hydroxide. The average values of $(H_{\mathrm{IIIa}} + H_{\mathrm{IVa}})/(H_{\mathrm{IIIa}} + H_{\mathrm{IVa}} + H_e)$ and $H_{\mathrm{IIIa}}/(H_{\mathrm{IIIa}} + H_{\mathrm{IVa}})$ in 3 g.l.p. chromatograms of the ether solution, which weighed 54 g., were (1.84 ± 0.08) 10^{-2} and 0.77 ± 0.01, respectively, indicating that the conversion was 58% and that the product was 77% IIIa and 23% IVa.

Miscellaneous Reactions of N-(2-Haloallyl)ethylamines with Various Bases.—Treatment of 8.2 g. of N-(2-bromoallyl)ethylamine (Ia) with 2 g. of sodium amide in 100 ml. of ether at 25° for 5 hr. and room temperature for 24 hr., gave a 29% conversion to IVa. No IIIa was detected by means of g.l.p.c. A 6.0-g. sample of N-(2-chloroallyl)ethylamine (IIa) was treated in the same manner. No indication of the presence of IIIa or IVa in the ether solution was obtained by g.l.p.c.

Treatment of 36 g. of Ia with 300 ml. of *N*-methylmagnesium bromide in ether at reflux for 4 hr. and at room temperature for 16 hr., gave a 10% yield of a mixture of 24% IIIa and 76% IVa. Formation of IIIa and IVa was confirmed by means of infrared spectroscopy, and 29 g. (80%) of Ia was recovered. N-(2-Chloroallyl)isopropylamine (35 g.) was treated in the same manner. Traces of the corresponding III and IV (~90% IV), estimated as <0.5 g. (<2%), were detected by g.l.p.c.

Compound Ia (36.0 g.) was treated with 2.8 g. of lithium aluminum hydride in 300 ml. of ether at reflux for 2.5 hr. The mixture had darkened considerably after 1 hr. The mixture was allowed to stand overnight, and 10 ml. of water was added cautiously with stirring. After 1 hr., the ether solution was decanted from the dark precipitate and dried with sodium hydroxide. Presence of <0.6 g. (<4%) of IIIa and IVa consisting of more than 90% IIIa was detected by means of g.l.p.c. Only 18.5 g. (51%) of Ia was recovered. Compound IIa (18.0 g.) was also treated with 2.8 g. of lithium aluminum hydride in the same manner. No trace of either IIIa or IVa was detected in the concentrated ether solution from the reaction.

A mixture prepared from 4.0 g. of coarsely powdered sodium hydroxide, 8.2 g. of Ia, and 100 ml. of liquid ammonia was stirred at reflux for 10 hr. Ether (50 ml.) was added to the stirred mixture, and the ammonia was allowed to evaporate. Formation of 1.0 g. (24%) of IVa was detected by means of g.l.p.c.; formation of IVa was confirmed by means of infrared spectroscopy.

Dihalomalonaldehydes

S. TROFIMENKO

Contribution No. 879 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware

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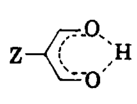
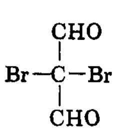
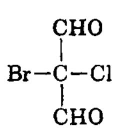
There are numerous examples of monosubstituted malonaldehydes,[1] depicted best by the "pseudoaromatic" structure I. By contrast, disubstituted malonaldehydes devoid of this "aromaticity" are little known. While acetals of dibromomalonaldehyde[2] and dimethylmalonaldehyde[3] have been reported, they were prepared indirectly and, until recently,[4] could not be converted to the free dialdehydes. This paper reports the first synthesis of negatively disubstituted malonaldehydes, dibromomalonaldehyde (II), and bromochloromalonaldehyde (III).


I



$$\mathrm{Br{-}C(CHO)_2{-}Br}$$

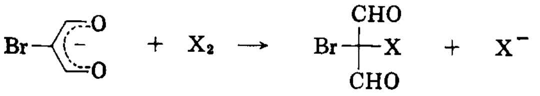
II



$$\mathrm{Br{-}C(CHO)_2{-}Cl}$$

III

Both of these compounds were prepared by the action of the appropriate halogen on the sodium salt of bromomalonaldehyde, under scrupulously anhydrous conditions.[5]

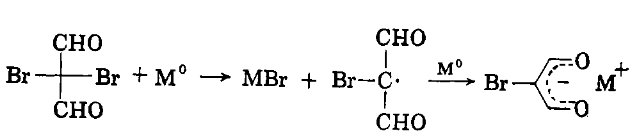


Dibromomalonaldehyde was obtained in better yields and was studied in more detail. It is readily soluble in common organic solvents; in water or aqueous tetrahydrofuran it dissolves with the formation of an isolable hydrate. Aqueous solutions of dibromomalonaldehyde can be titrated with base, the hydrate being cleaved to formic acid and dibromoacetaldehyde.

Dibromomalonaldehyde exhibits surprising thermal stability, remaining unchanged when refluxed at its boiling point (186°) for two hours. Even under such drastic conditions as passage over quartz chips at 390 and 450°, 50 and 40%, respectively, of the starting material is recovered.

In contrast to the thermal stability of dibromomalonaldehyde is its high sensitivity to radicals. When solutions of dibromomalonaldehyde (in benzene or carbon tetrachloride) are exposed to light or azo initiators, a rapid and complex reaction ensues; hydrogen bromide is evolved, and bromomalonaldehyde precipitates as an isolable product. When the reaction is allowed to proceed further, a complex mixture of acid bromides is obtained. It is noteworthy that bromomalonaldehyde by itself does not react under those conditions, nor does dibromomalonaldehyde in the absence of a solvent.

Dibromomalonaldehyde reacts with metals or metal carbonyls, presumably *via* two one-electron transfers, and yielded the metal salt of bromomalonaldehyde.



The bromomalonaldehyde radical gave no evidence of coupling in any of the preceding reactions; in fact, the most pronounced characteristic of dibromomalonaldehyde (or bromomalonaldehyde radical) is its tendency to revert to the aromaticity of bromomalonaldehyde anion, as a metal or proton chelate. In almost all reactions tried, including pyrolysis of anhydrous bromomalonaldehyde salts, bromomalonaldehyde could be sublimed out of the reaction mixture.

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(1) (a) Z = R or Ar [Z. Arnold and F. Sorm, *Collection Czech. Chem. Commun.*, **23**, 452 (1958)]; (b) Z = –CN [S. Trofimenko (unpublished results)]; (c) Z = –CHO [Z. Arnold and J. Zemlicka, *Collection Czech. Chem. Commun.*, **25**, 1318 (1958)]; (d) Z = $-NO_2$ [H. B. Hill, *Ber.*, **15**, 1906 (1882); *Am. Chem. J.*, **22**, 89 (1899)]; (e) Z = –COOR [L. Panizzi, *Gazz. chim. ital.*, **76**, 56 (1946)]; (f) Z = Br [M. J. Grard, *Compt. rend.*, **190**, 187 (1930); *Ann.*, **13**, 336 (1930)]; (g) Z = Cl [W. Diekmann, *Ber.*, **37**, 4638 (1904)]; (h) Z = OH (reductone) [T. Reichstein and R. Oppenauer, *Helv. Chim. Acta*, **16**, 988 (1933)]; (i) Z = –CRO [Z. Arnold and A. Holy, *Collection Czech. Chem. Commun.*, **28**, 869 (1963)].

(2) S. M. McElvain and L. R. Morris, *J. Am. Chem. Soc.*, **73**, 206 (1957).

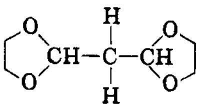
(3) K. C. Brannock, *J. Org. Chem.*, **25**, 258 (1960).

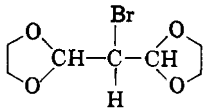
(4) After this work has been completed, a report of the successful hydrolysis of dimethylmalonaldehyde tetraethyl acetal appeared: L. A. Yanovskaya, B. A. Rudenko, V. F. Kucherov, R. N. Stepanova, and J. A. Kogan, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 2189 (1962).

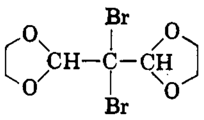
(5) The question whether direct C-halogenation or O-halogenation, followed by some secondary process, takes place, remains open; only O-acylation has been reported for malonaldehydes [T. V. Protopopova and A. P. Skoldinov, *Zh. Obshch. Khim.*, **28**, 240 (1958); Z. Arnold and J. Zemlicka, *Collection Czech. Chem. Commun.*, **25**, 1318 (1960)].

Dibromomalonaldehyde gives the usual aldehyde reactions. Spectral data (infrared, ultraviolet, n.m.r.) are also in accord with the assigned structure.

The effect of the two bromine atoms makes the acetalization of dibromomalonaldehyde difficult; on the other hand, the cyclic acetal VI is very resistant to hydrolysis, more so than the analogous acetals IV and V. Nuclear magnetic resonance peaks of the dioxolane portion in IV and V fall close to those reported for 2,2′-bis-1,3-dioxolane[6]; in the case of VI a substantial shift to lower τ is observed.


IV


V


VI

Experimental

Bromomalonaldehyde.—1,1,3-Trimethoxy-3-ethoxypropane[7] (1127 g., 6.33 moles) was stirred with 1127 ml. of water and 45 ml. of concentrated hydrochloric acid until a homogeneous solution resulted. Bromine (1021 g., 6.33 moles) was added slowly to the stirred and cooled (below 35°) solution. After the addition was complete, the clear yellow solution was concentrated at reduced pressure and temperatures not exceeding 70° to yield a thick slurry. Filtration gave slightly yellowish crystals that were washed with cold 50% ethanol and dried in a vacuum desiccator. The yield was 616 g. (65%), m.p. 155° dec.; lit.[1f] m.p. 148°; Ultraviolet: λ_{max}^{EtOH} 248 mμ, log ε 4.16. (Note: The contact of metal with the product is to be avoided, as it induces decomposition.)

Sodium Salt of Bromomalonaldehyde.—The sodium salt was prepared by treating bromomalonaldehyde with an equivalent amount of aqueous sodium hydroxide. The solution was concentrated *in vacuo* and diluted with much acetone. Shiny crystals of the solvated salt separated; they lost their luster on preliminary drying at room temperature and were then dried *in vacuo* at 80° until the -OH band in the infrared disappeared; Ultraviolet: $\lambda_{max}^{H_2O}$ 277, log ε 4.38. N.m.r. (D_2O), 5.31 τ (singlet.

For larger runs, the water was removed by azeotropic distillation with benzene. Yields ranged from 60 to 78%. The salt darkens from 180–310° without melting.

Dibromomalonaldehyde (II).—Dry sodium salt of bromomalonaldehyde (118 g., 0.682 mole) was stirred in 700 ml. of carbon tetrachloride. Bromine was added slowly to the cooled solution (20–30°) until the red color persisted. The suspension was stirred for another 10 min. at room temperature, then filtered, and the cake washed with three 100-ml. portions of carbon tetrachloride. The organic phases were combined, dried with magnesium sulfate and filtered, and the solvent was removed at reduced pressure. Distillation of the residue on a spinning-band column gave 119 g. (76%) of dibromomalonaldehyde, b.p. 55° (9 mm.), n^{20}_{D} 1.5492.

Anal. Calcd. for $C_3H_2Br_2O_2$: C, 15.7; H, 0.9; Br, 69.5; mol. wt., 230. Found: C, 16.2; H, 1.1; Br, 70.4; mol. wt., 210 (cryoscopic in benzene).

Infrared: 3.50, 5.75, 7.40, 9.14, 10.13, 10.7 (w), and 11.7 (w) μ. Ultraviolet: λ_{max} 261 mμ, ε 64. n.m.r.: singlet at τ 0.275.

Dibromomalonaldehyde stores well at room temperature provided moisture is scrupulously excluded.

Bromochloromalonaldehyde (III).—When chlorine was substituted for bromine in the reaction, bromochloromalonaldehyde, b.p. 38 (9 mm.), n^{20}_{D} 1.5245, was obtained in 32% yield (considerable losses due to volatility occurred during solvent removal).

Anal. Calcd. for C_3H_2BrCl: C, 19.4; H, 1.08. Found: C, 18.9; H, 1.26.

Infrared is the same as that of II except for a band at 12.7 μ instead of 11.7 μ.

The Hydrate of Dibromomalonaldehyde.—To a solution of dibromomalonaldehyde in tetrahydrofuran was added an excess of water, and the solution was stirred at room temperature for 2 hr. It was then evaporated *in vacuo* yielding a white solid. It could be recrystallized from water (rhombic plates) but melted unsharply (95–110°). It gave the 2,4-dinitrophenylhydrazine derivative of dibromomalonaldehyde.

The infrared spectrum of the solid had characteristic bands at 2.95, 3.10, 7.6, 9.08, 9.25, 9.60, 10.02, 10.68, and 12.16 μ.

Titration of Dibromomalonaldehyde.—Two dibromomalonaldehyde samples (4.5 and 4.8 mmoles, respectively) were each stirred in 15 ml. of water until solution resulted and were titrated with 0.1 *N* sodium hydroxide to phenolphthalein end point. The samples consumed 4.6 and 4.8 mmoles of base, respectively.

Addition of excess 2,4-dinitrophenylhydrazine reagent yielded the derivative of glyoxal in 96% yield, known to be formed from dihaloacetaldehyde.[8]

Pyrolysis of Dibromomalonaldehyde.—Dibromomalonaldehyde was pyrolyzed by being passed dropwise through a 30-cm. tube packed with quartz chips and maintained at the appropriate temperature by means of an electric furnace. The products were swept with nitrogen into a −80° trap. At 450°, 40% of dibromomalonaldehyde was recovered; at 390°, 50% dibromomalonaldehyde and 29% bromomalonaldehyde was obtained.

Free Radical Reactions of Dibromomalonaldehyde. A.—Dibromomalonaldehyde was refluxed in a small amount of benzene with azobisisobutyronitrile. Hydrogen bromide was evolved and after about 10 min. solid started separating. It was identified as bromomalonaldehyde by comparison with an authentic sample.

B.—Dibromomalonaldehyde was dissolved in benzene and exposed to sunlight. Within a few minutes hydrogen bromide was evolved and bromomalonaldehyde started precipitating. If the bromomalonaldehyde was not removed and the irradiation continued, the solid went back into solution and a strongly acidic sirup was obtained on evaporation of solvent. The same behavior was observed when a sunlamp was used as the light source and carbon tetrachloride as the solvent.

No reaction took place when pure dibromomalonaldehyde was irradiated. Upon dilution with benzene the reaction promptly commenced and proceeded as before.

C.—A 1.71-g. sample of nickel carbonyl was added to a solution of 2.30 g. of dibromomalonaldehyde in 5 ml. of benzene. After stirring for 3 hr. at room temperature there was obtained 3.0 g. of a hygroscopic solid. It gave positive ferric chloride and 2,4-dinitrophenylhydrazine tests and yielded bromomalonaldehyde upon acidification and sublimation.

Similar results were obtained upon refluxing dibromomalonaldehyde in xylene with molecular silver.

Malonaldehyde Bisethylene Acetal (IV).—1,1,3-Trimethoxy-3-ethoxypropane (178 g., 1.0 mole) was mixed in a 1-l. flask with redistilled ethylene glycol (140 g., 2.2 moles), 10 drops of sulfuric acid was added, and the mixture was heated in an oil bath at 140°. The alcohol was distilled slowly through a helices-packed column. After about 2 hr. the distillation almost ceased. The pot residue was mixed with 600 ml. of dilute potassium carbonate solution and extracted with six 200-ml. portions of ether. After drying and removal of ether, there was obtained 102 g. (64%) of a crude oil. Distillation gave a pure fraction, b.p. 85°, (1 mm.), which solidified. Recrystallization from ether–ligroin gave crystals, m.p. 42–43°.

Anal. Calcd. for $C_{17}H_{12}O_4$: C, 52.5; H, 7.55. Found: C, 52.8; H, 7.72.

The n.m.r. spectrum showed three kinds of protons in a 1:4:1 ratio resolved as triplet, A_2B_2 multiplet, and triplet, centered at 5.00, 6.07, and 8.02 τ, respectively (*J* = 5.5).

Bromomalonaldehyde Bisethylene Acetal.—Bromomalonaldehyde (134 g., 0.89 mole) was mixed with ethylene glycol (110 g., 1.78 moles) and 350 ml. of benzene. The mixture was stirred and refluxed, and the water was collected in a separator. When water separation ceased, the solution was cooled, 50 ml. of ether was added, and the organic phase extracted with dilute base and then with water. Drying of the organic layer gave, after solvent removal, 150 g. (70%) of an oil. It was distilled

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(6) E. Caspi, T. A. Wittstruck, and D. M. Piatak, *J. Org. Chem.*, **27**, 3183 (1962).

(7) Available from Kay-Fries Chemicals, Inc., 180 Madison Ave., New York 16, N. Y. Other 1,1,3,3-tetraalkoxypropanes gave comparable results.

(8) F. D. Chattaway and L. H. Farinholt, *J. Chem. Soc.*, 96 (1930).

on a spinning-band column, b.p. 100–104° (1 mm.); yield, 128 g. (60%).

Anal. Calcd. for $C_7H_{11}BrO_4$: C, 35.1; H, 4.54; Br, 33.4. Found: C, 35.4; H, 4.66; Br, 33.0.

The infrared spectrum contains bands at 3.30, 3.40, 6.75, 7.27, 7.98, 8.12, 8.25, 8.65 (vs), 8.90, 9.30, 9.5 (broad), 10.0, 10.50 (broad), 11.25, and 12.95 μ.

The n.m.r. spectrum consists of a doublet and a narrow A_2B_2 multiplet with an area ratio (by integration) of 2:9, indicating coincidence of the central hydrogen with the methylene groups.

Dibromomalonaldehyde Bisethylene Acetal (VI).—Dibromomalonaldehyde (32 g., 0.139 mole) was refluxed in 200 ml. of benzene with ethylene glycol (18.1 g., 0.291 mole) and sulfuric acid (5 drops). Water was removed continuously. After refluxing overnight, 4.2 ml. of water had been collected. The solution was washed with dilute alkali, the organic layer dried, and the solvent removed.

The residual sirup was distilled *in vacuo*. A viscous oil distilled that contained -OH and carbonyl bands. The pot residue solidified and was recrystallized from carbon tetrachloride, yielding 2.6 g. (6%) of VI, m.p. 70–75°. Two recrystallizations from hexane raised the m.p. to 81–82°.

Anal. Calcd. for $C_7H_{10}Br_2O_4$: C, 26.4; H, 3.14; Br, 50.3. Found: C, 26.9; H, 3.24; Br, 49.7.

The n.m.r. spectrum consisted of a singlet at 4.72 τ and a narrow A_2B_2 multiplet centered at 5.81 τ with an area ratio of 1:4.

Hydrolysis Rates of Acetals IV, V and VI.—Samples of IV, V, and VI were dissolved in minimum amounts of ethanol and treated with 2,4-dinitrophenylhydrazine reagent. Derivative formation, as evidenced by precipitation of a colored solid (which later redissolved in the case of VI) took place in about 30 sec. with compounds IV and V. The acetal VI required about 12 hr. for derivative formation.

Effect of Solvent Composition on the Kinetics of the Cyanoethylation of Methanol

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Received April 18, 1963

In previous work,[1] the kinetics and mechanism of the alkali metal alkoxide-catalyzed nucleophilic addition of alcohols to acrylonitrile in alcoholic solvents were studied; the rate equation obtained was $R = k[\text{acrylonitrile}][CH_3O^-]$. We have investigated further the cyanoethylation of methanol in solvent mixtures of methanol and aprotic solvents such as dimethylformamide (DMF) and dioxane. Dipolar solvents were found to change the nucleophilicity order of nucleophiles in bimolecular substitutions.[2] Rates of nucleophilic substitution reactions in which anions participate were found to be accelerated by a factor of 10^5–10^7 or more[3,4] on passing from protic to dipolar aprotic solvents[5]; this phenomenon was used with great advantage in the syntheses of many compounds.[5] It was presumed that this solvent effect must be due largely to the greater reactivity of anions poorly solvated, relative to the transition states of their reactions in dipolar aprotic solvents.[5] A similar solvent effect is to be expected in the case of cyanoethylation and related addition reactions, involving a nucleophilic attack of anions on acidic double bonds. Very little is known at present in this field; thus, the rate of addition of *p*-toluene thiolate to phenylacetylene in ethanol–dimethylformamide mixtures was found to increase greatly in the presence of high dimethylformamide concentrations.[6]

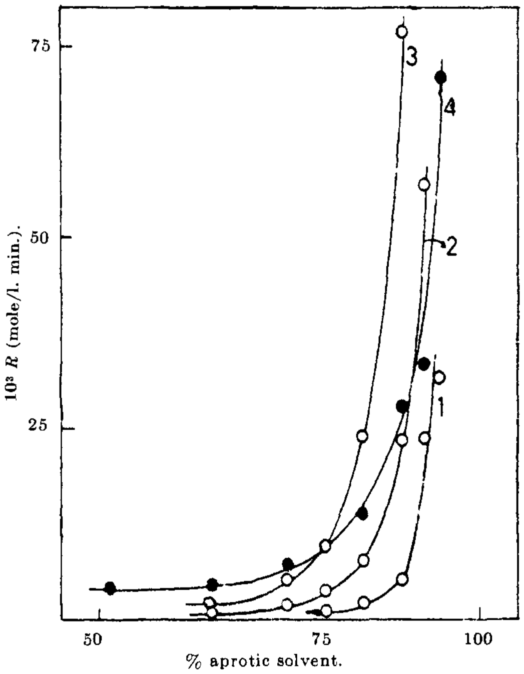

Fig. 1.—Plots of per cent aprotic solvent in the mixed methanol-aprotic solvent against initial rate (mole/l. min.) in methanol–dimethylformamide mixed solvent: (1) at 0°; (2) at 15°; (3) at 25°; (4) methanol–dioxane mixed solvent at 20°.

Results and Discussion

The kinetics of the cyanoethylation of methanol was studied in mixtures of methanol–dimethylformamide, at various temperatures, using lithium methoxide as basic catalyst, and in methanol–dioxane mixtures at 20° using potassium methoxide. Rates of reaction were calculated from the initial slopes of conversion *vs.* time plots. The rate increased progressively with decrease in the proportion of methanol in the mixed solvents (Fig. 1). A very great increase in rate was noticed in the range of low methanol concentrations, which in the case of methanol–dioxane mixtures obviously cannot be attributed solely to the effect of lowering of the dielectric constant on the rate of reaction between an ion and a neutral molecule.[7] In the case of methanol (ϵ 34)[8] and dimethylformamide (ϵ 37.6)[9] mixtures, the increase in rate has but little to do with change in the dielectric constant.

In all cases the rate of reaction was first order in acrylonitrile. First-order rate constants were calculated from the linear plots of log $[\text{acrylonitrile}]_t$ *vs.* time (Tables I, II). The rate of reaction was also approximately first order in catalyst; its value was 1.2

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[1] B.-A. Feit and A. Zilkha, *J. Org. Chem.*, **28**, 406 (1963).

[2] S. Winstein, L. G. Savedoff, S. G. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Letters*, No. **9**, 24 (1960).

[3] J. Miller and A. J. Parker, *J. Am. Chem. Soc.*, **83**, 117 (1961); A. J. Parker, *J. Chem. Soc.*, 1328 (1961).

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[5] A. J. Parker, *Quart. Rev.* (London), **16**, 163 (1962).

[6] W. E. Truce and R. F. Heine, *J. Am. Chem. Soc.*, **81**, 592 (1959).

[7] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1960, p. 135.

[8] H. L. Schlafer and W. Schaffernicht, *Angew. Chem.*, **72**, 618 (1960).

[9] S. Olive, *Makromol. Chem.*, **42**, 251 (1961).