

SHORT  
COMMUNICATIONS

## Synthesis of Triketones from Meldrum's Acid

M. I. Skuratova, O. V. Fedotova, and V. G. Kharchenko

Chernyshevskii Saratov State University, Astrakhanskaya 83, Saratov, 410026 Russia

Received July 10, 2001

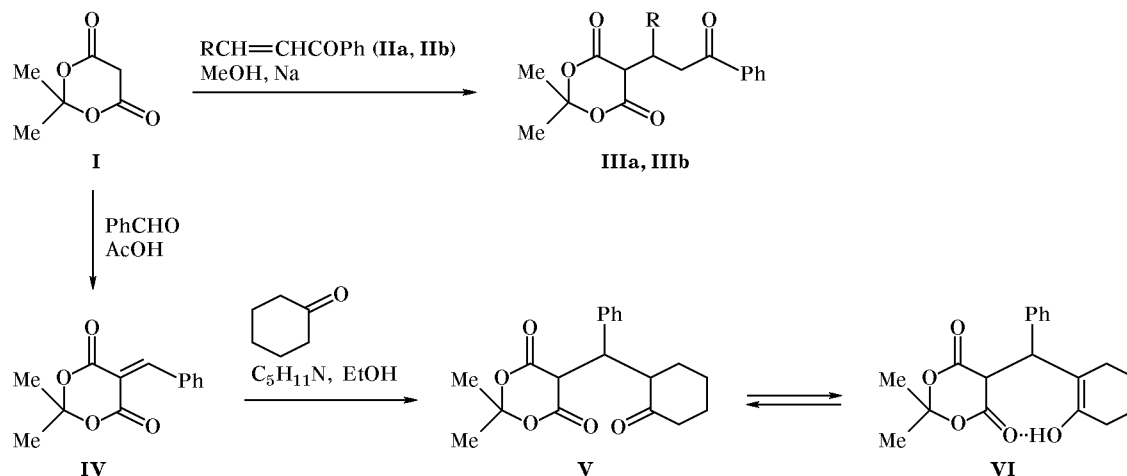
We were the first to synthesize triketones having a Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) fragment. Meldrum's acid, like barbituric acid and its analogs, exhibits a depressant effect on the central nervous system and possesses a low toxicity [1]. This makes it promising to search for new pharmacologically active substances in the series of 5-substituted 2,2-dimethyl-1,3-dioxane-4,6-diones.

Triketones **IIIa** and **IIIb** were synthesized by Michael addition of Meldrum's acid (**I**) to  $\alpha,\beta$ -unsaturated ketones **IIa** and **IIb**, respectively, in basic medium (Scheme 1). Meldrum's acid is a CH acid capable of forming the corresponding sodium salt. The latter was generated *in situ* and was treated with chalcone **II**. 5-Benzylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (**IV**) reacted with cyclohexanone to afford unsymmetrical bicyclic oxo-1,5-diketone **V** which exists in equilibrium with enol form **VI** (Scheme 1). Functionalization of tricarbonyl compounds via introduction of a Meldrum's acid moiety considerably extends their synthetic potential, thus stimulating

development of the chemistry of such specific oxo-1,5-diketones.

**5-(1,3-Diphenyl-3-oxopropyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (IIIa).** To a solution of 1.44 g of Meldrum's acid [2] in 20 ml of anhydrous methanol we added with stirring a solution of 0.7 g of sodium in 10 ml of anhydrous methanol and, after 10 min, a solution of 2.08 g of chalcone **IIa** in 20 ml of anhydrous methanol. The mixture was stirred for 5–6 h at room temperature, 3 ml of concentrated hydrochloric acid was added, and the precipitate of NaCl was filtered off. The filtrate was diluted with water and extracted with chloroform. The extract was dried over magnesium sulfate and evaporated, and the oily residue was ground with hexane. Yield 0.3 g (41%), mp 97–98°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1774, 1738, 1690 (C=O).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.34 s (3H,  $\text{CH}_3$ ), 1.67 s (3H,  $\text{CH}_3$ ), 3.69–3.8 m (2H,  $\text{CH}_2$ ), 4.28–4.4 m (1H,  $\text{PhCH}$ ), 4.52–4.76 m (1H, CH), 7.43–8.17 m (10H,  $\text{H}_{\text{arom}}$ ). Found, %: C 72.03; H 5.95.  $\text{C}_{21}\text{H}_{20}\text{O}_5$ . Calculated, %: C 71.59; H 5.68.

Scheme 1.



R = Ph (a),  $\text{C}_6\text{H}_4\text{OCH}_3$ -4 (b).

**5-[1-(4-Methoxyphenyl)-3-oxo-3-phenylpropyl]-2,2-dimethyl-1,3-dioxane-4,6-dione (IIIb)** was synthesized in a similar way. Yield 36%, mp 116–117°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1774, 1736, 1696 (C=O).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 0.83 s (6H,  $\text{CH}_3$ ), 1.0–1.39 m (2H,  $\text{CH}_2$ ), 3.24 s (3H,  $\text{OCH}_3$ ), 4.1–4.9 m (2H,  $\text{CHCHC}_6\text{H}_4$ ), 6.77–7.94 m (9H,  $\text{H}_{\text{arom}}$ ). Found, %: C 68.91; H 5.75.  $\text{C}_{22}\text{H}_{22}\text{O}_6$ . Calculated, %: C 69.11; H 5.76.

**2,2-Dimethyl-5-[2-oxocyclohexyl(phenyl)methyl]-1,3-dioxane-4,6-dione (V)**. A mixture of 0.5 g of 5-benzylidene-2,2-dimethyl-1,3-dioxan-4,6-dione (**IV**), 5 ml of anhydrous ethanol, 0.2 g of cyclohexanone, and 1 ml of piperidine was heated for 3 h at 50–60°C. The solvent was removed, and the oily residue was subjected to column chromatography on  $\text{Al}_2\text{O}_3$  using hexane–diisopropyl ether as eluent. Yield 0.35 g (50%), mp 140–141°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2700–

2500 ( $\text{OH}_{\text{chelate}}$ ); 1665, 1706 (C=O); 1648 (C=C).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.48–1.64 d (6H,  $2\text{CH}_3$ ), 2.12–2.32 m (2H,  $\text{COCH}_2$ ), 2.86 br.s (1H,  $\text{CH}_2\text{CH}$ ), 3.66–3.92 m (1H,  $\text{COCH}$ ), 4.24–4.44 d (1H,  $\text{CHPh}$ ), 5.92 br.s (1H, OH), 6.98–7.68 m (5H,  $\text{H}_{\text{arom}}$ ). Found, %: C 69.46; H 7.05.  $\text{C}_{19}\text{H}_{22}\text{O}_5$ . Calculated, %: C 69.05; H 6.66.

The IR spectra were recorded on a Specord M-80 spectrometer. The  $^1\text{H}$  NMR spectra were measured on a Varian FT-80A instrument (80 MHz) in  $\text{CDCl}_3$  using TMS as internal reference.

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