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 CCl_4 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-acetylthiophene and 2-acetylpyridine we were unable to obtain hetaryl-substituted 2-trichloromethyloxiranes in pure form, which were recorded only chromato-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 ^{35}Cl, respectively). In the reaction of 4-acetylpyridine with CCl_4/OH^-, not even trace amounts of any product could be obtained

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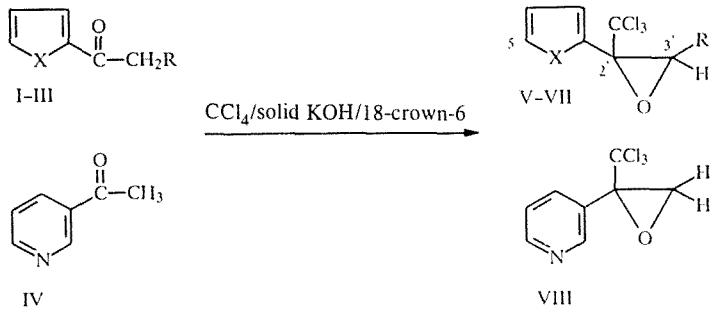
Scheme 1



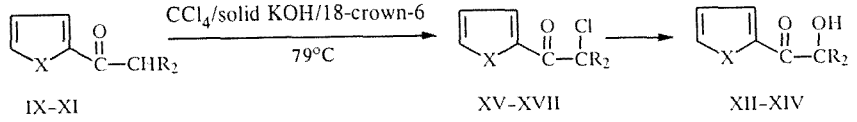
X = O, R = H (I, V); X = S, R = H (II, VI); X = S, R = CH_3 (III, VII)

The identification of oxiranes V-VIII obtained was carried out with ^1H and ^{13}C NMR (VI and VII) and mass-spectrometrically. In the ^1H-NMR spectrum of oxirane V, a multiplet A 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 $^{13}C-^1H$.

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 α-hydroxy ketones XII-XIV (scheme 2):

Scheme 2



IX, XII, XV X = S, X = CH_3; X, XIII, XVI X = S, R = C_2H_5; XI, XIV, XVII X = O, R = CH_3

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 α-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 α-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 α-hydroxy ketones XII-XIV were isolated as the main products in this case.

EXPERIMENTAL

The ^1H- 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 chromato-mass spectrometer with 70-eV ionizing electrons. The GLC analysis was carried out with a Chrom-5 chromatograph

with a flame ionization detector on a glass column packed with the phase 5% OV-17 on W-HP chromosorb (80...100 mesh); analysis temperature, 140-160°C.

2-Acetylthiophene, 2-acetylfuran, 2-, 3-, and 4-acetylpyridines and 18-crown-6 were products of the Fluka Co.; 1-(2-thienyl)-1-propanone III was obtained by acylating thiophene with propionyl chloride by the Friedel–Crafts reaction [17]; 2-methyl-1-(2-thienyl)-1-propanone IX and 1-(2-thienyl)-2-ethyl-1-butanone X were synthesized by alkylating 2-acetylthiophene with the corresponding alkyl halides under PTC conditions according to [18]; 2-methyl-1-(2-furyl)-1-propanone XI was obtained by alkylating 2-acetylfuran with methyl iodide [18].

The results of the elemental analysis of the synthesized compounds are consistent with the calculated results.

2-(2-Furyl)-2-trichloromethyloxirane (V). To a solution of 9.90 g (90 mmole) of 2-acetylfuran I and 0.71 g (2.7 mmole) of 18-crown-6 in 200 ml of CCl_4 is added 25.2 g (0.45 mole) of fine KOH powder. The reaction mixture is stirred for 8 h at room temperature, filtered through L 5/40 silica gel, and excess CCl_4 is driven off on a rotary evaporator. Vacuum distillation yields compound V. b.p. 71-72°C/1 Torr. ^{1}H NMR spectrum: 3.35 and 3.73 (2H, dd, J = 5.1 Hz, CH_2). 6.43 (1H, dd, J = 3.4 and 1.8 Hz, 4-H); 6.77 (1H, dd, J = 3.4 and 0.7 Hz, 3-H); 7.46 (1H, dd, J = 1.8 and 0.7 Hz, 5-H). Mass spectrum, m/z (I_{rel}, %): 226 (28, M^+), 161 (35), 148 (100), 133 (78), 109 (46), 95 (93), 81 (92), 63 (54), 53 (27), 39 (22). Yield, 3.20 g (16%).

Oxiranes VI-VIII are similarly obtained.

2-(2-Thienyl)-2-trichloromethyloxirane (VI) is obtained from 2-acetylthiophene II. The reaction takes 15 h. b.p. 102-103°C/1.5 Torr. ^{1}H-NMR spectrum: 3.13 and 3.76 (2H, dd, J = 5.3 Hz, CH_2); 7.02 (1H, dd, J = 5.1 and 3.6 Hz, 4-H); 7.37 (1H, dd, J = 5.1 and 1.2 Hz, 5-H); 7.44 (1H, dd, J = 3.6 and 1.2 Hz, 3-H). ^{13}C-NMR spectrum: 55.16 ($CH_{(3')}$); 64.86 ($CH_{(2')}$); 99.44 (CCl_3); 126.30 ($C_{(3)}$); 127.00 ($C_{(5)}$); 129.76 ($C_{(4)}$); 135.08 ($C_{(2)}$). Mass spectrum, m/z (I_{rel}, %): 242 (26, M^+); 177 (63), 142 (74), 125 (18), 111 (70), 97 (100), 69 (18), 58 (13), 45 (19). Yield, 12%.

3-Methyl-2-(2-thienyl)-2-trichloromethyloxirane (VII) is obtained from 1-(2-thienyl)-1-propanone III in 5 h. B.P. 95-97°C/1 Torr. ^{1}H-NMR spectrum: 1.18 (3H, d, J = 5.3 Hz, 3'-CH_3); 3.99 (1H, q, J = 5.3 Hz, $\underline{CH}CH_3$); 7.06 (1H, dd, J = 5.1 and 3.6 Hz, 4-H); 7.33 (1H, dd, J = 5.1 and 1.2 Hz, 5-H); 7.43 (1H, dd, J = 3.6 and 1.2 Hz, 3-H). ^{13}C-NMR spectrum: 14.46 (q.d, J = 128.0 and 5.9, Hz, CH_3); 60.47 (d.q., J = 177.2 and 5.9 Hz, $C_{(3')}$); 69.27 (s, $C_{(2')}$); 100.60 (s, CCl_3); 126.39 (ddd, J = 169.3, 5.9, and 3.9 Hz, $C_{(3)}$); 127.28 (ddd, J = 187.0, 9.8, and 5.9 Hz, $C_{(5)}$); 130.30 (ddd, J = 169.3, 9.8, and 5.9 Hz, $C_{(4)}$); 133.76 (m, $C_{(2)}$). Mass spectrum, m/z (I_{rel}, %): 256 (3, M^+), 212 (10), 194 (86), 177 (100), 142 (87), 111 (60), 97 (10), 84 (72), 63 (20), 45 (20). Yield, 22%.

2-(3-Pyridyl)-2-trichloromethyloxirane (VIII) is obtained from 3-acetylpyridine in 8 h. b.p. 150°C/1 Torr. ^{1}H-NMR spectrum: 6.04 and 6.28 (2H, d.d, J = 3.0 Hz, CH_2); 8.10 (1H, m, 5-H); 8.75 (1H, m, 4-H); 8.96 (1H, m, 6-H); 9.27 (1H, m, 2-H). Mass spectrum, m/z (I_{rel}, %): 237 (13, M^+), 174 (15), 172 (15), 160 (13), 138 (13), 120 (100), 110 (10), 106 (46), 102 (11), 92 (45), 84 (14), 78 (21), 75 (17), 65 (20), 51 (26). Yield, 8%.

2-Hydroxy-2-methyl-1-(2-thienyl)-1-propanone (XII). To a solution of 4.62 g (30 mmole) of 2-methyl-1-(2-thienyl)-1-propanone IX and 0.24 g (0.9 mmole) of 18-crown-6 in 60 ml of CCl_4, fine KOH powder (16.8 g, 0.3 mole) is added in 0.1-mole portions. The reaction mixture is refluxed for 8 h, then filtered, and excess CCl_4 is driven off on a rotary evaporator. Vacuum distillation of the residue yields product XII. b.p. 142-144°C/10 Torr. Lit. data [14]: b.p. 150°C/10 Torr. ^{1}H NMR spectrum: 1.59 (6H, s, $2CH_3$); 4.12 (1H, br.s, OH); 7.14 (1H, dd, J = 5.0 and 4.0 Hz, 4-H); 7.68 (1H, dd, J = 5.0 and 1.0 Hz, 5-H); 7.98 (1H, dd, J = 4.0 and 1.0 Hz, 3-H). Mass spectrum, m/z (I_{rel}, %): 170 (0.6, M^+), 127 (3), 111 (20), 84 (8), 59 (100), 43 (28). Yield, 1.93 g (38%).

Ketones XIII and XIV are similarly synthesized.

2-Hydroxy-2-ethyl-1-(2-thienyl)-1-butanone (XIII) is obtained from 2-ethyl-1-(2-thienyl)-1-butanone X in 29 h. b.p. 185-188°C/10 Torr. ^{1}H-NMR spectrum: 0.82 (6H, t, J = 7.5 Hz, CH_3); 1.97 (4H, q, J = 7.5 Hz, $2CH_2$); 3.93 (1H, br.s, OH); 7.16 (1H, dd, J = 5.0 and 4.0 Hz, 4-H); 7.69 (1H, dd, J = 5.0 and 1.1 Hz, 5-H); 7.90 (1H, dd, J = 4.0 and 1.1 Hz, 3-H). Mass spectrum, m/z (I_{rel}, %): 198 (1, M^+), 180 (2), 169 (3), 141 (14), 111 (26), 87 (100), 69 (18), 57 (57), 45 (96), 39 (33). Yield, 28%.

2-Hydroxy-2-methyl-1-(2-furyl)-1-propanone (XIV) is obtained from 2-methyl-1-(2-furyl)-1-propanone XI in 11 h. b.p. 109-110°C/10 Torr. Lit. data [16]: b.p. 107°C/14 Torr. ^{1}H-NMR spectrum: 1.60 (6H, s, $2CH_3$); 4.08 (1H, s, OH); 6.60 (1H, dd, J = 3.6 and 1.8 Hz, 4-H); 7.43 (1H, dd, J = 3.6 and 0.8 Hz, 3-H); 7.65 (1H, dd, J = 1.8 and 0.8 Hz, 5-H). Mass spectrum, m/z (I_{rel}, %): 154 (3, M^+), 111 (4), 95 (18), 68 (9), 59 (100), 43 (18), 39 (13). Yield, 44%.

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