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TRISUBSTITUTED 1,3,5-TRIAZINES. 6*. SYNTHESIS OF 2,4,6-TRIS-(ACETONYL)-1,3,5-TRIAZINE

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Acylation of 2,4,6-tris(tert-butoxycarbonylmethyl)-1,3,5-triazine with acetic anhydride in the presence of lithium hydride with subsequent removal of the tert-butoxycarbonyl groups with trifluoroacetic acid leads to 2,4,6-tris(acetonyl)-1,3,5-triazine, the cyclic analog of α-cyanoacetone. The special spectral features of this compound compared with triazines obtained previously are discussed.

Keywords: 2,4,6-tris(acetonyl)-1,3,5-triazine, 2,4,6-tris(*tert*-butoxycarbonylmethyl)-1,3,5-triazine, *tert*-butoxycarbonyl group, acylation.

We recently reported the synthesis of 2,4,6-tris(*tert*-butoxycarbonylmethyl)-1,3,5-triazine (**1**) by the selective decarboxylation of the corresponding hexahydrotriazine [2] and obtained from it substituted 2,4,6-tris(hydroxyiminomethyl)-1,3,5-triazines [3]. The present communication is devoted to developing a method of synthesis of 2,4,6-tris(acetonyl)-1,3,5-triazine (**2**), a compound of interest as the precursor of a whole series of difficultly available triazines.

Our previous attempts to synthesize acylmethyl-1,3,5-triazines were unsuccessful. Reactions of cyanuric chloride with silyl enol ethers led to substitution of only one chlorine atom [4]. The acylation of 2,4,6-tris[di(*tert*-butoxycarbonyl)methylene]hexahydro-1,3,5-triazine and its sodium salt with anhydrides and acid chlorides of aliphatic and aromatic acids was not carried out successfully [2]. The interaction, which is described in the literature [5], of cyanuric chloride and its derivatives with sodioacetoacetic ester led to a complex mixture of products. Under the reaction conditions 4,6-dichloro-2-methoxy-1,3,5-triazine with sodioacetoacetic ester undergoes ketonic and acidic breakdown of the introduced carbethoxyacetylmethyl residues.

Also described in the literature are the preparation of 2,4,6-tris(formyl-R-methyl)-1,3,5-triazines, existing in the tautomeric form of tris(formylalkylidene)hexahydro-1,3,5-triazines (R = ethyl, phenyl, substituted phenyl), from the 2,4,6-trialkyl-1,3,5-triazines and Vilsmeier reagents [6]. However the authors of this work did not attempt to synthesize tris(formylmethyl)-1,3,5-triazine from 2,4,6-trimethyl-1,3,5-triazine and chloromethyleniminium salts.

Convenient methods of synthesis of 2,4,6-tris(acylmethyl)-1,3,5-triazines have therefore not been developed up to the present time.

* For Part 5 see [1].

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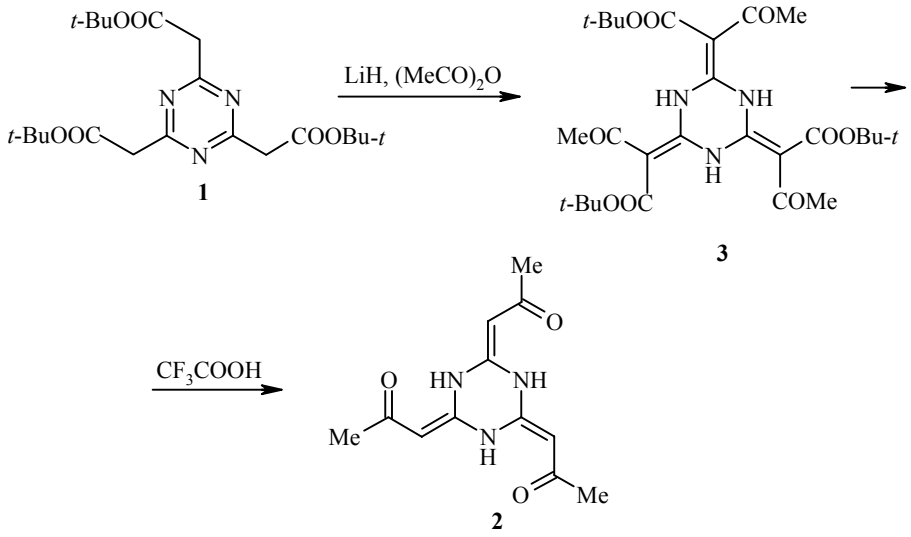
With the aim of obtaining compound **2** we investigated the interaction of triazine **1** with acetic anhydride in the presence of lithium hydride. It was shown that under the conditions studied C-alkylation occurs smoothly at the methylene group of triazine **1** with the formation of 2,4,6-tris(*tert*-butoxycarbonylacetylmethylene)-hexahydro-1,3,5-triazine (**3**), treatment of which with trifluoroacetic acid leads to triazine **2**.



As in the case of 2,4,6-tris[di(*tert*-butoxycarbonyl)methylene]hexahydro-1,3,5-triazine (**4**) synthesized previously by us [7], compound **3** exists in the hexahydrotriazine form as four isomers, characterized by different spatial environments of the NH group. If the acetyl group is designated at side **A**, and the *tert*-butoxycarbonyl group at side **B**, then it may be seen that any NH group may be found with equal probability in an **AA**, **BB**, **AB**, and **BA** environment (in the reaction Scheme compound **3** is depicted as **ABABAB**). Due to the absence of elements of symmetry in the molecule of **3** (except for the mirror plane coinciding with the plane of the triazine ring) **AB** ≠ **BA**. This leads to the fact that together with the four signals of the NH group in the ^{1}H NMR spectrum, in the ^{13}C spectrum of this compound there are four signals for each of the chemically nonequivalent carbon atoms. Using the spectral characteristics of hexahydrotriazine **4** it may be more or less safe to assign the fragments belonging to the **BB** environment. In the ^{1}H NMR spectrum this is the signal of the NH group at 12.9-13.1 ppm, and in the ^{13}C spectrum the signals at 166.9, 145.9, 85.7, and 81.0 ppm (the closest value is underlined in the description of the ^{13}C NMR spectrum in Experimental). In difference to precursor **3**, compound **2** exists as a single isomer, the structure of which is seemingly stabilized by hydrogen bonds. It is interesting to note that tris(nitromethyl)-1,3,5-triazine synthesized previously [8] and the initial triazine **1** exist exclusively in the triazine form. Judging by the literature sources [9-12], tautomeric conversions are extremely widespread in the azinylmethane series, which are convenient models for establishing the general rules for tautomerism of the azinyl–ylidene type. Examples of the tautomeric equilibrium of alkylazines–alkylidenedihydroazines are known for substituted methylpyridines, pyridazines, pyrazines, pyrimidines, and triazines, while only for pyrimidines and triazines are examples known of noncatalyzed equilibria displaced completely to the side of the ylidene form [9-11]. In spite of numerous attempts at analysis (the BMO method, comparison of charts of charge differences, topological criteria) no general approach has been made up to the present time to considering equilibria of the azinyl–ylidene type, enabling assessment of the effects of structure, type of substituent, solvent, and temperature on the form of existence of substituted alkylazines [12].

EXPERIMENTAL

The IR spectra were taken on a Specord UR-20 instrument in KBr disks. The ^{1}H, ^{13}C, and ^{14}N NMR spectra were obtained on a Bruker AM-300 instrument (300, 75, and 21 MHz respectively), internal standard was TMS. Melting points were determined on a Boetius type hot stage with a heating rate of 4°C/min at the point of melting. The mass spectra were obtained on a Varian CH-6 instrument with direct insertion of samples into the ion source, energy of ionizing electrons was 70 eV, accelerating voltage 1.75 kV, and emission current 100 mA.

2,4,6-Tris(*tert*-butoxycarbonylacetylmethylene)hexahydro-1,3,5-triazine (3). Finely powdered lithium hydride (0.9 g, 113 mmol) was added to a solution of 2,4,6-tris(*tert*-butoxycarbonylmethyl)-1,3,5-triazine (**1**) (7.1 g, 17 mmol), obtained by the procedure of [2], in a mixture of THF (30 ml) and acetic anhydride (13 ml). The mixture was heated on a boiling water bath for 30 min, and then kept at room temperature for 22 h. The reaction mass was at first gelatinous, yellow-orange in color, after heating and standing it became mobile again. The mixture was diluted with water to 150-200 ml, the precipitated solid was filtered off, washed with hot water, dried on the filter, washed with acetone or ether, and air-dried to constant weight. Compound **2** (7.4 g, 80%) was obtained as a white powder; mp 203-205°C. ^{1}H NMR spectrum ($CDCl_3$–DMSO-d_6, 1:1), δ, ppm: 1.52 [27H, s, $(C\underline{H}_3)_3C$]; 2.30, 2.31, 2.32, 2.33 (9H, four singlets for nonequivalent $C\underline{H}_3CO$ groups); 14.62, 14.84, 14.87, 15.42 (3H, four singlets for nonequivalent NH groups). ^{13}C NMR spectrum ($CDCl_3$–DMSO-d_6, 1:1), δ, ppm: 195.34; 195.17; 194.83; 194.64 ($\underline{C}OCH_3$); 165.67; 165.52; 164.90; 164.79 ($\underline{C}OO$); 147.31; 146.70; 146.10; 145.24 (C=$\underline{C}$N); 92.99; 92.49; 92.10; 91.72 ($\underline{C}$=CN); 80.64; 80.35 [$(CH_3)_3\underline{C}$]; 30.28; 30.14; 30.08; 29.96 ($CO\underline{C}H_3$); 26.30 [$(\underline{C}H_3)_3C$]. IR spectrum (KBr), ν, cm^{-1}: 3100-2800, 2990, 2890, 1695, 1635, 1580, 1460, 1420, 1400, 1360, 1325, 1250, 1200, 1150, 1065, 1020. Mass spectrum, *m/z* (*I*, %): 549 (8) $[M]^+$, 381 (20) $[M\text{-}3C_4H_8]^+$, 363 (29) $[381\text{-}H_2O]^+$, 345 (19) $[363\text{-}H_2O]^+$, 57 (100) $[C_4H_9]^+$, 43 (68) $[COCH_3]^+$, 41 (73) $[CH_2CN+H]^+$. Found, %: C 58.57; H 7.46; N 7.90. $C_{27}H_{39}N_3O_9$. Calculated, %: C 59.00; H 7.15; N 7.65.

2,4,6-Tris(acetonyl)-1,3,5-triazine or 2,4,6-Tris(2-oxopropylidene)hexahydro-1,3,5-triazine (2). Trifluoroacetic acid (5 ml) was added to a solution of 2,4,6-tris(*tert*-butoxycarbonylacetylmethylene)hexahydro-1,3,5-triazine (**3**) (550 mg, 1 mmol) and the reaction mass was stirred for 30 min at room temperature. The acid was distilled off on a rotary evaporator, the residue was diluted with water (20 ml), and extracted with methylene chloride (3 × 10 ml). The extract was dried with calcined Na_2SO_4, filtered through a thin layer of silica gel, the solvent was evaporated, and the residue obtained was triturated with a small volume of acetone. The resulting crystals were filtered off. Compound **2** (190 mg, 76%) was obtained; mp 131-132°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.11 (9H, s, $C\underline{H}_3CO$); 5.10 (3H, s, $\underline{H}C$=C). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 195.33 ($\underline{C}OCH_3$); 148.26 (C=$\underline{C}$N); 85.99 ($\underline{C}$=CN); 28.60 ($CO\underline{C}H_3$). IR spectrum (KBr), ν, cm^{-1}: 3350, 1680, 1675, 1650, 1560, 1480, 1355, 1280, 1010, 970. Mass spectrum, *m/z* (*I*, %): 249 (53) $[M]^+$, 234 (99) $[M\text{-}CH_3]^+$, 207 (12) $[M\text{-}CH_2CO]^+$, 192 (29) $[207\text{-}CH_2CO]^+$, 165 (10), 150 (5), 123 (5), 84 (28) $[CH_3COCH_2CN\text{-}H]^+$, 68 (25) $[CH_3COCH_2CN\text{-}CH_3]^+$, 43 (100) $[COCH_3]^+$. Found, %: N 17.44. $C_{12}H_{15}N_3O_3$. Calculated, %: N 16.86.

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