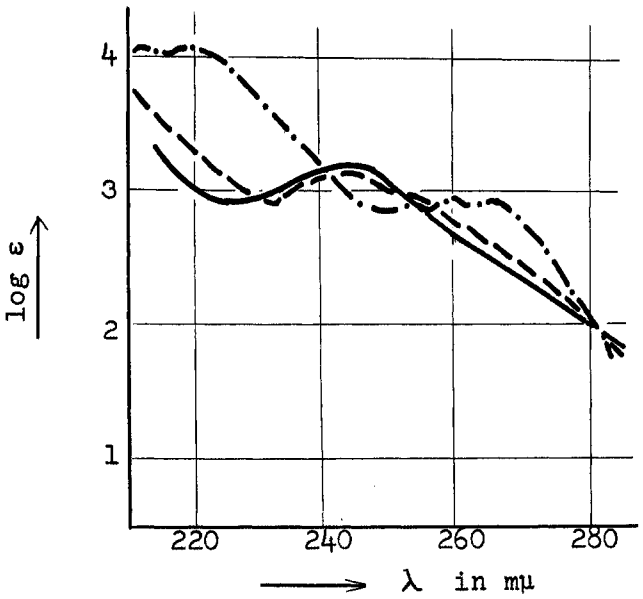


Figure 1.—Uv spectra of carbomethoxymercury compounds I (——), II (-·-·-), and III (- - -) in ethanol.

Authentic Materials.—Methyl tetrahydrofuroate, α-phenyltetrahydrofuran, and α,α′-bistetrahydrofuranyl were prepared by catalytic hydrogenation of methyl furoate,[9] by the methods of Shima, *et al.*,[10] and Mitsui, *et al.*,[11] respectively. Methyl formate, dimethyl oxalate, and bicyclohexyl were commercially availabel (from Wako Pure Chemical Industries, Ltd.).

Photochemical Reaction of Bis(carbomethoxy)mercury in THF.—Bis(carbomethoxy)mercury (4.8 g, 0.015 mol) was irradiated in THF (82 ml) for 12 hr by a 120-W low-pressure mercury lamp under nitrogen at room temperature. During the reaction, metallic mercury precipitated. Evolved gas was introduced into a cylindrical gas holder filled with a saturated aqueous solution of sodium chloride. The gaseous products (230 ml) consisted of carbon monoxide (55%), methane (24%), and carbon dioxide (22%) by glpc, using a 3-m, activated carbon column (80°, He carrier). After distillation of the reaction mixture, a lower boiling fraction, bp 30–68°, contained 0.9 g of methyl formate, which was identified by comparison with authentic material on glpc, using a 1.5-m, tricresyl phosphate on Celite 545 column (80°, He carrier gas flow rate of 46 ml/min). The glpc retention time was 1.2 min. The higher boiling fraction (1.75 g), bp 40–124° (24 mm), consisted of α,α′-bistetrahydrofuranyl (0.92 g), methyl tetrahydrofuroate (0.42 g), and dimethyl oxalate (0.10 g), which were identified by comparison with authentic materials on glpc, using a 1.5-m, silicone DC 550 on Celite 545 column (147°, H_2 carrier gas flow rate of 65 ml/min). The glpc retention times were 11.7, 6.5, and 2.4 min, respectively. Further identification by glpc using another column, 1.5 m, polyethylene glycol 6000 on Celite 545 (200°, H_2 carrier) supported the above results. The products, methyl formate, methyl tetrahydrofuroate, and α,α′-bistetrahydrofuranyl, were isolated by further distillation and preparative glpc, although dimethyl oxalate could not be isolated due to the small amount. The infrared spectra of products isolated were identical with those of authentic materials. The distillation residue was 0.2 g.

The photochemical reactions of carbomethoxymercuric chloride and phenyl(carbomethoxy)mercury were carried out under the same conditions and the reaction mixture was similarly treated.

Photolysis of Diphenylmercury in THF and Cyclohexane.—Diphenylmercury (3.5 g, 0.01 mol) was photolyzed in the mixed solvents (100 ml) at various molar ratios of THF and cyclohexane for 5 hr by a 120-W low-pressure mercury lamp. The reaction mixtures were treated as described above, and the yields of THF dimer and bicyclohexyl in higher boiling fractions were determined by glpc analysis.

(9) B. H. Wojcik, *Ind. Eng. Chem.*, **40**, 210 (1948).
(10) K. Shima and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, **36**, 121 (1963).
(11) S. Mitsui and H. Saito, *Nippon Kagaku Zasshi*, **81**, 289 (1960).

Registry No.—I, 10507-39-8; II, 19638-01-8; III, 17261-26-6; IV, 100-56-1; V, 587-85-9; THF, 109-99-9.

Reaction of Diethyl Bromomalonate with Sodium Phenoxide

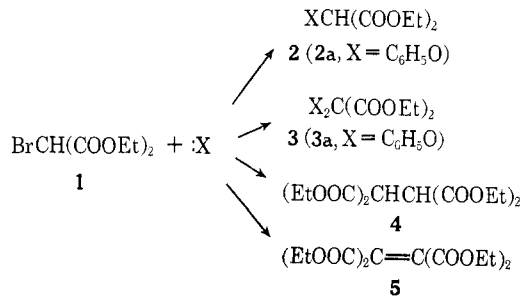
K. H. TAKEMURA,* MARIETTA PULICKAL,[1a] AND FRANCES O. HOFF[1b]

Department of Chemistry, Creighton University, Omaha, Nebraska 68131

Received March 24, 1971

The major product(s) of the reaction of diethyl bromomalonate (**1**) with nucleophiles has been found to be dependent upon the base employed (Scheme I). Thus,

SCHEME I



the diazido compound **3** (X = N_3) is formed in the reaction with sodium azide,[2] and tetraethyl 1,1,2,2-ethanetetracarboxylate (**4**) is obtained with the sodium salts of diethyl phosphite,[3] diethyl thiophosphite,[4] and thiophenol.[5] Reagents which give the unsaturated ester, tetraethyl ethenetetracarboxylate (**5**), have been summarized.[6] Both monoaroxy- and diaroxymalonates (**2** and **3**, X=ArO) are produced when bromo ester **1** is treated with phenoxide, 3-methylphenoxide, or 4-nitrophenoxide ion.[7] The ratio of these two products formed in the reaction was reported to be solvent-dependent.

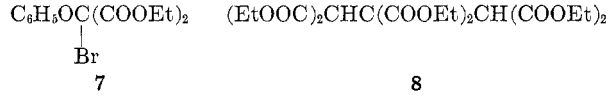
The purpose of the present work was to establish a reaction path for the formation of diphenoxymalonate (**3a**) in the reaction of **1** with sodium phenoxide. In addition, it was of interest to investigate further the effect of solvent on the course of the reaction.

Results and Discussion

The reaction of **1** with sodium phenoxide was carried out in the following solvents: absolute alcohol, 85% alcohol, tetrahydrofuran, benzene, and ether.

(1) Abstracted in part from the M.S. Theses, Creighton University, of (a) S. M. P., 1968; (b) F. O. H., 1969.
(2) H. Bretschneider and N. Karpitschka, *Monatsh. Chem.*, **84**, 1091 (1953).
(3) A. E. Arbuzov and V. S. Abramov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 223 (1946).
(4) A. N. Pudovik and R. I. Tarasova, *Zh. Obshch. Khim.*, **34**, 293 (1964); *Chem. Abstr.*, **60**, 10579 (1964).
(5) K. H. Takemura and D. J. Tuma, *J. Org. Chem.*, **34**, 252 (1969).
(6) A. H. Blatt, Ed., "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 273.
(7) J. B. Niederl and R. T. Roth, *J. Amer. Chem. Soc.*, **62**, 1154 (1940).

In addition to the previously reported aroxymalonates (**2a** and **3a**), the crude reaction product was found to contain the tetracarboxylates **4** and **5**, together with diethyl malonate (**6**), diethyl α-bromophenoxymalonate (**7**), and hexaethyl 1,1,2,2,3,3-propanehexacarboxylate



7 **8**

(**8**). The results of our experiments are summarized in Table I.

TABLE I

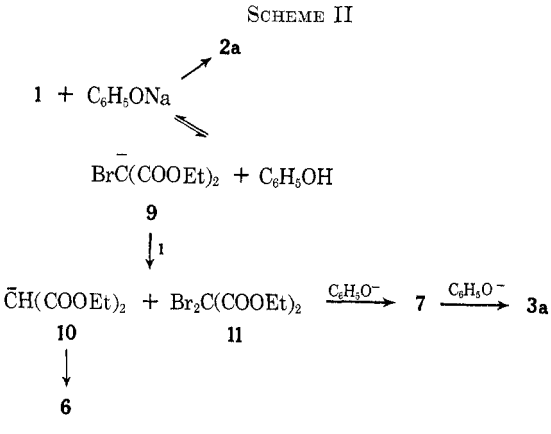
PRODUCTS OF REACTION OF DIETHYL BROMOMALONATE WITH SODIUM PHENOXIDE[a]

	Weight per cent of reaction product[b]						
Solvent	**2a**	**3a**	**4**	**5**	**6**	**7**	**8**
Absolute alcohol	43	28	4	11	9	3	2
85% alcohol[c]	40	27	3	10	15		
Tetrahydrofuran	41	30	10	3	4		10
Benzene	23	41	4	12	14	4	1
Ether	13	37	9	11	16	5	8

[a] Equimolar quantities (0.030 mol) in 50 ml of solvent, heated for 1 hr. [b] Excluding any traces of bromomalonate and phenol present; average of two to three experiments. [c] Several unidentified materials present.

The formation of diphenoxymalonate (**3a**) and α-bromophenoxymalonate (**7**) is most easily explained by reactions of phenoxide ion with dibromomalonate (**11**).[8] We therefore propose the sequence of reactions in Scheme II to account for **3a** and **7**, together with the

SCHEME II



monophenoxy compound **2a** and diethyl malonate (**6**) which are also products of the reaction.

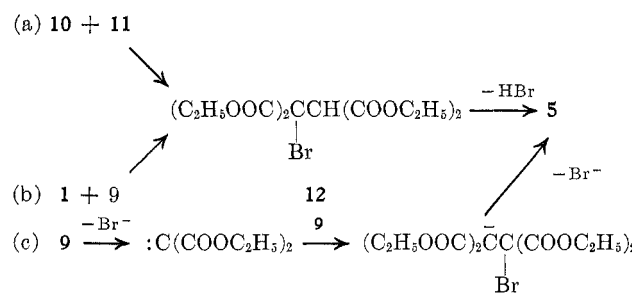
Diethyl bromomalonate (**1**) may be considered as an ambident substrate. Possible sites for reaction with nucleophiles include bromine, α carbon, and α hydrogen. Attack on bromine has been observed.[5] The generally expected displacement on carbon leads to **2a**. We suggest that, in the reaction of phenoxide ion with **1**, reversible attack on hydrogen also occurs to give bromomalonate anion **9**. The latter then combines with the bromine of a second molecule of **1** to give malonate anion (**10**) and dibromomalonate (**11**).

(8) The possibility of **2a** as an intermediate in the formation of **3a** has been excluded on the basis of the reaction of **1** with sodium phenoxide in the presence of 4-nitrophenoxymalonate. There was no evidence for the formation of phenoxy(4-nitrophenoxy)malonate.[1b]

The behavior of chloromalonate is consistent with these ideas. This halo ester with sodium phenoxide in absolute alcohol gave more than 88% of monophenoxy compound **2a**. Only a trace amount of diphenoxymalonate (**3a**) was detected.[9] Although conversion of choromalonate to its anion would be expected to proceed more readily than with **1**, the subsequent reaction at halogen to give the dihalomalonate is greatly diminished. The latter can be attributed to the decreased polarizability of chlorine as compared to bromine.[5,10]

Other products arising from the reaction of **1** with phenoxide may be accounted for by reactions which relate readily with those given in Scheme II. Bromo ester **1** and malonate anion (**10**) can give the saturated tetracarboxylate **4**.[11] Three reaction paths are possible for the formation of the unsaturated ester **5** (Scheme III). In two of these, a and b, **5** is produced by elimination of hydrogen bromide from the intermediate bromotetracarboxylate **12**. Compound **12** can arise from malonate anion (**10**) and dibromomalonate (**11**) (route a), or from attack of bromomalonate anion (**9**) at the carbon of **1** with displacement of bromide ion (route b).[12] In route c, loss of bromide from anion **9** yields a carbenoid intermediate (overall α elimination from **1**). The reaction of the latter with **9**, followed by loss of halide ion, leads to unsaturated ester **5**.[13] We are unable to exclude any of these three possible reaction routes.

SCHEME III



The hexaester **8** can be formed in two ways: the Michael addition of diethyl malonate (**6**) to unsaturated ester **5**,[14] or the reaction of malonate anion (**10**) with dibromomalonate (**11**). The latter was employed in the preparation of **8** in this work. Which of the two routes is followed in our experiments with **1** is undetermined.

In their studies of the reaction of **1** with sodium phenoxide, Niederl and Roth[7] found that the ratio of monophenoxy- (**2a**) to diphenoxymalonate (**3a**) produced

(9) In some experiments, trace amounts of the unsaturated ester **5** were also found. In all cases minor quantities of several unidentified substances were also present.

(10) It is interesting to note that diazidomalonate (**3**, X = N_3) was obtained from **1**,[2] and also from dichloromalonate, but chloromalonate gave no identifiable organic product with sodium azide [M. O. Forster and R. Muller, *J. Chem. Soc.*, 126 (1910)].

(11) C. A. Bischoff, *Ber.*, **29**, 1276 (1896).

(12) D. Bethell, *J. Chem. Soc.*, 666 (1963). A mechanism analogous to (b) was suggested for the formation of bifluorenylidene from 9-bromofluorene and base.

(13) The reactions of 4-nitrobenzyl derivatives with base to give 4,4′-dinitrostilbene have been explained by similar reaction routes. See S. B. Hanna, Y. Iskander, and Y. Riad, *J, Chem. Soc.*, 217 (1961); C. G. Swain and E. R. Thornton, *J. Amer. Chem. Soc.*, **83**, 4033 (1961); I. Rothberg and E. R. Thornton, *ibid.*, **85**, 1704 (1963).

(14) S. Ruhemann and A. V. Cunnington, *J. Chem. Soc.*, 1013 (1898).

was 2:3 in absolute alcohol and 3:2 in 85% alcohol.[15] We have noted little difference in the relative amounts of the two products in these two solvents (Table I). In both, **2a** was found to predominate, the product ratio being in each case about 3:2.

It is noteworthy that the diphenoxy compound **3a** was the major product in those reactions in which sodium phenoxide was insoluble in the solvent (ether and benzene).[16] However, when the phenol salt was soluble (alcoholic and tetrahydrofuran solvents), the principal product was the monophenoxy compound **2a**. It appears that the protic or aprotic nature of the solvent is relatively unimportant. The possibility that these solvent effects might be attributed to differences in the concentration of phenoxide ion available for reaction with bromo ester **1** was considered. The slow addition of phenoxide to **1** had no significant effect upon the ratio of **2a** to **3a**. At the present, the solvent effects noted remain unexplained.

Experimental Section

Melting points were determined on a Fisher–Johns hot state and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were recorded on a Beckman IR-8 spectrophotometer, and nuclear magnetic resonance spectra in carbon tetrachloride (unless otherwise specified) on a Varian T-60 spectrometer. Chemical shifts are expressed in parts per million downfield relative to TMS (δ scale). Glpc analyses were made with an Aerograph A-90-P gas chromatograph using an 8 ft × 0.25 in. column of 20% SE-30 on Chromosorb W at a column temperature of 115°, programmed to 225°, using helium (100 cc/min) as carrier.

Materials.—Reagent grade diethyl bromomalonate (**1**) (Aldrich Chemical) was redistilled, bp 54–55° (0.08 mm), n^{20}D 1.4512. Glpc analysis showed less than 2% dibromo compound. Sodium phenoxide (>97% purity) was prepared as previously described.[17] Reagent grade solvents were employed. Tetrahydrofuran was distilled from lithium aluminum hydride and stored under nitrogen.

Diethyl monophenoxymalonate (2a) was isolated in 50% yield from the reaction of sodium phenoxide and diethyl chloromalonate in alcohol. The crude reaction product (glpc analysis) contained 88% of **2a**. The recrystallized product (alcohol) melted at 51–52° (lit.[7] mp 52–53°): ir (KBr) 1755, 1220, 1100, and 1030 cm^{-1}; nmr 7.05 (m, 5 H), 5.03 (s, 1 H), 4.19 (q, 4 H), and 1.25 (t, 6 H).

Diethyl diphenoxymalonate (3a) was prepared from dibromomalonate and sodium phenoxide in alcohol: bp 158–161° (0.3 mm) [lit.[18] bp 250–260° (60 mm)]; n^{24}D 1.5272; ir (neat) 1765, 1220, 1080, 755, and 695 cm^{-1}; nmr 7.22 (m, 10 H), 4.17 (q, 4 H), and 1.03 (t, 6 H).

Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.21; H, 5.92.

Tetraethyl 1,1,2,2-ethanetetracarboxylate (4) was obtained from **1** and sodium diethyl phosphite as previously described,[3] mp 76° (lit.[3] mp 76°).

Tetraethyl ethenetetracarboxylate (5) was synthesized according to the published procedure,[6] mp 52–53° (lit.[6] mp 52.5–53°).

Diethyl α-bromophenoxymalonate (7) was isolated in 10% yield from equimolar quantities of dibromomalonate and sodium phenoxide in alcohol: bp 135–137° (0.4 mm); n^{24}D 1.5125; ir (neat) 2985, 1750, 1230, 1135, 1050, 1020, 760, and 695 cm^{-1}; nmr 7.22 (m, 5 H), 4.30 (q, 4 H), and 1.27 (t, 6 H).

Anal. Calcd for $C_{13}H_{15}BrO_5$: C, 47.15; H, 4.57. Found: C, 47.40; H, 4.83.

Hexaethyl 1,1,2,2,3,3-propanehexacarboxylate (8) was prepared in 38% yield from dibromomalonate and diethyl sodiomalonate in alcohol: bp 178–179° (0.1 mm) [lit.[18] bp 246° (15 mm)]; n^{26}D 1.4532; ir (CCl_4) 1745, 1245, 1115, and 1040 cm^{-1}; nmr ($CDCl_3$) 4.30 (q, 12 H), 4.33 (s, 2 H), and 1.30 (t, 18 H). The quartet and singlet were superimposed; the quartet and triplet peaks appeared as unresolved doublets.

Anal. Calcd for $C_{21}H_{32}O_{12}$: C, 52.94; H, 6.77. Found: C, 53.08; H, 6.91.

Reaction of Diethyl Bromomalonate (1) with Sodium Phenoxide.—In a typical run, 7.2 g (0.030 mol) of **1** in 10 ml of solvent was added in one portion with stirring to 3.5 g (0.030 mol) of sodium phenoxide in 40 ml of solvent. The addition of **1** resulted in an exothermic reaction with rapid precipitation of sodium bromide. (In ether solvent, it was necessary to moderate the reaction by dropwise addition of **1**.) The mixture was heated (bath 90–95°) and stirred under nitrogen for 1 hr.

In the case of water-soluble solvents, the solvent was removed under reduced pressure (water aspirator) at 100°, and the residue was treated with water. With solvents insoluble in water, the reaction mixture was diluted directly with water. The organic materials were isolated in the usual manner by extraction with ether. The crude oily product (6–7.5 g) was dissolved in toluene for glpc analysis. Components were identified by retention times and by admixture with authentic materials. Weight ratios of the substances present were established from peak areas, with appropriate modifications based upon preliminary studies with known mixtures.

The dropwise addition (20-min period) of sodium phenoxide in 40 ml of alcohol to **1** dissolved in 15 ml of solvent afforded a crude product which contained **2a** and **3a** in the ratio of 3:1.8.

Registry No.—**1**, 685-87-0; **2a**, 4525-70-6; **3a**, 4525-71-7; **7**, 31593-62-1; **8**, 5435-96-1; sodium phenoxide, 139-02-6.

(15) The analytical methods employed were based upon differential solublilities of the substituted malonic acids and preferential amide formation. In our hands, using known mixtures of **2a** and **3a**, these methods gave unsatisfactory results (unpublished observations).

(16) Compound **3a** was reported to be the principal product of the reaction in xylene and in absence of solvent.[7] We assume that similar conditions existed in these reactions.

(17) N. Kornblum and A. P. Lurie, *J. Amer. Chem. Soc.*, **81**, 2705 (1959).

(18) M. Conrad and C. Bruckner, *Ber.*, **24**, 2993 (1891).

An Improved Method of Resolution of Coniine[1]

J. CYMERMAN CRAIG* AND A. R. PINDER

Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California 94122

Received October 2, 1970

The hemlock alkaloids[2] constitute a large group of optically active 2-substituted piperidines of which coniine (2-*n*-propylpiperidine) is the major representative. Considerable current interest in these substances is due not only to the conflicting hypotheses for their biogenesis[3-5] but also to the recent extension of methods of optical rotatory dispersion and circular dichroism to the determination of their absolute configuration.[6-9]

The need for large quantities of optically pure enantiomers of coniine revealed that the published method[10]

(1) Acknowledgment is made to the U. S. Public Health Service (Research Grant HE-05881) for support of this research.

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(3) B. T. Cromwell and M. F. Roberts, *Phytochemistry*, **3**, 369 (1964); B. T. Cromwell in "Biosynthetic Pathways in Higher Plants," A. M. S. Pridham and T. Swain, Ed., Academic Press, New York, N. Y., 1965, p 147.

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(7) K. H. Michel, F. Sandberg, F. Haglid, T. Norin, J. C. Craig, and R. P. K. Chan, *Acta Chem. Scand.*, **23**, 3479 (1969).

(8) G. Fodor, E. Bauerschmidt, and J. C. Craig, *Can. J. Chem.*, **47**, 4393 (1969).

(9) J. C. Craig, A. R. Pinder, and W. E. Pereira, Jr., unpublished results.

(10) A. Ladenburg, *Justus Liebigs Ann. Chem.*, **247**, 1 (1888); K. Hess and W. Weltzien, *Ber.*, **53**, 139 (1920).