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NEW METHOD FOR OBTAINING 2,6-DIAZABICYCLO[2.2.2]-OCTANE-3,5-DIONES

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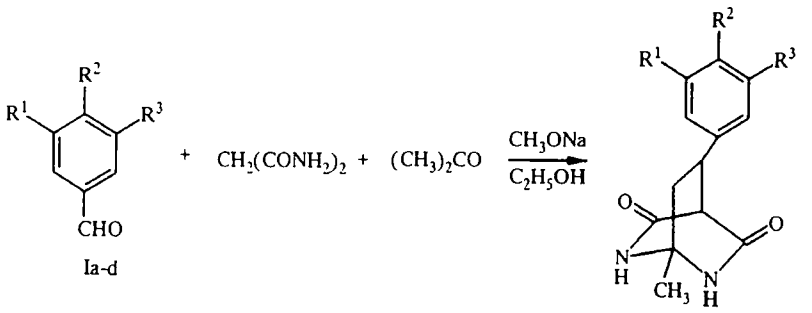
2,6-Diazabicyclo[2.2.2]octane-3,5-diones have so far been a relatively unstudied group of compounds, obtained as a result of intermolecular condensation of pyrimidines with butatriene derivatives [1] or as a result of intramolecular condensation of 3-carbamoyl derivatives of 3,4-dihydropyridines [2].

We have established that it is more convenient to synthesize 2,6-diazabicyclo[2.2.2]octane-3,5-diones II in a one-step three-component condensation from the corresponding aldehydes I, acetone, and malonodiamide in equimolar ratios in the presence of sodium methoxide.



I, II a $R^1 = R^2 = R^3 = H$; b $R^1 = R^2 = H$, $R^3 = OCH_3$; c $R^1 = R^2 = R^3 = OCH_3$; d $R^1 = R^2 = H$, $R^3 = NO_2$

Compared with the method in [2], in this case we no longer need preliminary synthesis of α,β-unsaturated ketones, which often is a laborious task [3].

Compounds IIa-d were obtained by boiling a mixture of 7 mmoles of the corresponding aldehyde I, 7 mmoles malonodiamide, and 14 mmoles acetone in 10 ml ethanol for 30 min. The reaction mixture was cooled; on the next day compounds IIa-d were filtered off and recrystallized from ethanol and acetic acid (10:1).

1-Methyl-8-phenyl-2,6-diazabicyclo[2.2.2]octane-3,5-dione (IIa, $C_{13}H_{14}N_2O_2$). Yield, 40%. T_{mp} 249-251°C. According to the data in [2], T_{mp} 250-251°C.

1-Methyl-8-(*p*-methoxyphenyl)-2,6-diazabicyclo[2.2.2]octane-3,5-dione (IIb, $C_{14}H_{16}N_2O_3$). Yield, 30%. T_{mp} 254-256°C (EtOH – AcOH). PMR spectrum (DMSO-D_6): 1.48 (3H, s, CH_3); 1.90 and 2.30 (2H, dd, 7-H_2); 2.86 (1H, d, 4-H); 3.44 (1H, m, 8-H); 3.63 (3H, s, 4-OCH_3); 6.98 (4H, m, 8-C_6H_4); 8.78 and 8.88 ppm (2H, d, 2– and 6-NH).

1-Methyl-8-(3,4,5-trimethoxyphenyl)-2,6-diazabicyclo[2.2.2]octane-3,5-dione (IIc, $C_{16}H_{20}N_2O_5$). Yield, 35%. T_{mp} 229-231°C (EtOH – AcOH). PMR spectrum (DMSO-D_6): 1.50 (3H, s, CH_3); 1.97 and 2.33 (2H, dd, 7-H_2); 2.95 (1H, d, 4-H); 3.40 (1H, m, 8-H); 3.63 (3H, s, 4-OCH_3); 3.74 (6H, s, 3- and 5-OCH_3); 6.55 (2H, s, 8-C_6H_2); 8.8 and 8.98 ppm (2H, d, 2- and 6-NH).

1-Methyl-8-(3-nitrophenyl)-2,6-diazabicyclo[2.2.2]octane-3,5-dione (IId, $C_{13}H_{13}N_3O_4$). Yield, 47%. T_{mp} 224.5-226.5°C (EtOH – AcOH). PMR spectrum (DMSO-D_6): 1.50 (3H, s, CH_3); 2.20 and 2.24 (2H, dd, 7-H_2); 3.00 (1H, d, 4-H); 3.76 (1H, m, 8-H); 7.63-8.10 (4H, m, 8-C_6H_4); 8.86 and 9.90 ppm (2H, d, 2- and 6-NH).

The elemental analysis data for C, H, and N correspond to the calculated values.

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