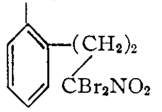
TABLE VIII

$\alpha,\alpha,\omega,\omega$-TETRABROMO-$\alpha,\omega$-DINITRO PARAFFINS $[(CH_2)_n-(CNO_2Br_2)_2(I)]$ FROM CYCLIC KETONES

Ketone	I.[a] n	Yield, THF[b]	% in Et_2O	Formula	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Bromine, % Calcd.	Bromine, % Found
Cyclopentanone	2[c]	72	62	$C_4H_4N_2O_4Br_4$	99–100	...	...	..	..	..	..	...	...
Cyclohexanone	3[c]	53	..	$C_5H_6N_2O_4Br_4$	40–41	...	...	..	..	..	..	...	...
Cycloheptanone	4	54	44	$C_6H_8N_2O_4Br_4$	85–86	14.65	14.66	1.63	1.65	5.70	5.82	...	...
Cycloöctanone	5	35	..	$C_7H_{10}N_2O_4Br_4$	35–36	16.32	16.45	1.99	2.09	5.54	5.60	63.19	63.30
α-Tetralone	CO_2H	40	..	$C_{10}H_9NO_4Br_2$	127–128	44.50	44.49	2.96	3.01	5.18	5.20	29.62	29.53



[a] All compounds were crystallized from hexane.

[b] THF = tetrahydrofuran. [c] See ref. 7.

mometer after the flame was removed. Explosion points, taken in this manner, were reproducible to ±2°.

Anal. Calcd. for $C_5H_4N_2O_5K_2$: C, 23.95; H, 1.61; N, 11.19. Found: C, 22.85; H, 2.65; N, 11.06.

Method B.—A better method of purification consisted of recrystallizing the salt from 30% potassium hydroxide, washing the green needles with methanol until the filtrate became colorless and neutral and drying at 56° (1 mm.). The yield of the pure salt was 55%.

Anal. Found: C, 23.24; H, 2.03; N, 11.44.

1,1,4,4-Tetrabromo-1,4-dinitrobutane.—Dipotassium 2,5-dinitrocyclopentanone (9.4 g., 0.038 mole) purified by method A, was dissolved in 75 ml. of water and added rapidly at 0° to a solution of potassium hypobromite. The latter was prepared by adding dropwise 27.6 g. of bromine to a solution of 24.8 g. of potassium hydroxide (85% assay) in 150 ml. of water at 0°. The product was separated by filtration and recrystallized from hexane. The yield of 1,1,4,4-tetrabromo-1,4-dinitrobutane, m.p. 101–102° (lit. value[7] 100°) was 16.6 g. or 72%.

1,1,4,4-Tetrachloro-1,4-dinitrobutane.—A solution of 5 g. of purified dipotassium 2,5-dinitrocyclopentanone (0.02 mole) in 50 ml. of water was added rapidly to a solution of 12 g. of HTH (calcium hypochlorite) in 150 ml. of water at 0°. The reaction mixture was filtered and the filter cake was extracted with ether. The solvent was distilled off and the remaining product was then recrystallized from aqueous methanol yielding 4.54 g. (79.3%) of 1,1,4,4-tetrachloro-1,4-dinitrobutane, m.p. 50–50.5°.

Anal. Calcd. for $C_4H_4N_2O_4Cl_4$: C, 16.81; H, 1.40; N, 9.78. Found: C, 16.90; H, 1.47; N, 9.78.

Potassium *t*-Butoxide.—In a 500-ml. filter flask equipped with a Y-neck adapter to which a condenser surmounted by a calcium chloride drying tube was attached, 200 ml. of -butyl alcohol (distilled over sodium) was heated to reflux by means of an oil-bath. Potassium, 45.4 g. (1.16 mole), was added in small pieces, followed by 50 ml. of additional *t*-butyl alcohol and the reaction mixture was refluxed for 16 hours to assure complete reaction of the potassium. The excess *t*-butyl alcohol was evaporated at 120° (1 mm.) for four hours. The product obtained at this point titrated for 64% base, expressed as potassium *t*-butoxide. The solid cake was then purified by vacuum sublimation at 220° (1 mm.), in 30-g. portions, and 130 g. (72.5%) of 99% pure potassium *t*-butoxide was obtained.

Sodium *t*-Butoxide.—To 5.75 g. (0.125 mole) of sodium sand, prepared by the method of Fieser,[14] 70 ml. of *t*-butyl alcohol (distilled over sodium) was added in a 200-ml. flask. The reaction mixture was refluxed for 12 hours and the excess *t*-butyl alcohol was evaporated at 120° (1 mm.) for four hours. The crude sodium *t*-butoxide was purified by vacuum sublimation at 180° (1 mm.) to yield 20 g. (83%) of 99.5% pure sodium *t*-butoxide. Prior to sublimation it was found to be 99% pure.

Determination of Solubility of Potassium and Sodium Alkoxides.—A saturated solution of the sublimed alkoxide was prepared by shaking an excess amount of the alkoxide with the purified solvent, for 12 hours at 25°. The suspension was allowed to settle, and a portion of the clear supernatant liquid was transferred under dry nitrogen pressure to a flask. The solvent was evaporated *in vacuo*, the residue was dissolved in distilled water and aliquots of the aqueous solution were titrated with standard hydrochloric acid to phenolphthalein end-point.

Acknowledgment.—We are indebted to the Office of Naval Research for the financial support of this work and to the Ethyl Corporation for a generous gift of amyl nitrate.

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[14] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 368.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE R. B. WETHERILL LABORATORY OF CHEMISTRY, PURDUE UNIVERSITY]

The Synthesis and Reactions of Brominated N-Methylolamides[1]

BY HENRY FEUER AND JAKE BELLO

RECEIVED MARCH 28, 1956

The bromination of N-methylolacrylamide (I) gives the normal addition product N-methylol-2,3-dibromopropionamide (II) while that of N-methylolmethacrylamide (III) results in the unexpected formation of N,N′-methylenebis-(2,3-dibromoisobutyramide) (IV) instead of N-methylol-2,3-dibromoisobutyramide (V). The latter has now been prepared by bromination of methacrylamide followed by methylolation under basic conditions. In the dark, in the complete absence of acid, compound V is converted to IV by bromine, but not by iodine. It is proposed that compound V is an intermediate in the conversion of III to IV.

Previous work in this Laboratory[2] has shown that the reaction of bromine with N-methylolmethacrylamide (III) gave N,N′-methylenebis-(2,3-dibromoisobutyramide) (IV) instead of the expected N-methylol-2,3-dibromoisobutyramide (V). In contrast, bromination of N-methylolacrylamide (I) gave the normal addition product, N-methylol-2,3-dibromopropionamide (II).

The formation of N,N′-methylenebisamides by condensing an amide with formaldehyde in an acidic medium has been known for a long time.[3]

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[1] This paper was presented before the Division of Organic Chemistry at the New York City Meeting of the American Chemical Society, September 15, 1954.

[2] H. Feuer and U. E. Lynch, THIS JOURNAL, **75**, 5027 (1953).

[3] G. Pulvermacher, *Ber.*, **25**, 318 (1892).

The possibility existed therefore that a small amount of acidic impurities present in the bromine used catalyzed the formation of compound IV from

$$\underset{\text{III}}{H_2C{=}C(CH_3)CONHCH_2OH} \xrightarrow[CCl_4]{Br_2} \underset{\text{IV}}{(H_2CBrCBr(CH_3)CONH)_2CH_2}$$

$$\underset{\text{I}}{H_2C{=}CHCONHCH_2OH} \xrightarrow[CCl_4]{Br_2} \underset{\text{II}}{H_2CBrCHBrCONHCH_2OH}$$

III. However, this did not agree with the fact that compound I afforded the normal bromine adduct II, and that II was converted to N,N'-methylenebis-(2,3-dibromopropionamide) (VI) in the presence of a catalytic amount of acid. Moreover, the bromine

$$\text{II} \xrightarrow{H^+} \underset{\text{VI}}{(H_2CBrCHBrCONH)_2CH_2}$$

which was used in all experiments was carefully distilled, and infrared as well as mass spectrograph analyses did not give evidence of any impurities.

In the formation of compound IV from III it was considered possible that N-methylol-2,3-dibromoisobutyramide (V) is an intermediate. Compound V was prepared by brominating methacrylamide and allowing the resulting 2,3-dibromoisobutyramide (VII) to react with formaldehyde in an alkaline medium.

$$H_2C{=}C(CH_3)CONH_2 \xrightarrow{Br_2} \underset{\text{VII}}{H_2CBrCBr(CH_3)CONH_2}$$

$$\text{VII} \xrightarrow[OH^-]{CH_2O} \underset{\text{V}}{H_2CBrCBr(CH_3)CONHCH_2OH}$$

When compound V was treated with bromine *in the dark* or *in the light* and *in the absence of any acid*, compound IV resulted in high yield (86%). That the bromine atoms in IV were still at the same positions as in V was established by hydrolyzing[4] IV in acidic medium to 2,3-dibromoisobutyric acid. The identity of compound IV with that obtained from the direct bromination of III was established by a mixed melting point determination which showed no depression. It is significant for our discussion of the mechanism that upon treatment with iodine in anhydrous ethylene chloride, and in the light, compound V was recovered in 95% yield. As expected, heating of compound V with sulfuric acid or hydrogen bromide in ethylene chloride also gave IV. However, treatment with hydrochloric acid in ethylene chloride resulted in hydrolysis of V with the formation of 2,3-dibromoisobutyric acid.

Attempts to prepare compound II by the procedure which was successful for the synthesis of V failed. Upon allowing 2,3-dibromopropionamide to react with formaldehyde in the presence of aqueous sodium hydroxide, dehydrobromination occurred with the formation of sodium bromide dihydrate and with the recovery of a small amount of the amide. Substituting sodium hydroxide with potassium carbonate gave some polymer and potassium bromide as the only products.

Discussion

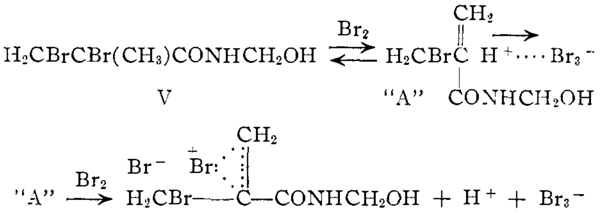
The fact that both compounds III and V are converted to compound IV by bromine in the dark indicates that a free radical mechanism is not involved in this transformation. The formation of IV, however, can be explained on the basis of an ionic reaction between bromine and the tertiary bromide to produce Br_3^- and a carbonium ion. This carbonium ion might then lose a proton to provide the acid required for the transformation of compound V to IV.

The observation that iodine fails to cause the transformation argues against this interpretation. Iodine would be expected to be as effective as bromine in facilitating the ionization of a tertiary bromide.

$$RBr + Br_2 \longrightarrow R^+Br_3^-$$

$$RBr + I_2 \longrightarrow R^+BrI_2^-$$

A possible way out of this difficulty is to postulate that the halogen reacts to produce the π-complex form[5] of the carbonium ion. This π-complex form ("A") would be capable of reacting with bromine, but not with iodine to liberate acid.[6]

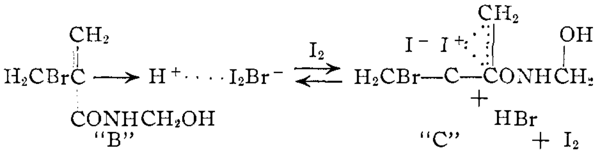


$$\underset{\text{V}}{H_2CBrCBr(CH_3)CONHCH_2OH} \underset{}{\overset{Br_2}{\rightleftarrows}} \underset{\text{"A"}}{H_2CBr\overset{\overset{CH_2}{\|}}{\underset{\underset{CONHCH_2OH}{|}}{C}}\ \overrightarrow{H^+\cdots Br_3^-}}$$

$$\text{"A"} \xrightarrow{Br_2} \overset{Br^-\ \ \overset{+}{Br}{:}\ \ CH_2}{H_2CBr\text{—}C\text{—}CONHCH_2OH} + H^+ + Br_3^-$$

$$\text{V} \xrightarrow{H^+} (H_2CBr\text{-}CBr(CH_3)CONH)_2CH_2$$

While iodine would also be expected to react with V to give the π-complex form ("B"), a significant amount of hydrogen bromide is not produced because the equilibrium in the formation of the iodonium ion ("C") lies far to the left.



$$\underset{\text{"B"}}{H_2CBr\overset{\overset{CH_2}{\|}}{\underset{\underset{CONHCH_2OH}{|}}{C}} \longrightarrow H^+\cdots I_2Br^-} \overset{I_2}{\rightleftarrows} \underset{\text{"C"}}{\overset{I^-\ \ I^+{:}\ \ CH_2\qquad OH}{H_2CBr\text{—}C\text{—}CONHCH_2}} + HBr + I_2$$

Experimental Part[7]

The bromine used in these experiments was dried by phosphorus pentoxide and then distilled.

2,3-Dibromoisobutyramide (VII).—A stirred slurry of methacrylamide, 17 g. (0.20 mole) in 300 ml. of dry carbon tetrachloride, was treated dropwise with 33.6 g. (0.21 mole) of bromine. The solvent was removed *in vacuo* and the residue distilled to yield 30 g. (61% conversion) of 2,3-dibromoisobutyramide, b.p. 116° at 2 mm. The distillation was stopped when the fresh drops of distillate were tan. Higher yields can be obtained only at the expense of purity. Recrystallization from methylene chloride gave crystals of VII, m.p. 53-54°.

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[4] We are indebted to Michael Israel, Purdue University, for carrying out this experiment.

[5] R. W. Taft, Jr., THIS JOURNAL, **74**, 5372 (1952); J. B. Levy, R. W. Taft, Jr., and L. P. Hammett, *ibid.*, **75**, 1253 (1953).

[6] G. A. Russell and H. C. Brown, *ibid.*, **77**, 4025 (1955).

[7] All melting points are uncorrected.

Anal. Calcd. for $C_4H_7NOBr_2$: C, 19.58; H, 2.86; N, 5.71; Br, 65.31. Found: C, 19.73; H, 2.78; N, 5.44; Br, 65.25.

N-Methylol-2,3-dibromoisobutyramide (V).—To a mixture consisting of 12.5 g. (0.05 mole) of 2,3-dibromoisobutyramide, 5 ml. (0.062 mole) of 37% formalin solution and three pellets of sodium hydroxide was added sufficient ethanol to dissolve the amide. After standing at 25° for 16 hours, the solution was concentrated *in vacuo* and the solid residue was crystallized from ethyl acetate or acetone to give 7 g. (50.9%) of pure product, m.p. 125–126°.

Anal. Calcd. for $C_5H_9NO_2Br_2$: C, 21.82; H, 3.27; N, 5.09. Found: C, 21.87; H, 3.28; N, 5.11.

Reactions of N-Methylol-2,3-dibromoisobutyramide. (a) **With Hydrochloric Acid.**—A mixture consisting of 1.4 g. (0.005 mole) of N-methylol-2,3-dibromoisobutyramide, 10 ml. of ethylene chloride and two drops of 38% hydrochloric acid was refluxed for 20 minutes, filtered from gummy matter, and cooled to yield 0.7 g. (81.3%) of 2,3-dibromoisobutyric acid,[8] m.p. 48–49°. A mixed melting point determination with an authentic sample of the acid was 48–49°.

(b) **With Hydrogen Bromide.**—A mixture of 2 g. (0.0073 mole) of N-methylol-2,3-dibromoisobutyramide and 100 ml. of ethylene chloride was saturated with hydrogen bromide at 25° and allowed to stand for one hour. After filtration, which yielded 0.8 g. of starting material, dry air was bubbled through the solution to remove hydrogen bromide and to concentrate the solution. This procedure afforded 0.6 g. (33% conversion 55% yield) of N,N′-methylenebis-(2,3-isobutyramide),[2] m.p. 205° after recrystallization with ethylene chloride.

(c) **With Sulfuric Acid.**—A mixture consisting of 1 g. (0.0036 mole) of N-methylol-2,3-dibromoisobutyramide, 20 ml. of ethylene chloride and one drop of concd. sulfuric acid was refluxed for 15 minutes. The mixture was concentrated to a volume of 10 ml. and decanted from a small amount of gum. Upon cooling, 0.85 g. (94%) of N,N′-methylenebis-(2,3-dibromoisobutyramide) was obtained.

(d) **With Bromine.**—N-Methylol-2,3-dibromoisobutyramide (2 g., 0.0073 mole) and 1 g. (0.006 mole) of bromine were allowed to react in the dark for 12 hours in a closed flask at 25°. The bromine was then removed in the dark and the remaining residue (1.85 g.) melted at 188–196°. Recrystallization from ethylene chloride raised the melting point to 204–206°. A total of 1.6 g. (86%) of crystals was obtained and identified as N,N′-methylenebis-(2,3-dibromoisobutyramide).[2] A mixed melting point determination with an authentic sample was 205°.

(e) **With Iodine.**—A mixture consisting of 2.75 g. (0.01 mole) of N-methylol-2,3-dibromoisobutyramide, 0.25 g. of iodine and 200 ml. of dry ethylene chloride was kept in a closed container for 12 hours at 25°. After evaporation, 2.6 g. (94.2%) of the starting material was recovered.

Hydrolysis of N,N′-Methylenebis-(2,3-dibromoisobutyramide) (IV).—A mixture consisting of 5.0 g. (0.01 mole) of N,N′-methylenebis-(2,3-dibromoisobutyramide) and 175 ml. of concd. hydrochloric acid was refluxed until dissolution was complete (22 hours). The mixture was then cooled and extracted with three 50-ml. portions of carbon disulfide. Evaporation of the solvent and cooling of the residual oil yielded 1.5 g. (30%) of crystals, m.p. 46–47°, which were identified as 2,3-dibromoisobutyric acid.[8] A mixed melting point determination with an authentic sample showed no depression.

N,N′-Methylenebis-(2,3-dibromopropionamide) (VI).—A solution of 0.2 g. (0.77 mmole) of N-methylol-2,3-dibromopropionamide[2] in 20 ml. of ethylene chloride, to which one drop of concd. sulfuric acid had been added, was boiled for 15 minutes. Upon cooling, 0.1 g. (55%) of N,N′-methylenebis-(2,3-dibromopropionamide) was obtained, m.p. 207–208° after recrystallization with ethylene chloride.

Anal. Calcd. for $C_7H_{10}O_2N_2Br_4$: C, 17.72; H, 2.11; N, 5.91. Found: C, 18.0; H, 2.39; N, 5.46.

2,3-Dibromopropionamide.—A slurry of 35 g. (0.57 mole) of acrylamide in 100 ml. of carbon tetrachloride was treated with 80 g. (0.5 mole) of bromine. The precipitate was filtered off, washed with carbon tetrachloride and recrystallized from absolute ethanol. A yield of 70 g. (63%) of 2,3-dibromopropionamide, m.p. 132–133°, lit. value[9] 130–133°, resulted.

Attempted Methylolation of 2,3-Dibromopropionamide. (a) **With Sodium Hydroxide.**—A solution of 23 g. (0.1 mole) of 2,3-dibromopropionamide and 3 g. (0.1 mole) of 37% formalin solution in ethanol was basified with sodium hydroxide. The solution became neutral on standing and additional base was added to maintain a *p*H of 9–10. After 12 hours, the solvent was removed *in vacuo* at 25° and filtration yielded 10.3 g. of sodium bromide dihydrate (73% based on removal of one mole of hydrobromic acid per mole of dibromopropionamide), m.p. 51°. Distillation of the filtrate yielded 4.5 g. of unreacted starting material.

(b) **With Potassium Carbonate.**—The experimental procedure was the same as above except that potassium carbonate was used instead of sodium hydroxide. Pure potassium bromide was isolated in 30% conversion and a tough, slightly tacky translucent polymer in 60% conversion if the material is considered to be a polymer of α-bromoacrylamide.

Acknowledgments.—The authors are indebted to Professor Herbert C. Brown for many stimulating discussions and to the Office of Naval Research for the financial support of this work.

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[8] C. Kolbe, *J. prakt. Chem.*, [2] **25**, 373 (1882).

[9] M. Moureu, *Ann. chim. phys.*, [7] **2**, 177 (1894).

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

The Stereochemistry of Raney Nickel Action. VII. Catalytic Hydrogen–Deuterium Exchange in the 2-Phenylpropionamide Series

BY WILLIAM A. BONNER AND JOHN A. ZDERIC

RECEIVED FEBRUARY 20, 1956

The relative rates of racemization and hydrogen–deuterium exchange when (+)-2-phenylpropionamide is treated with deuterated Raney nickel in refluxing deutero-ethanol have been investigated. Isotope exchange occurs at the α-hydrogen, in the α-methyl group and in the aromatic ring considerably more rapidly than racemization occurs, results which may be rationalized in terms of a stereospecifically adsorbed carbonium ion intermediate. 1-Phenylethanol and ethylbenzene similarly underwent isotope exchange in both the side chain and nucleus.

It has recently been reported[1] that both α-hydrogen atoms and nuclear hydrogen atoms in mandelamide and phenylacetamide undergo exchange with deuterium when treated with deuterated Raney nickel in refluxing deuteroethanol. Similarly, the slow racemization of compounds such as ethyl (+)-2-phenylpropionate and (+)-2-phenylpropionamide under the influence of Raney nickel in refluxing ethanol has been reported.[2] It seemed to us of considerable interest to investigate quantitatively any relationship which might exist in the rate of

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[1] W. A. Bonner, THIS JOURNAL, **76**, 6350 (1954).

[2] W. A. Bonner, J. A. Zderic and G. A. Casaletto, *ibid.*, **74**, 5086 (1952).