Triazines from Formaldehyde and Nitriles[1]

BY THOMAS L. GRESHAM AND THOMAS R. STEADMAN

The recent publication of a description[2] of the reaction of nitriles with formaldehyde (I) to yield hexahydro-1,3,5-tris-acyl-*s*-triazines prompts us to record such of our own independently performed experiments as will supplement those of Gradsten and Pollock.

We found that the reactions were best conducted in the presence of an excess of the nitrile, employing either α-polyoxymethylene or trioxane as the source of I. In the case of the preparation of hexahydro-1,3,5-tris-acrylyl-*s*-triazine (II), Gradsten and Pollock emphasized the need for freshly distilled acrylonitrile. We found in a series of five experiments that better yields and more easily controlled reactions consistently resulted from using commercially available acrylonitrile.[3] We believe this finding may be explained by the tendency of the impurities in the acrylonitrile to inhibit polymerization, since reactions involving freshly distilled acrylonitrile occasionally became uncontrollably violent, with consequent loss of material through polymerization and charring. Evidence for the identity of the products beyond that furnished by Gradsten and Pollock[2] was obtained by hydrolysis to recognizable fragments and molecular weight determinations.

The triazines described in this note are under study at the Sloan-Kettering Institute for Cancer Research. A preliminary report from Dr. C. Chester Stock has indicated that the results with hexahydro-1,3,5-tris-isobutyryl-5-triazine against mouse leukemia and sarcoma 180 have been encouraging enough to make this class of compounds worthy of further investigation. A full description of these chemotherapeutic studies will be published elsewhere.

Experimental

Hexahydro-1,3,5-tris-acrylyl-5-triazine (II).—In a two-liter three-necked flask fitted with a Hershberg tantalum wire stirrer, a reflux condenser and a dropping funnel, was placed 150 ml. of commercial acrylonitrile and 15 ml. of concentrated sulfuric acid. This solution was heated to 70° and a slurry of 90 g. of α-polyoxymethylene in 350 ml. of acrylonitrile was added over a period of an hour, during which time the temperature of the reaction mixture remained at 80° without further heating. After all of the slurry had been added, the reaction mixture was allowed to cool and the crystalline product filtered from the ice-cold mother liquors. These crystals were washed with 500 ml. of 1% sodium hydroxide and then with 500 ml. of water. The dried, crude product weighed 148 g. Recrystallization from ethanol gave 129.5 g. of II (52% yield). It should be noted that II polymerized quite readily, even in boiling alcohol or chloroform. Rapid cooling of clarified, saturated solutions of II ensured the absence of polymer in the product.

Anal. Calcd. for $C_{12}H_{15}N_3O_3$: C, 57.81; H, 6.07; mol. wt., 249.2. Found[4]: C, 57.70, 57.87; H, 6.17, 6.17; mol. wt.[5] (cryoscopic in acetic acid), 236, 228.

Hydrogenation of 1.50 g. of II in ethanol over Adams catalyst required 93 minutes at 30°, yielding 1.3 g. of hexahydro-1,3,5-tripropionyl-*s*-triazine (III), m. p. 149–150° (cor.) (in a sealed tube) after one recrystallization from ethanol. When crystals of III were held in a sealed tube for a few minutes at a temperature a little above the melting point, the melt resolidified and melted subsequently at 170–171° (cor.). Comparison of the infrared absorption curves[6] showed that the substances melting at these two temperatures were identical. In other experiments, the higher melting form was isolated directly as fluffy white needles.

Anal. Calcd. for $C_{12}H_{21}N_3O_3$: C, 56.45; H, 8.29; N, 16.46; mol. wt., 255. Found[7]: C, 56.65, 56.63; H, 8.21, 8.28; N, 16.37, 16.49; mol. wt. (ebullioscopic, benzene), 265, 261.[5]

Hydrolysis of 1.8 g. of III by 50 ml. of 10% sulfuric acid gave formaldehyde, which was identified as the 2,4-dinitrophenylhydrazone (m. p. 163° after one recrystallization from alcohol), and propionic acid, which was converted to the *p*-toluidide for identification, m. p. 124.5–125.5°. A mixed melting point showed no depression. Ammonia was liberated from the acid hydrolysis residue when it was made alkaline.

Hexahydro-1,3,5-trimethacrylyl-*s*-triazine.—To a solution of 90 g. of trioxane in 201 g. of inhibited methacrylonitrile[8] was added 10 ml. of concentrated sulfuric acid. The temperature of the reaction rose to 90°, and some formaldehyde was lost from the reaction vessel. After one hour at 90° (using external heating as necessary), a solution of 8 g. of sodium hydroxide in 200 ml. of water was added to the reaction mixture. The oily product crystallized on cooling and scratching to give 122 g. of crude product (41.9% yield). Recrystallization from ethanol resulted in 113.5 g. of crystals, m. p. 149.5–151° (cor.). In contrast with II this substance showed no signs of undergoing thermally induced polymerization at temperatures as high as its melting point.

Anal. Calcd. for $C_{15}H_{21}N_3O_3$: C, 61.83; H, 7.27; N, 14.42; mol. wt., 291.3. Found: C, 61.80, 61.83; H, 7.24, 7.38; N, 14.41, 14.47[4]; mol. wt., 292 ± 2 (ebullioscopic, benzene).[5]

From the hydrogenation of 2 g. of hexahydro-1,3,5-trimethacrylyl-*s*-triazine in ethanol over Adams catalyst there was isolated 1.5 g. of hexahydro-1,3,5-tris-isobutyryl-*s*-triazine (IV), m. p. 149–150° (cor.).

Anal. Calcd. for $C_{15}H_{27}N_3O_3$: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.81, 60.82; H, 9.15, 9.28; N, 14.04, 14.05.[4]

Hydrolysis of 7.5 g. of IV with 10% sulfuric acid gave formaldehyde, ammonium sulfate and isobutyric acid, which was identified as the *p*-toluidide, m. p. 108–109°. A mixed melting point with an authentic specimen showed no depression.

---

(1) Presented before the Division of Organic Chemistry at the 114th Meeting of the American Chemical Society, St. Louis, Missouri, September 6, 1948.

(2) Gradsten and Pollock, THIS JOURNAL, **70**, 3079 (1948).

(3) American Cyanamid Co., New York 20, N. Y.

(4) Analysis by J. R. Kubik.

(5) Determination by D. M. Kurtz.

(6) Data by J. J. Shipman.

(7) Huffman Microanalytical Laboratories, Denver 2, Colorado.

(8) Shell Development Co., Emeryville, California.

B. F. GOODRICH RESEARCH CENTER
BRECKSVILLE, OHIO
RECEIVED DECEMBER 23, 1948

Dearrangement of Nitroaminoguanidine in a Solution of Ammonium Carbonate

BY RONALD A. HENRY AND G. B. L. SMITH

Nitroguanidine dearranges rapidly in hot, aqueous ammonium carbonate solution with the evolution of nitrous oxide and the formation of guanidine carbonate in practically quantitative