118°. Optical rotation of these samples varied from +50 to +80°.

Cholest-4-ene-7β-ol Benzoate (VI).—A solution of 31 g. of the crude reduction product in a mixture of 500 ml. of pyridine and 66 ml. of benzoyl chloride was stored at 10° for 24 hours. The reaction mixture then was poured into a solution of 80 ml. of 12 *N* hydrochloric acid in 1 l. of water. The benzoate was extracted with a total of 1250 ml. of Skellysolve B and this non-aqueous extract washed with dilute hydrochloric acid, water, 10% sodium bicarbonate, and finally water. The neutral yellow hexane solution was dried over Drierite and shaken during one-half hour with 250 g. of alumina. The alumina was filtered off to give a colorless filtrate. When evaporated the filtrate deposited 24.7 g. of white solid which was crystallized from an ether–methanol pair. The product, weighing 13.5 g. (33%), consisted of glistening, thick needles, m.p. 158-160°, $[\alpha]^{26}\text{D}$ +94° (*c* 0.558).

Anal. Calcd. for $C_{34}H_{50}O_2$: C, 83.21; H, 10.27. Found: C, 83.35; H, 10.11.

Cholest-4-ene-7β-ol (I).—To 0.68 g. of the benzoate VI was added 50 ml. of a 95% ethanol solution containing 4.0 g. of potassium hydroxide. The resulting solution was refluxed for five hours. After this time water was added to the hot solution until turbidity was produced. After overnight cooling the solution had deposited 0.43 g. (86%) of small prisms, m.p. 122–124°. Recrystallization from acetone–water gave needles, m.p. 122.5-124, $[\alpha]^{26}\text{D}$ +90 (*c* 0.628).

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.89; H, 12.00. Found: C, 83.67; H, 11.78.

The acetate was prepared in the usual fashion giving mica-like plates, m.p. 96-97°, $[\alpha]^{27}\text{D}$ +78° (*c* 2.200).

Anal. Calcd. for $C_{29}H_{48}O_2$: C, 81.25; H, 11.29. Found: C, 81.09; H, 11.07.

The tosylate was prepared in a fashion similar to that previously described.[11] The tosylate was precipitated from the pyridine solution with water and the solid recrystallized from acetone–water. The stocky rods melted 125.5-126° dec. typical of tosylates, $[\alpha]^{27}\text{D}$ +27.6°.

Anal. Calcd. for $C_{34}H_{52}O_3S$: C, 75.51; H, 9.69. Found: C, 75.71; H, 9.58.

Cholest-4-ene-3-one-7β-ol Benzoate (VII).—During a period of 1.5 hours, 6.0 g. of chromic acid was added to a suspension of 13.4 g. of the benzoate VI in 280 ml. of glacial acetic acid. The solution was kept between 52 and 54°. Stirring at this temperature was continued for one-half hour after the addition was complete. When the solution was cooled, 8 ml. of ethanol was added to destroy the excess chromic acid and the mixture was evaporated to dryness. After washing with water, the residue was extracted with 300 ml. of ether and this ether extract washed with water, 10% sodium bicarbonate, and again water. The resulting ethereal solution was filtered through a short column of alumina and the filtrate was evaporated to a solid residue. This residue was crystallized from 95% ethanol to give 2.0 g. (14.5%) of white solid, m.p. 142-153°. Four recrystallizations from ethanol gave 1.2 g. of fine needles melting at 158-159° with partial resolidification followed by remelting at 168°. Chromatography of this material on a 6 × 1 cm. column of 60–100 mesh Florisil gave the pure keto-benzoate VII, m.p. 165-167°, $[\alpha]^{28}\text{D}$ +79° (*c* 1.368).

Anal. Calcd. for $C_{34}H_{48}O_3$: C, 80.90; H, 9.58. Found: C, 80.66; H, 4.40.

Oppenauer Oxidation of Cholest-5-en-3β,7β-diol 7-Benzoate.—A mixture of 1.0 g. of the 7-benzoate, 1.0 g. of aluminum isopropoxide, 35 ml. of dry cyclohexanone and 35 ml. of dry toluene was refluxed gently for one hour. After this time 0.3 ml. of acetic acid was added and steam was passed through the mixture for 1.5 hours. The resulting solution was extracted with ether which, after washing, was evaporated to 610 mg. of a yellow oil. Purification of this oil by chromatography produced mostly oily residue, but gave 80 mg. of cholest-5,7-diene-3-one as a crystalline material, undepressed upon admixture with authentic dienone.

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[11] R. H. Baker and Q. R. Petersen, THIS JOURNAL, **73**, 4080 (1951).

Preparation of Methylenebisamides[1]

BY CHARLES W. SAUER AND ROBERT J. BRUNI

RECEIVED JUNE 2, 1954

Knudsen[2] has reported the preparation of methylenediformamide from paraformaldehyde and formamide in 30% yield. In searching for a method to improve this yield, we investigated the use of trioxane, monochlorodimethyl ether, di-(chloromethyl) ether and hexamethylenetetramine as a source of the methylene group. The only one giving the desired product was the last of these.

The literature[3] contains numerous references to the use of hexamethylenetetramine as a source of formaldehyde. All of these reactions are reported to take place under conditions in which formaldehyde is liberated from the hexamethylenetetramine prior to formation of the final product; while it is difficult to visualize the formation of formaldehyde under the conditions of the reactions reported here. Descude[4] has reported the reaction of hexamethylenetetramine with benzamide at 200° to give azotrimethylenetribenzamide, but no product resembling the methylenedibenzamide we have obtained from hexamethylenetetramine and benzamide.

The reaction of formamide with hexamethylenetetramine gave a low (30 to 50%) yield of methylenediformamide, as had the Knudsen procedure. However, reuse of the mother liquor as solvent for succeeding runs gave yields of 70 to 100% based on added formamide and hexamethylenetetramine, which was not the case when paraformaldehyde was used instead of hexamethylenetetramine. Normally for the reaction, the mother liquor from a run was refreshed with amounts of hexamethylenetetramine and formamide equivalent to the amount of methylenediformamide obtained in the previous run. No determination was made of the optimum number of runs for reuse of the mother liquor, but it is at least 15 to 20. A typical reaction is outlined in Table I, which gives some yields obtained by this method. Other experiments reusing the mother liquor up to 15 times have been run. Infrared spectra of the products from paraformaldehyde and from hexamethylenetetramine were compared, and no significant differences were observed.

The reaction of hexamethylenetetramine with amides has been extended to the formation of methylenediacetamide, methylenebis-(malonamide), and methylenedibenzamide from acetamide, malonamide and benzamide, respectively. Their preparation is given in the Experimental section.

Experimental

Methylenediformamide A.—A mixture of 540 g. (12 moles) of formamide and 70 g. (0.5 mole) of hexamethylenetetramine is heated at a pot temperature of 140° for 5 hours. The mixture is cooled to ice temperature and the product is collected on a filter and washed with 90 g. (2 moles) of form-

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[1] This work was done under Contracts DA-19-020-ORD-12 and DA-19-020-ORD-47 with the Office of the Chief of Ordnance and has been released by the Office of Public Information, Department of Defense, for publication.

[2] P. Knudsen, *Ber.*, **47**, 2698 (1914).

[3] J. F. Walker, "Formaldehyde," 2nd Edition, Reinhold Publ. Corp., New York, N. Y., 1953, p. 416 *et seq.*

[4] M. Descude, *Ann. chim. phys.*, [7] **29**, 533 (1903).

amide. The product may be recrystallized from ethanol. Before recrystallization, it is desirable to elute the crude product with ethanol saturated with methylenediformamide from previous recrystallizations. Decolorizing charcoal is used to remove colored material when necessary. Methylenediformamide melts at 142–143°.

B.—The formamide mother liquor (from A in the first pass or B in the later passes) is treated with Darco G60 to decolorize it, and then it is combined with the wash formamide (90 g.) and 23 g. (0.167 mole) of hexamethylenetetramine and the above procedure is repeated. The yields of crude product from a typical series of runs are recorded in Table I.

TABLE I

METHYLENEDIFORMAMIDE FROM HEXAMETHYLENETETRAMINE WITH 100% EXCESS FORMAMIDE

Run	Mother liquor from run	Hexamine, mole	Formamide, moles	Yield, G.	Yield, %	Total yield G.	Total yield %
1		0.5	12	162	53	162	53
2	1	.167	2	124	121	286	70
3	2	.167	2	108	106	394	77
4	3	.167	2	97	95	491	80
5	4	.167	2	95	93	586	82
6	5	.167	2	95	93	681	83

Methylenediacetamide.—This compound was prepared from acetamide and hexamethylenetetramine in the same manner as methylenediformamide using quinoline as solvent. The product, melting at 198–200° after recrystallization from isopropyl alcohol, did not depress the melting point of an authentic sample of methylenediacetamide.

Methylenebis-(malonamide).—This compound was prepared from malonamide and hexamethylenetetramine in refluxing dimethylformamide. The yield of product, melting at 252° dec. after recrystallization from 90% formic acid or from formamide, was 82.5%.

Anal. Calcd. for $C_7H_{12}O_4N_4$: C, 38.89; H, 5.59; N, 25.92. Found: C, 39.12, 38.90; H, 5.72, 5.50; N, 25.55, 25.73.

Methylenedibenzamide.—This compound was prepared from benzamide and hexamethylenetetramine in refluxing quinoline. The product, melting at 216–220° after recrystallization from isopropyl alcohol, did not depress the melting point of an authentic sample of methylenedibenzamide.

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Nitramines. I. Methylenedinitramine[1]

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RECEIVED JUNE 2, 1954

Recently it became necessary to prepare a quantity of methylenedinitramine. This compound has been prepared previously from hydrolysis of 1,3-dinitro-1,3,5-triazacyclohexane 5-nitrate with barium hydroxide and isolation through its barium salt, and also from methylenediacetamide by nitration to methylenedi-(nitroacetamide) followed by hydrolysis.[2]

Since the formyl group has been found very useful where a labile protecting group is desired, as in the synthesis of amino acids, the use of methylenediformamide instead of methylenediacetamide for the synthesis of this compound was investigated. Nitration of a suspension of methylenediformamide (MDF)[3] in acetic anhydride by anhydrous nitric acid produced methylenedi-(nitroformamide), which on hydrolysis gave methylenedinitramine in nearly quantitative yield.

Since this new procedure gave substantially superior yields to previous methods for the preparation of nitramines, variables influencing yield have been investigated. The use of this reaction for the preparation of other nitramines also is being investigated and will be reported later.

In initial work on the nitration process, all of our studies were made using a 9/4/1 ratio[4,5] of anhydrous nitric acid to acetic anhydride to methylenediformamide, with a nitration and aging temperature of 0°. The yield of methylenedi-(nitroformamide) was found to increase with aging time until a nearly quantitative yield was obtained with a four-hour aging period.

Table I shows the influence of increased nitration temperature on the yield of crude methylenedinitramine. A study of various nitrating mixtures showed that no methylenedi-(nitroformamide) was obtained using nitric acid alone or in mixture with sulfuric acid, which is similar to the finding of Brian and Lamberton[4] for the nitration of methylenediacetamide. With acetic anhydride–nitric acid mixtures, decreasing amounts of nitroamide were obtained when the amount of water in the nitric acid used was increased; this, however, could be overcome by the pre-addition of enough anhydride to the acid to react with the water present. Any decrease in the ratio of acetic anhydride or nitric acid to methylenediformamide, or the substitution of ammonium nitrate for a portion of the nitric acid, was found to cause a decrease in the yield of methylenedinitramine. However, when trifluoroacetic anhydride was substituted for acetic anhydride, the ratio of acid to anhydride to methylenediformamide could be reduced to 3/3/1 to obtain a quantitative yield. No decrease in yield was obtained with acetic anhydride–nitric acid mixtures when the order of addition was changed. Contrary to

TABLE I

INFLUENCE OF NITRATION TEMPERATURE WITH TIME ON YIELD OF METHYLENEDINITRAMINE

Mole of MDF	Nitration[a] temp., °C.	Aging temp., °C.	Aging time, hr.	Crude yield, %
1	0	2	4	95
0.5	10	10	1	97
0.5	10	10	2	100
0.5	10	10	4	93
1	25–30	15–30	3	99

[a] An acid/anhydride/MDF ratio of 9/4/1 was used. Formic acid was added for the hydrolysis, and the methylenedinitramine was isolated by azeotropic distillation with xylene at reduced pressure.

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[1] This work was done under Contracts DA-19-020-ORD-12 and DA-19-020-ORD-47 with the Office of the Chief of Ordnance and has been released for publication by the Office of Public Information, Department of Defense.

[2] A. H. Lamberton, *Quart. Revs.*, **5**, 75 (1951).

[3] P. Knudsen, *Ber.*, **47**, 2699 (1914); C. W. Sauer and R. J. Bruni, THIS JOURNAL, **77**, 2259 (1955).

[4] R. C. Brian and A. H. Lamberton, *J. Chem. Soc.*, 1635 (1949).

[5] Heat of reaction data for the nitration reaction were calculated by Dr. G. R. Handrick, Arthur D. Little, Inc., from heat of combustion data obtained by a new method which will be given in detail in a forthcoming publication. $CH_2(NHCHO)_2 + 4(CH_3O)_2O + 9HNO_3 \rightarrow CH_2(N(NO_2)CHO)_2 + 6CH_3COOH + 5HNO_3 + 2CH_2C(O)ONO_2 +$ 30.4 kcal./mole (heat evolved). The heat evolved on nitration was determined experimentally by Dr. J. W. Lawrence, Atlas Powder Co., as 29.5 kcal./mole.