TRISUBSTITUTED 1,3,5-TRIAZINES.

2. SYNTHESIS OF 1,3,5-TRIAZINES FROM 2,4,6-TRIS[DI(tert-BUTOXYCARBONYL)METHYLENE]HEXAHYDRO-1,3,5-TRIAZINE

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A study was carried out on electrophilic addition and hydrolytic dissociation of 2,4,6-tris[di(tert-butoxy-carbonyl)methylene]hexahydro-1,3,5-triazine. Chloro, bromo, and methyl derivatives of tris[di(tert-butoxy-carbonyl)methyl]-1,3,5-triazine were synthesized for the first time as well as 2,4,6-tris-[tert-butoxycarbonylmethyl]-1,3,5-triazine.

In previous work [1], we reported the synthesis of 2,4,6-tris[di(tert-butoxycarbonyl)nitromethyl]-1,3,5-triazine and 2,4-bis[di(tert-butoxycarbonyl)nitromethyl]-6-di(tert-butoxycarbonyl)methyl-1,3,5-triazine in the nitration of 2,4,6-tris[di(tert-butoxycarbonyl)methylene]hexahydro-1,3,5-triazine (I) using a mixture of nitric acid and acetic anhydride. This reaction may be seen as the addition of a nitronium cation to an activated double bond in I with subsequent aromatization of the hexahydrotriazine ring to give a triazine ring.

In the present work, we studied the reaction of hexaester I with halogenating, alkylating, and acylating reagents as well as its saponification with loss of the tert-butyl groups.

The chlorination and bromination of hexaester I proceeds under mild conditions to give the corresponding trichloro- (II) and tribromotriazines (III) in high yield:

\[
\begin{align*}
&\text{II: } \text{Hal} = \text{Cl}, \text{III: } \text{Hal} = \text{Br} \\
&\text{II: } \text{Hal} = \text{Cl}, \text{III: } \text{Hal} = \text{Br}
\end{align*}
\]

Attempts to carry out iodination using molecular iodine under analogous conditions proved unsuccessful. Hexaester I was recovered from the reaction unchanged.

The alkylation of I was studied in its reaction with methyl iodide. This reaction does not proceed in the absence of strong bases. On the other hand, the sodium salt of hexahydrotriazine I is methylated readily and the corresponding derivative is formed in 85% yield.

Attempts to acylate and benzoylate both I and its sodium salts by acetyl and benzoyl chlorides proved unsuccessful.

In the electrophilic addition reactions studied, the formation of the triazine ring is probably the driving force of the reaction and the labile tert-butyl groups are not affected. We attempted to find conditions, under which it would be possible to saponify several or all of the ester groups in these compounds. In previous work [2], we showed that the reaction of hexaester I with trifluoroacetic acid leads to saponification of the six CO\textsubscript{2}Bu-t groups and formation of 2,4,6-tris-di(carboxy)methylene]hexahydro-1,3,5-triazine. The hydrolytic dissociation of I also proceeds under analogous conditions [1]. The acids obtained are readily decarboxylated to give the corresponding 1,3,5-triazines [1, 2].

*For Communication 1, see ref. [1].

The ease of removal of the tert-butyl groups and tendency of triazinecarboxylic acids to undergo spontaneous decarboxylation permitted us to synthesize 2,4,6-tris(tert-butoxycarbonylmethyl)-1,3,5-triazine \( V \) from hexaester \( I \) in almost quantitative yield. Three ester groups are smoothly saponified upon using approximately a two-fold molar excess of trifluoroacetic acid per tert-butoxycarbonyl group with subsequent decarboxylation according to the following scheme:

\[
\text{CH(COOBu-t)}_2 \text{CH(COOBu-t)}_2 \xrightarrow{\text{H}^+} \text{CH(COOBu-t)}_2 \text{CH(COOBu-t)}_2 \xrightarrow{3\text{CO}_2} \text{CH(COOBu-t)}_2 \text{CH(COOBu-t)}_2
\]

The saponification of triazine \( II \) under analogous conditions leads to 2,4,6-tris(chloromethyl)-1,3,5-triazine \( VI \):

\[
\text{II} \xrightarrow{\text{H}^+} \text{CH(COOBu-t)}_2 \text{CH(COOBu-t)}_2 \xrightarrow{3\text{CO}_2} \text{CH(COOBu-t)}_2 \text{CH(COOBu-t)}_2
\]

Triazine \( VI \) holds interest as a heterocyclic analog of ethyl cyanoacetate, permitting us to obtain various 1,3,5-triazine derivatives at the activated methylene group by means of electrophilic addition.

**EXPERIMENTAL**

The IR spectra were taken on a Specord spectrometer for KBr pellets. The \(^1\text{H} \) and \(^{13}\text{C} \) NMR spectra were taken on a Bruker AM-300 spectrometer at 300 and 75.5 MHz, respectively, with TMS as the internal standard. The melting points were obtained on a Boetius heating block. The temperature was raised at 4°C/min in the vicinity of the melting point.

The synthesis of 2,4,6-tris[di(tert-butoxycarbonylmethylene)]hexahydro-1,3,5-triazine was described in our previous work [2].

\( 2,4,6-\text{Tris[di(tert-butoxycarbonylmethylene)]chloromethyl}-1,3,5-\text{triazine} \) (II). A stream of chlorine was introduced into a solution of 7.24 g (10 mmole) hexaester \( I \) in 100 ml CHCl\(_3\) and 100 ml saturated aqueous NaHCO\(_3\) with cooling on an ice bath (5-10°C) and stirring until the organic layer was no longer colored. The reaction mixture was stirred at this temperature for an additional 30 min. The organic layer was separated, washed with 100 ml aqueous NaHCO\(_3\), 100 ml aqueous Na\(_2\)S\(_2\)O\(_3\), three 100-ml portions of water, and dried over CaCl\(_2\). The solvent was distilled off and the residue was recrystallized from ethanol or hexane to give 7.68 g (93%) triazine \( II \), mp 114-115°C. IR spectrum: 3000, 2970, 1760, 1750, 1520, 1495, 1400, 1380, 1370, 1295, 1270, 1250, 1170, 1080, 960, 850 cm\(^{-1}\). PMR spectrum in CDCl\(_3\): 1.59 ppm (54H, s, 18CH\(_3\)). \(^{13}\text{C} \) NMR in CDCl\(_3\): 174.14 (C=C=N), 162.20 (CO\(_2\)), 84.94 [\( \delta \)(CH\(_3\))\(_3\)], 73.65 (C–Cl), 27.45 ppm (CH\(_3\)). Found: C, 52.92;