Organic Chemistry

Alkylation of β-dicarbonyl compounds with 1,2-dibromocyclohexane

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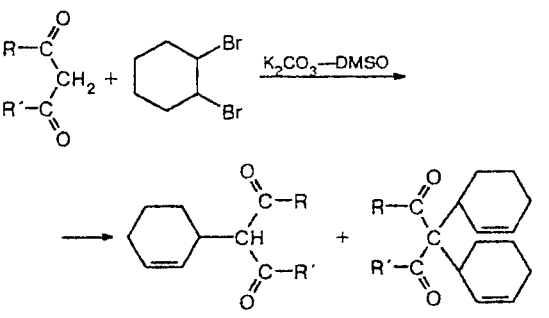
Alkylation of acetylacetone, ethyl acetoacetate, and diethyl malonate with 1,2-dibromocyclohexane in the presence of K_2CO_3 in DMSO occurs only as *C*-alkylation accompanied by dehydrobromination, whereas a similar reaction of dimedone follows both *C*- and *O*-alkylation pathways.

Key words: β-dicarbonyl compounds, alkylation with 1,2-dibromocyclohexane.

Alkylation of β-dicarbonyl compounds with α,ω-dibromoalkanes in the K_2CO_3—DMSO system has been studied fairly comprehensively.[1,2] However, no systematic data on the alkylation of β-dicarbonyl compounds with cyclic dibromides have been reported. This work is devoted to the study of alkylation of some β-dicarbonyl compounds with 1,2-dibromocyclohexane in the K_2CO_3—DMSO system.

Previously,[1,2] it has been noted that the direction of alkylation of β-dicarbonyl compounds with α,ω-dibromoalkanes depends both on the structure of the initial β-dicarbonyl compound and on the number of C atoms in the dibromide. By analogy with published data,[1,2] it might be expected that alkylation of β-dicarbonyl compounds with 1,2-dibromocyclohexane in the K_2CO_3—DMSO system would give *C*-mono-, *C,C*-di-, *C,C*-cyclo-, *O*-, and *C,O*-alkylation products. We found that the alkylation of acyclic β-dicarbonyl compounds, *viz.*, acetylacetone, ethyl acetoacetate, and diethyl malonate, occurs mainly as *C*-monoalkylation and gives compounds **1**, **3**, **5** as the major products and compounds **2**, **4**, **6** as minor *C,C*-dialkylation products (Scheme 1).

Scheme 1



1, **3**, **5** **2**, **4**, **6**

1, **2**: R = R′ = Me
3, **4**: R = Me, R′ = OEt
5, **6**: R = R′ = OEt

The structures of products **1**—**6** were confirmed by synthesizing them by an alternative route, *i.e.*, by alkyla-

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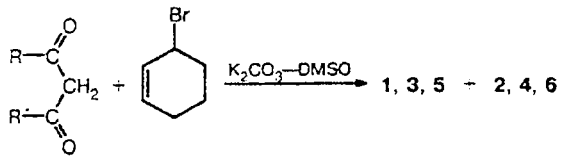
tion of the above-mentioned β-dicarbonyl compounds with 3-bromocyclohexene in the K_2CO_3—DMSO system (Scheme 2).

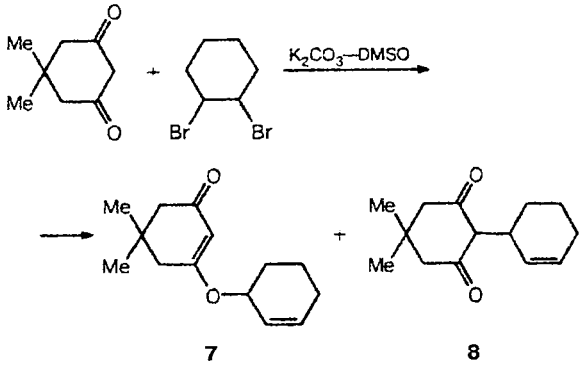
Scheme 2



To elucidate the order in which alkylation and dehydrobromination occur during the reaction of β-dicarbonyl compounds with 1,2-dibromocyclohexane, we studied the behavior of the latter compound under the alkylation conditions (80 °C, 10 h) and found that it remains unchanged. Hence, it can be assumed that the carbanion generated from a dicarbonyl compound under the action of the catalytic system attacks the 1,2-dibromocyclohexane molecule to give the intermediate 2-bromocyclohexyl derivative, which is then debrominated.

Unlike the alkylation of acetylacetone, ethyl acetoacetate, and ethyl malonate, the alkylation of dimedone with 1,2-dibromocyclohexane carried out under the same conditions follows both *O*- and *C*-alkylation pathways and affords compounds **7** and **8** in nearly equal yields (Scheme 3).

Scheme 3



Thus, the direction of alkylation of β-dicarbonyl compounds with 1,2-dibromocyclohexane in the K_2CO_3—DMSO system depends on the structure of the substrate.

Experimental

NMR spectra were recorded on an FT-80A spectrometer (80 and 20 MHz for ^1H and ^{13}C nuclei, respectively) in $CDCl_3$ using tetramethylsilane as the internal standard.

The starting 1,2-dibromocyclohexane and 3-bromocyclohexene were obtained by known procedures.[3,4]

General procedure of alkylation. 1,2-Dibromocyclohexane (24.2 g, 0.1 mol) was added to an intensely stirred mixture of a β-dicarbonyl compound (0.1 mol) and calcined potassium carbonate (34.5 g, 0.25 mol) in 50mL of DMSO. The reaction with 3-bromocyclohexene (16.1 g, 0.1 mol) was carried out in the presence of 21 g (0.15 mol) of K_2CO_3. The reaction mixture was stirred for 10 h at 80 °C, cooled, diluted with water until K_2CO_3 dissolved, and extracted with benzene. The benzene extracts were washed with water and dried with anhydrous $CaCl_2$. After evaporation of the benzene, the residue was distilled *in vacuo*.

The reaction of acetylacetone (10 g) and 1,2-dibromocyclohexane gave compounds **1** and **2**.

3-(Cyclohex-2-enyl)pentane-2,4-dione (1), yield 13.8 g (76.7%), b.p. 77—79 °C (2 Torr), n_D^{20} 1.4872, d_4^{20} 1.0501. Found (%): C, 73.09; H, 8.91. $C_{11}H_{16}O_2$. Calculated (%): C, 73.33; H, 8.89. ^1H NMR, δ: 1.27—1.65 (m, 4 H, 2 CH_2); 1.97 (m, 2 H, CH_2); 2.18 (s, 6 H, 2 CH_3); 3.00 (m, 1 H, CH); 3.61 (d, 1 H, CH); 5.18 (d, 1 H, CH=); 5.75 (m, 1 H, CH=). ^{13}C NMR, δ: 20.25, 24.49, 26.18, 29.68 (C(sp^3) of the cyclohexene ring); 35.18 and 35.24 (2 CH_3); 74.14 (CH); 126.80 (CH=); 129.42 (CH=); 149.17 (C=O); 149.38 (C=O).

3,3-Di(cyclohex-2-enyl)pentane-2,4-dione (2), yield 2.2 g (8.6%), b.p. 102—103 °C (1 Torr), n_D^{20} 1.4897, d_4^{20} 0.9874. Found (%): C, 78.42; H, 9.22. $C_{17}H_{24}O_2$. Calculated (%): C, 78.46; H, 9.23. ^1H NMR, δ: 1.12—1.69 (m, 8 H, 4 CH_2); 1.99 (m, 4 H, CH_2); 2.20 (s, 6 H, 2 CH_3); 3.08 (m, 2 H, 2 CH); 5.20 (d, 2 H, 2 CH=); 5.71 (m, 2 H, 2 CH=).

The reaction of acetylacetone (10 g) with 3-bromocyclohexene gave compounds **1** (yield 14.6 g, 81.1%) and **2** (yield 3.1 g, 11.9%), whose characteristics coincided with those given above.

The reaction of ethyl acetoacetate (13 g) and 1,2-dibromocyclohexane gave compounds **3** and **4**.

Ethyl 2-(cyclohex-2-enyl)acetoacetate (3), yield 15.24 g (72.6%), b.p. 97—99 °C (2 Torr), n_D^{20} 1.4722, d_4^{20} 1.0553. Found (%): C, 68.48; H, 8.53. $C_{12}H_{18}O_3$. Calculated (%): C, 68.57; H, 8.57. ^1H NMR, δ: 1.25 (t, 3 H, CH_3); 1.27—1.75 (m, 4 H, CH_2); 1.99 (m, 2 H, CH_2); 2.21 (s, 3 H, CH_3); 2.95 (m, 1 H, CH); 3.40 (d, 1 H, CH); 4.21 (q, 2 H, CH_2O); 5.42 (t, 1 H, CH); 5.72 (d, 1 H, CH=). ^{13}C NMR, δ: 13.56 (CH_3); 20.36, 24.48, 26.18, 29.09 (C(sp^3) of the cyclohexene ring); 34.44 (CH_3); 34.52 (CH_3); 60.63 (CH_2); 64.61 (CH); 126.95 (CH=); 129.01 (CH=); 168.11 (C=O); 168.14 (C=O).

Ethyl 2,2-di(cyclohex-2-enyl)acetoacetate (4), yield 4.5 g (15.5%), b.p. 132—134 °C (2 Torr), n_D^{20} 1.4850, d_4^{20} 1.0308. Found (%): C, 74.49; H, 8.97. $C_{18}H_{26}O_3$. Calculated (%): C, 78.48; H, 8.96. ^1H NMR, δ: 1.24 (t, 3 H, CH_3); 1.25—1.79 (m, 8 H, 4 CH_2); 2.00 (m, 4 H, 2 CH_2); 2.20 (s, 3 H, CH_3); 2.99 (m, 2 H, 2 CH); 4.25 (q, 2 H, CH_2O); 5.40 (m, 2 H, 2 CH=); 5.70 (d, 2 H, 2 CH=).

The reaction of ethyl acetoacetate and 3-bromocyclohexene gave compounds **3** (yield 16.2 g, 77.1%) and **4** (yield 3.9 g, 13.4%), whose characteristics coincided with those given above.

The reaction of diethyl malonate (16 g) and 1,2-dibromocyclohexane gave compounds **5** and **6**.

Diethyl cyclohex-2-enylmalonate (5), yield 17.8 g (74.2%), b.p. 109—111 °C (2 Torr), n_D^{20} 1.4610, d_4^{20} 1.0542. Found (%): C, 64.03; H, 8.37. $C_{13}H_{20}O_4$. Calculated (%): C, 64.97; H, 8.33. ^1H NMR, δ: 1.15 and 1.17 (t, 6 H, 2 CH_3); 1.19—1.97 (m, 4 H, 2 CH_2); 2.30 (m, 1 H, CH); 3.22 (d, 1 H, CH); 4.20 and 4.22 (q, 4 H, 2 CH_2O); 5.57 (d, 1 H, CH=); 5.79 (d, 1 H, CH=). ^{13}C NMR, δ: 13.58 and 13.68 (2 CH_3); 20.58, 24.54, 26.22, 34.85 (C(sp^3) of the cyclohexene ring); 56.67

(CH): 60.77 and 61.64 (2 CH_2O); 127.27 (CH=); 128.87 (CH=); 167.91 and 167.98 (2 C=O).

Diethyl di(cyclohex-2-enyl)malonate (6), yield 3.9 g (12.3%), b.p. 138—142 °C (2 Torr), m.p. 75—76 °C (from EtOH). Found (%): C, 71.31; H, 8.78. $C_{19}H_{28}O_4$. Calculated (%): C, 71.25; H, 8.75. ^{1}H NMR, δ: 1.16—1.18 (t, 6 H, 2 CH_3); 1.20—1.97 (m, 8 H, 4 CH_2); 2.97 (m, 2 H, 2 CH); 4.20 and 4.23 (q, 4 H, 2 CH_2O); 5.57 (d, 2 H, 2 CH=); 5.75 (d, 2 H, 2 CH=).

The reaction of diethyl malonate (16 g) and 3-bromocyclohexene gave compounds **5** (yield 18.9 g, 78.7%) and **6** (yield 4.0 g, 12.5%), whose characteristics coincided with those given above.

The reaction of dimedone (14 g) and 1,2-dibromocyclohexane gave compounds **7** and **8**.

5,5-Dimethyl-3-(cyclohex-2-enyloxy)cyclohex-2-enone (7), yield 9.15 g (41.6%), b.p. 172—173 °C (2 Torr), a yellowish resin-like substance. Found (%): C, 76.32; H, 9.08. $C_{14}H_{20}O_2$. Calculated (%): C, 76.36; H, 9.09. ^{1}H NMR, δ: 1.18 (s, 6 H, 2 CH_3); 1.30—1.90 (m, 4 H, 2 CH_2); 2.12 (m, 2 H, CH_2); 2.26 (s, 2 H, CH_2); 2.34 (s, 2 H, CH_2); 3.71 (m, 2 H, CHO); 5.81 (d, 1 H, CH=); 6.08 (d, 1 H, CH=); 7.25 (s, 1 H, CH=). ^{13}C NMR, δ: 21.30, 24.89, 27.57 (C(sp^3) of the cyclohexene ring); 28.09 (CH_3); 28.44 (CH_3); 31.57 (CH_2); 42.83 (CH_2); 50.17 (CH_2); 50.27 (CHO); 116.72 (CH=); 130.53 (CH=); 132.35 (CH=); 173.40 (=C—O); 189.14 (C=O).

5,5-Dimethyl-2-(cyclohex-2-enyl)cyclohexane-1,3-dione (8), yield 8.1 g (36.8%), b.p. 189—191 °C (2 Torr), a yellowish resin-like substance. Found (%): C, 76.30; H, 9.08. $C_{14}H_{20}O_2$. Calculated (%): C, 76.36; H, 9.09. ^{1}H NMR, δ: 1.12 (s, 6 H, 2 CH_3); 1.28—1.86 (m, 4 H, 2 CH_2); 2.10 (m, 2 H, CH_2); 2.29 (s, 2 H, CH_2); 2.45 (s, 2 H, CH_2); 3.12 (m, 1 H, CH); 5.61 (d, 1 H, CH=); 5.77 (d, 1 H, CH=); 7.01 (br.s, 1 H, OH).

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