Soc. Exp. Biol., **27**, 1305 (1968); (c) C. J. Pedersen, *J. Org. Chem.*, **36**, 254, 1690 (1971); N. S. Poonia, *J. Amer. Chem. Soc.*, **96**, 1012 (1974).
(3) (a) D. St. C. Black and I. A. McLean, *Tetrahedron Lett.*, 3961 (1969); (b) W. Rosen and D. H. Busch, *J. Amer. Chem. Soc.*, **91**, 4694 (1969); (c) W. Rosen and D. H. Busch, *Inorg. Chem.*, **9**, 262 (1970); (d) L. F. Linday and D. H. Busch, *J. Amer. Chem. Soc.*, **91**, 4690 (1969).
(4) (a) N. B. Tucker and E. E. Reid, *J. Amer. Chem. Soc.*, **55**, 775 (1933); (b) S. R. Meadow and E. E. Reid, *ibid.*, **56**, 2177 (1934).
(5) (a) B. Dietrich, J. M. Lehn, and J. P. Sauvage, *Chem. Commun.*, 1055 (1970); 440 (1971); (b) *Tetrahedron Lett.*, 2990 (1969).
(6) H. K. Freusdorff, *J. Amer. Chem. Soc.*, **93**, 600 (1971).
(7) (a) R. M. Izatt, J. H. Rytting, D. P. Nelson, B. L. Haymore, and J. J. Christensen, *Science*, **164**, 44 (1969); (b) G. Eisenman, S. M. Ciani, and G. Szobo, *Fed. Proc., Fed. Amer. Soc. Exp. Biol.*, **27**, 1289 (1968); (c) B. C. Pressman, *ibid.*, **27**, 1283 (1968); (d) L. Lardy, *ibid.*, **27**, 1278 (1968); (e) A. Thore, D. L. Keister, N. Shani, and A. San Pietro, *Biochemistry*, **7**, 3499 (1968).
(8) L. A. Ochrymowycz and J. M. Michna, unpublished results.
(9) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963); **89**, 1827 (1967).
(10) (a) B. T. Kilbourn, J. D. Dussitz, L. A. R. Pioda, and W. Simon, *J. Mol. Biol.*, **30**, 559 (1967); (b) V. T. Ivanov, I. A. Laine, N. D. Abduleav, L. B. Senyavina, E. M. Popov, Y. A. Ovchinnikov, and M. M. Shemyakin, *Biochem. Biophys. Res. Commun.*, **38**, 803 (1969).
(11) M. Russo, L. Mortillaro, L. Credali, and C. de Checchi, *Polym. Lett.*, **3**, 455 (1965).
(12) J. L. Down, J. Lewis, B. Moore, and G. Wilkinson, *J. Chem. Soc.*, 3767 (1959).
(13) W. H. Carothers, *J. Amer. Chem. Soc.*, **51**, 2548, 2560, (1929); **52**, 314, 711, 3292 (1930); **54**, 1559, 1566, 1569, 1579 (1932); **55**, 5023, 5031 (1933); *Chem. Rev.*, **8**, 353 (1931).
(14) The proposed nomenclature supplements the abbreviated nomenclature introduced by Rosen and Busch[3] and Pedersen's "oxy-crown" nomenclature.[2a]
(15) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, p 188.
(16) (a) E. L. Eliel, N. L. Albinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Wiley, New York, N. Y., 1965; (b) H. R. Allcock, "Heteroatom Ring Systems and Polymers," Academic Press, New York, N. Y., 1967, Appendix II; (c) G. W. Frank, P. J. Degen, and F. A. L. Anet, *J. Amer. Chem. Soc.*, **94**, 4792 (1972).
(17) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N. Y., 1959, p 572, and references cited therein.
(18) O. Kamm and C. S. Marvel, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 25.
(19) A. S. Speziole, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 401.
(20) W. H. Mueller and M. Dines, *J. Heterocycl. Chem.*, **6**, 627 (1969).
(21) H. Brintzinger, M. Langheck, and H. Ellwanger, *Chem. Ber.*, **87**, 320 (1954).
(22) R. C. Fuson, C. C. Price, R. A. Bauman, O. H. Bullitt, W. R. Hatehard, and E. W. Maynert, *J. Org. Chem.*, **11**, 469 (1946).
(23) G. M. Bennett and E. M. Whincap, *J. Chem. Soc.*, 1860 (1921).

Intramolecular Aromatic and Aliphatic Ullmann Reactions[1]

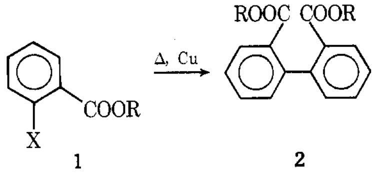
Melvin S. Newman* and James A. Cella[2]

Evans Chemical Laboratory, The Ohio State University, Columbus, Ohio 43210

Received January 22, 1974

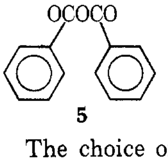
Intramolecular Ullmann cyclizations of several *o*-halobenzoic anhydrides have been shown to take place in high yields at temperatures near 60-70° in tetramethylethylenediamine (TMEDA), dimethylformamide (DMF), *N*-methylpyrrolidone (NMP), hexamethylphosphoramide (HMPA), and pyridine. In all cases except that of pyridine, appreciable (10-30%) to large (50-82%) amounts of reduction products accompany the coupling product. The coupling of aliphatic α-bromo-unsaturated anhydrides under comparable conditions has also been demonstrated.

The Ullmann coupling of 2-halo esters, **1**, to dialkyl diphenates, **2**, has often been effected.[3] In general the reaction has been carried out by long heating with copper at temperatures over 200°. We wished to find out if this type of reaction could be carried out under milder conditions than usual by changing the reaction from an intermolecular to an intramolecular type. In one case tried here earlier the synthesis of 6,6′-diethyldiphenic acid was markedly better when 3-ethyl-2-iodobenzoic anhydride was used instead of methyl 3-ethyl-2-iodobenzoate.[4] A few isolated cases in which intramolecular Ullmann reactions were tried are mentioned[3] but little study of this type of ring closure has been made. We had hoped that the synthesis of unsymmetrical diphenic acids might be improved by the use of unsymmetrical halo anhydrides, but this hope was not fully realized (see later, below).

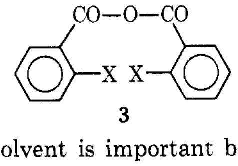


1 **2**

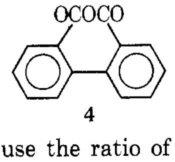
We have found out that Ullmann reactions are carried out much more easily if anhydrides are used instead of halo esters. Two general types of reactions have been studied: method A, in which the 2-halobenzoic acid anhydrides, **3**, are cyclized to diphenic anhydrides, **4**, in a variety of nitrogenous solvents by heating with copper powder at 60-70°; and method B, in which the anhydrides, **3**, are heated with copper powder in benzene containing catalytic amounts of nitrogenous complexing agents. The complexing agents were chosen with the thought that they might complex with any hypothetical organocopper intermediate which might be involved in the reaction.[5-7] For analysis of the results of most experiments the reaction mixtures were treated with methanol and with diazomethane to convert anhydrides into the corresponding methyl esters.



5



3



4

The choice of solvent is important because the ratio of ring-closed product, a diphenic anhydride, **4**, to reduced product, a benzoic anhydride, **5**, is markedly solvent dependent.

The experiments (method A) which illustrate these points are listed in Table I. In our experience, the best solvent for this type of reaction is pyridine. In 1 hr at 60-70° not only is the starting anhydride almost completely reacted but the ratio of diphenic anhydride to benzoic anhydride formed is greatest (see expt 5, 11, and 17 in Table I). Surprisingly, appreciable to large amounts of reduction product were obtained in all of the other solvents studied.[8] That reduction occurs prior to, and not on, quenching of the reaction mixture with water was shown in the case of 2-bromobenzoic anhydride in tetramethylethylenediamine (TMEDA) by quenching with D_2SO_4 in D_2O.

Table I
Effect of Solvent and Substrate in Ullmann Reactions of 2-Halobenzoic Anhydrides[a]

Expt	Substrate	Solvent	% reaction[b]	% coupling[c]	% reduction[d]
1	$(2\text{-ClC}_6\text{H}_4\text{CO})_2\text{O}$[e]	Neat	0	0	0
2	$(2\text{-ClC}_6\text{H}_4\text{CO})_2\text{O}$[e]	TMEDA	43	83	17
3	$(2\text{-ClC}_6\text{H}_4\text{CO})_2\text{O}$[e]	DMF	68	50	50
4	$(2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CO})_2\text{O}$	DMF	100	88	12
5	$(2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{CO})_2\text{O}$	Pyridine	93	96	4
6	$(2\text{-BrC}_6\text{H}_4\text{CO})_2\text{O}$	Neat	0	0	0
7	$(2\text{-BrC}_6\text{H}_4\text{CO})_2\text{O}$	TMED	87	25	75
8	$(2\text{-BrC}_6\text{H}_4\text{CO})_2\text{O}$	NMP[f]	84	77	23
9	$(2\text{-BrC}_6\text{H}_4\text{CO})_2\text{O}$	HMPA[g]	79	77	23
10	$(2\text{-BrC}_6\text{H}_4\text{CO})_2\text{O}$	DMF	100	90	10
11	$(2\text{-BrC}_6\text{H}_4\text{CO})_2\text{O}$	Pyridine	100	98	2
12	$(2\text{-IC}_6\text{H}_4\text{CO})_2\text{O}$	Neat	0	0	0
13	$(2\text{-IC}_6\text{H}_4\text{CO})_2\text{O}$	TMED	100	18	82
14	$(2\text{-IC}_6\text{H}_4\text{CO})_2\text{O}$	HMPA	84	69	31
15	$(2\text{-IC}_6\text{H}_4\text{CO})_2\text{O}$	DMF	76	74	26
16	$(2\text{-IC}_6\text{H}_4\text{CO})_2\text{O}$	NMP	76	85	15
17	$(2\text{-IC}_6\text{H}_4\text{CO})_2\text{O}$	Pyridine	100	98	2

[a] The reaction conditions are those described in the Experimental Section under Ullmann Reactions. Method A. [b] Determined (glpc) by subtracting from 100 the per cent of recovered methyl halobenzoate corresponding to starting anhydride. [c] Determined (glpc) from the amount of dimethyl diphenate produced. [d] Determined (glpc) from the amount of methyl benzoate produced. [e] In reaction by method A, no reactions occurred in *N*-methylpyrrolidine (NMP) acid hexamethylphosphoric triamide (HMPA). [f] *N*-Methylpyrrolidone. [g] Hexamethylphosphoric triamide.

Table II
Effect of Complexing Agent in Ullmann Reaction of 2-Bromobenzoic Anhydride[a,b]

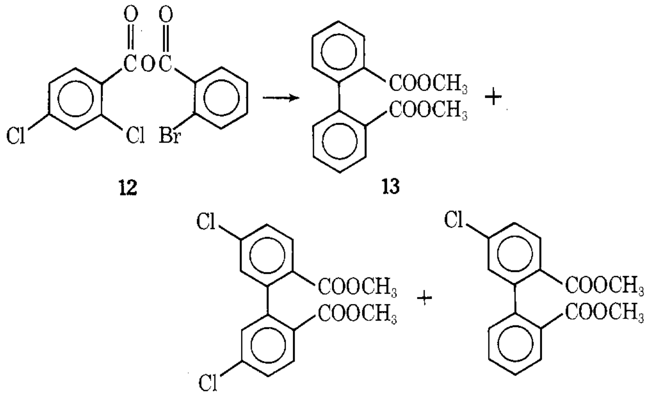
Complexing agent	% reaction	% coupling	% reduction
DMF	100	85	15
HMPA	100	87	13
TMEDA	86	32	68
4,5-Phenanthroline	100	95	5
2,2′-Bipyridine	100	98	2

[a] The per cent of reaction, coupling, and reduction were determined as described in Table I. [b] The reaction conditions are those described in the Experimental Section under Ullmann Reactions. Method B.

No deuterated methyl benzoate was detected. This experiment rules out the presence of an arylcopper species just prior to quenching. Any arylcopper compound formed under our reaction conditions (similar to expt 7, Table I) must have been reduced by the solvent prior to addition of D_2SO_4. This type of substitutive reduction in Ullmann-type reactions has been discussed.[6] Apparently NCH_3 groups in solvents readily engage in reductive processes.

As a standard experiment (method B) a solution of 2-bromobenzoic anhydride (6) in benzene containing less than 1 equiv of a complexing agent was held at reflux over copper powder for 24 hr. The results, summarized in Table II, indicate that the complexing agents of choice contain nitrogen-heterocyclic rings, *e.g.*, 4,5-phenanthroline and 2,2′-bipyridine. To show the generality of this type of reaction, 2,4-dichlorobenzoic anhydride (7) and 2-chloro-5-nitrobenzoic anhydride (8) in benzene containing 2,2′-bipyridine were converted into the corresponding 5,5′-dichlorodiphenic anhydride (10) and 4,4′-dinitrodiphenic anhydride (11) in excellent yields.

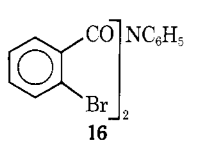
The results outlined above make it obvious that the Ullmann reaction to form diphenic acid derivatives is greatly facilitated by the use of anhydrides instead of esters. Accordingly, we next studied the use of unsymmetrical benzoic anhydrides[9] for obtaining unsymmetric diphenic anhydrides. Although the starting anhydrides used were undoubtedly mainly unsymmetric, on heating rapid disproportionation took place faster than coupling with the result that the two symmetric and the unsymmetric diphenic anhydrides were produced. For example, when the crude mixed anhydride, **12**, formed by treating 2,4-dichlorobenzoic acid in pyridine with 2-bromobenzoyl chloride[9] was heated under the conditions of method A or B a mixture of diphenic anhydrides was obtained. This mixture was hydrolyzed with alkali and the free acids obtained were esterified with diazomethane. Analysis of the esters showed that dimethyl diphenate (**13**), dimethyl 5,5′-dichlorodiphenate (**14**), and dimethyl 5-chlorodiphenate (**15**) were present in about the statistical ratio 1:1:2, respectively.



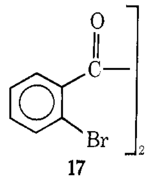
12 **13** **14** **15**

The same mixture of **13**, **14**, and **15** was obtained when an equimolar mixture of **6** and **7** was used as starting material. This fact suggests that, for example, an excellent yield of **15** might be obtained if a mixture of **7** and an excess of **6**, or a mixture of **6** and an excess of **7**, were used. In a given case the choice as to which anhydride should be used in excess would depend on which anhydride was least valuable.

In an effort to use a derivative which might not disproportionate as readily as do anhydrides, we prepared *N*-phenyl-2-bromobenzimide (**16**). An attempt at cyclization (method B) yielded mainly recovered **16** and small



16



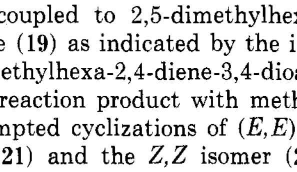
17

amounts of unidentified products, none of which corresponded to the desired *N*-phenyl diphenic imide. One attempt at cyclization of 2,2′-dibromobenzil (**17**) failed to produce any phenanthrenequinone.

Because of the success in the synthesis of diphenic anhydrides by intramolecular Ullmann reactions described above we carried out a few experiments in the aliphatic area. Intermolecular Ullmann reactions on substituted vinyl bromides and iodides have been carried out and the stereospecificity of the reactions determined and discussed.[5] We have found that 2-bromo-3-methylbutenoic anhydride (**18**) is readily coupled to 2,5-dimethylhexa-2,4-diene-3,4-dioic anhydride (**19**) as indicated by the isolation of dimethyl 2,5-dimethylhexa-2,4-diene-3,4-dioate (**20**) after treatment of the reaction product with methanol. The results of the attempted cyclizations of (*E,E*)-2-bromocinnamic anhydride (**21**) and the *Z,Z* isomer (**22**) were not very promising but are of some interest. The *E,E* anhydride, **21**, is not configurationally stable under the reaction conditions (method A). However, by chromatography of the methyl esters of the reaction product, a 22% yield of dimethyl (*Z,Z*)-1,4-diphenyl-1,3-butadiene-2,3-dioate (**23**) was isolated. The *Z,Z* anhydride, **22**, afforded 19% of dimethyl (*E,E*)-1,4-diphenyl-1,3-butadiene-2,3-oate (**24**).[10]

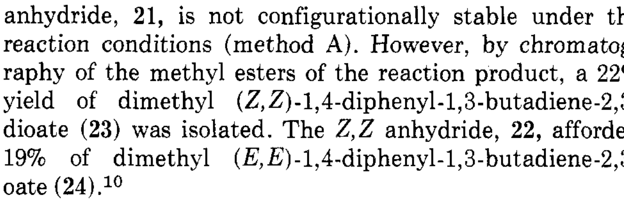
$[(CH_3)_2C{=}CBrCO]_2O$

18

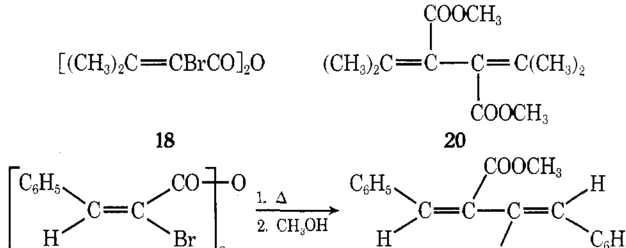


$(CH_3)_2C{=}C(COOCH_3){-}C(COOCH_3){=}C(CH_3)_2$

20



21 **23**



22 **24**

In each of the above coupling reactions some methyl cinnamate was produced. The proportion of this reduction product to coupled product was much larger in the case of the reaction involving **22**, undoubtedly because of greater hindrance to coupling because of the stereochemistry of the transition state which places the phenyl groups in opposition to each other.

The assignment of structures to **23** and **24** was made on the basis of uv and pmr spectra. The uv max for **23** (312 nm, log ϵ 3.5) lies at longer wavelength than that of **24** (278 nm, log ϵ 4.4), as does that of (*E,E*)-1,4-diphenyl-1,3-butadiene (328 nm) compared to (*Z,Z*)-1,4-diphenyl-1,3-butadiene (299 nm).[11] The *E,Z* form for either of the coupling products from **21** and **22** is ruled out because both **23** and **24** have singlets for the vinylic hydrogen at δ 6.92 and 7.92, respectively. If an *E,Z* compound were at hand there should be two singlets.

The fact that these reactions were effected in a short time (*ca.* 1.5 hr) at 80–90° as compared to the longer times at higher temperatures for intermolecular coupling[5] makes further study of intramolecular coupling of vinylic halides of interest.[12]

Experimental Section[13]

Preparation of Acid Chlorides. In a typical experiment 38.5 g of 2-bromobenzoic acid was slowly added to a stirred slurry of 40 g of PCl_5 and 200 ml of dry CH_2Cl_2. When the mixture had become homogeneous (*ca.* 15 min after addition) the solvent and $POCl_3$ were removed under reduced pressure and the residue was distilled to yield 34.0 g (82%) of 2-bromobenzoyl chloride,[14] bp 130–133° (15 mm). In a similar way were prepared 2-chlorobenzoyl chloride,[15] bp 65° (0.05 mm), 2-iodobenzoyl chloride,[16] bp 145° (13 mm), 2,4-dichlorobenzoyl chloride,[17] bp 115–117° (13 mm), and 2-bromo-3-methyl-2-butenoyl chloride,[18] bp 78–80° (15 mm), ir (neat) 5.69 μ (1757 cm^{-1}).

Preparation of Anhydrides. The method[19] we used (method 1) to prepare some anhydrides is illustrated by the synthesis of 2-iodobenzoic anhydride.[20] To an ice-cold solution of 8.7 g of 2-iodobenzoic acid and 3 ml of pyridine in 20 ml of benzene was added a solution of 9.3 g of 2-iodobenzoyl chloride in 20 ml of benzene. After 10 min the mixture was filtered and the filtrate was worked up as usual to yield 14.9 g (88%) of 2-iodobenzoic anhydride, mp 71–75°. In a similar way 2-chlorobenzoic anhydride,[21] mp 78–79°, 2-bromobenzoic anhydride, mp 76.0–77.5°, and 2,4-dichlorobenzoic anhydride, mp 105.0–106.5°, were prepared.

Anal. Calcd for $C_{14}H_8Br_2O_3$: C, 43.7; H, 2.1; *m/e* 383. Found: C, 43.3; H, 1.8; *m/e* 383 (center of triplet). Calcd for $C_{14}H_6Cl_4O_3$: C, 46.2; H, 1.7; *m/e* 365. Found: C, 46.5; H, 1.6; *m/e* 365.

The mixed anhydrides, 2,4-dichloro-2′-bromobenzoic anhydride and 3-bromo-2-naphthoic-2′-bromobenzoic anhydride, were prepared by this method but were not analyzed or characterized because of rapid disproportionation on heating.

By treatment with ethoxyacetylene[22] (method 2), (*E*)-2-bromocinnamic acid was converted into (*E,E*)-2-bromocinnamic anhydride,[23] mp 71–73°, the *Z* isomer into (*Z,Z*)-2-bromocinnamic anhydride,[23] mp 101–102°, and 2-chloro-5-nitrobenzoic acid into 2-chloro-5-nitrobenzoic acid anhydride, mp 145–146°.

Anal. Calcd for $C_{14}H_6Cl_2N_2O_7$: Cl, 18.4; N, 7.3. Found: Cl, 18.3; N, 7.1.

Ullmann Reactions. Method A (See Table I). In a typical experiment (expt 10, Table I) a mixture of 1.0 g of copper powder[24] in 5 ml of pure DMF containing 1.4 g of 2-bromobenzoic anhydride (**6**) was stirred magnetically in a flask held in a bath at 60–70°. After 1.5 hr the cooled mixture was diluted with ether and filtered. The filtrate was washed with water and the water wash was reextracted with ether (repeated once). The combined ether layer was washed with saturated salt solution and filtered through anhydrous $MgSO_4$. After distillation of the ether, the residue was heated at reflux with aqueous methanolic KOH for 20 min. The acids, obtained by ether extraction of the acidified hydrolysis solution, were taken into ether. The dried ether solution was treated with a slight excess of diazomethane and the solvent was distilled. There remained 0.90 g (92%) of an oil which solidified on cooling. Analysis by glpc on a 30% SE-30 (a silicone oil) on Chrome-A support in a 8 ft × 0.25 in. column at 225° using helium revealed that approximately 10% of methyl benzoate was present along with 90% of dimethyl diphenate. No methyl 2-bromobenzoate was present. The identity of each fraction was determined by use of authentic samples. The experiment with **6** in which quenching with D_2SO_4 was used (see discussion) was of the method A type.

Method B (See Table II). In a typical experiment a solution of 1.0 g (2.6 mmol) of **6** and 0.2 g (1.0 mmol) of 2,2′-bipyridine in 75 ml of dry benzene was held at reflux over 0.7 g (10.4 mg-atoms) of copper for 24 hr. The reaction mixture was filtered. The filtrate was extracted with water and dilute HCl. After the benzene solution was filtered through $MgSO_4$, the reaction products were worked up as described for method A to yield approximately 98% of dimethyl diphenate and 2% of methyl benzoate (expt 5, Table II).

In a similar experiment except that the solvents were removed after the unused copper was removed by filtration, there was isolated by crystallization from benzene 0.5 g (86%) of diphenic anhydride,[25] mp 218–220°. Similarly, 2,4-dichlorobenzoic anhydride (**7**) yielded 5,5′-dichlorodiphenic anhydride,[26] mp 201–203°, and 2-chloro-5-nitrobenzoic anhydride (**8**) yielded 4,4′-dinitrodiphenic anhydride,[27] mp 234–236°, in 86 and 80% yields, respectively.

Mixed Anhydride Experiments. The experiments involving freshly prepared 2-bromo-2′,4′-dichlorobenzoic anhydride (**12**) were carried out in HMPA by methods A and B. The results were essentially the same in each case; about 10% of methyl benzoate and methyl 4-chlorobenzoate (reduction products) were formed in addition to dimethyl diphenate (**13**), dimethyl 5,5′-dichlorodiphenate, and dimethyl 5-chlorodiphenate (**15**), in the ratio of approximately 1:1:2. The structure of **15** was assumed from nmr (CCl_4), δ 7.9 and 7.3 (m, 7, ArH), 3.6 (s, 3, OCH_3), 3.52 (s, 3, OCH_3), and mass spectrum, *m/e* 304. When equimolar mixtures of **6** and **7** were treated as described for methods A and B, reaction products closely analogous to those obtained with **12** were obtained.

N-Phenyl-2-bromobenzimide (16). To a slurry containing 0.2 g (5 mmol) of sodium hydride in 10 ml of DMF was added 1.3 g (4.9 mmol) of N-phenyl-2-bromobenzamide.[28] In a few minutes all of the hydrogen had been evolved and the mixture became homogeneous. To this was added 1.1 g (5 mmol) of 2-bromobenzoyl chloride. After standing overnight the mixture was heated to 65° for 30 min. After the usual work-up there was obtained about 2 g of an oil which was crystallized from benzene with little loss to yield **16**, mp 107–108°, which contained only ArH in the pmr, mass spectrum m/e 459, ir 5.92 μ. This compound was recovered unchanged from experiments of type A and B above.

2,2′-Dibromobenzil (17). 2-Bromobenzaldehyde, bp 120–130°, was prepared in 48% yield (crude) by a slight modification (use of aqueous alcoholic potassium hydroxide) of the 2-nitropropane oxidation[29] of 2-bromobenzyl bromide. A mixture of 10.0 g of this aldehyde and 1.0 g of sodium cyanide in 50 ml of NMP was held at 90–100° for 9 hr. The mixture was diluted with an equal volume of water and the crude product, isolated as usual, was treated with saturated aqueous sodium bisulfite to remove unreacted aldehyde. The resulting crude benzoin was treated with 35 ml of concentrated HNO_3 for 1.5 hr at 90–100°. The product from this reaction, isolated as usual, was chromatographed over Florisil to yield 12% of pure **17**, mp 120–123°, m/e 368. No attempt at maximization of yield was made.

Anal. Calcd for $C_{14}H_8Br_2O_2$: C, 45.7; H, 2.2. Found: C, 45.5; H, 2.2.

Dimethyl 2,5-Dimethylhexa-2,4-diene-3,4-dioate (20). Pure 2-bromo-3-methyl-2-butenoic acid, mp 90–91°, prepared essentially as described,[30] was converted by method 2 (using ethoxyacetylene) into the anhydride **18**, 8.5 g of which was immediately added to 60 ml of DMF containing 6.4 g of copper. After 1.5 hr at 80°, 60 ml of methanol was added and the mixture was held at reflux for 30 min. After cooling and dilution with water the product was taken into ether. The ether extract was treated with diazomethane. After the usual work-up distillation afforded 2.9 g (50%) of pure **20**, mp 73–74°, ir (KBr) 5.83 μ, nmr (CCl_4) δ 3.70 (s, 6, OCH_3), 2.15 (s, 6, $=CCH_3$), 1.68 (s, 6, $=CCH_3$), m/e 226, on crystallization from pentane.

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.6; H, 8.1. Found: C, 63.7; H, 8.0.

A small amount (*ca.* 10%) of reduction product, methyl 3-methyl-2-butenoate, was formed in the reaction as estimated by glpc (comparison of retention time with that of an authentic sample). When the reaction of **18** with copper was tried at reflux in benzene with 2,2′-bipyridine for 24 hr, no **20** was isolated, as tarry material was formed.

Dimethyl (Z,Z)1,4-Diphenyl-1,3-butadiene-2,3-dioate (23). (E)-2-Bromocinnamic acid, mp 115–116.5°, prepared essentially as described,[31] was converted into the anhydride with ethoxyacetylene (method 2 above). A mixture of 2.0 g of this and 1.6 g of copper in 10 ml of DMF was stirred at 85° for 1.5 hr. After the usual work-up and esterification to methyl esters, the product was chromatographed over silica gel. There could be isolated 0.4 g (22%) of **23**, mp 121–123°, uv max 318 nm (log ϵ 3.5), ir (KBr) 5.78 μ, pmr δ 7.36 (s, 10, ArH), 6.92 (s, 2, $=CH$), 3.77 (s, 6, OCH_3), after recrystallization from ether–hexane. No attempt was made to maximize the yield of this reaction.

Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.5; H, 5.6. Found: C, 74.7; H, 5.6.

Dimethyl (E,E)-1,4-Diphenyl-1,3-butadiene-2,3-dioate (24). On heating 8.0 g of (E)-2-bromocinnamic acid at 200° for 30 min, the product was crystallized from heptane to yield 5.5 g (69%) of (Z)-2-bromocinnamic acid,[31] mp 129–130°. After conversion to the anhydride with ethoxyacetylene (method 2 above), 5.0 g of the anhydride **22**, 4.0 g of copper, and 20 ml of DMF were held at 80–90° for 90 min. The mixture was diluted with methanol and refluxed for 1 hr. The resulting product was separated into neutral and acidic fractions by extraction with K_2CO_3 solution. The acid fraction was esterified with diazomethane and the esters were chromatographed on silica gel to yield 0.7 g (19%) of **24**,[32] mp 113–115°, uv max 278 nm (log ϵ 4.4), pmr δ 7.92 (s, 2, $=CH$), 7.33 (m, 10, ArH), 3.73 (s, 6, OCH_3).

Registry No.—$(2\text{-}ClC_6H_4CO)_2O$, 49619-43-4; $(2,4\text{-}Cl_2C_6H_3CO)_2O$, 51417-52-8; $(2\text{-}BrC_6H_4CO)_2O$, 49619-44-5; $(2\text{-}IC_6H_4CO)_2O$, 51417-53-9; **4**, 6050-13-1; **8**, 51417-54-0; **10**, 20872-20-2; **11**, 27007-55-2; **12**, 51417-55-1; **13**, 5807-64-7; **14**, 27007-54-1; **15**, 1035-83-2; **16**, 51417-56-2; **17**, 51417-57-3; **18**, 51417-58-4; **20**, 6117-26-6; **21**, 51417-59-5; **22**, 51417-60-8; **23**, 51417-61-9; **24**, 51417-62-0; Cu, 7440-50-8; 2-bromobenzoyl chloride, 7154-66-7; 2-chlorobenzoyl chloride, 609-65-4; 2-iodobenzoyl chloride, 609-67-6; (E)-2-bromocinnamic acid, 15894-30-1; (Z)-2-bromocinnamic acid, 15813-24-8; 2-chloro-5-nitrobenzoic acid, 2516-96-3; N-phenyl-2-bromobenzamide, 10282-57-2; 2-bromobenzaldehyde, 6630-33-7; 2-bromo-3-methyl-2-butenoic acid, 51263-40-2.

References and Notes

(1) This work was supported by Grant GP 12445 of the National Science Foundation.

(2) The work herein reported is contained in the Ph.D. Thesis of James A. Cella, The Ohio State University, 1973.

(3) P. E. Fanta, *Chem. Rev.*, **38**, 139 (1946); **64**, 613 (1964).

(4) M. S. Newman and M. W. Logue, *J. Org. Chem.*, **36**, 1398 (1971).

(5) T. Cohen and T. Poeth, *J. Amer. Chem. Soc.*, **94**, 4363 (1972), and references cited therein.

(6) For discussions of the role of complexing agents in reactions involving copper, see N. Kornblum and D. L. Kendall, *J. Amer. Chem. Soc.*, **74**, 5782 (1952); A. H. Lewin, M. J. Zovko, W. H. Rosewater, and T. Cohen, *Chem. Commun.*, 80 (1967).

(7) R. G. R. Bacon and H. A. O. Hill, *Quart. Rev., Chem. Soc.*, **19**, 95 (1965).

(8) In this connection, the efficacy of HMPA in the deamination of aryldiazonium tetrabromomercurates(II) in the presence of powdered glass is pointed out. See M. S. Newman and W. M. Hung, *J. Org. Chem.*, **39**, 1317 (1974).

(9) S. R. Sandler and W. Karo, "Organic Functional Group Preparations," Academic Press, New York, N. Y., 1972, pp 85–90.

(10) The facts that **21** yields **23** and **22** yields **24** do not mean that inversion of configuration has occurred. The change of *E,E* anhydride to *Z,Z* ester is a consequence in the change of priorities in assigning the configurations to starting and end products. The crude reaction product from **21** was shown not to contain **24** by the absence of absorption at 248 nm.

(11) J. H. Pinckard, B. Wille, and L. Zechmeister, *J. Amer. Chem. Soc.*, **70**, 1938 (1948).

(12) G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Amer. Chem. Soc.*, **93**, 1379 (1971), have shown that vinyl copper compounds couple with retention of stereochemistry.

(13) All melting points and boiling points are uncorrected. Microanalyses were performed by M-H-W Laboratories, Garden City, Mich. Ir spectra were recorded on a Perkin-Elmer Infracord using sodium chloride disks or potassium bromide pellets. Pmr spectra, taken on an A-60 instrument, Varian Associates, Palo Alto, Calif., are reported as δ units relative to $(CH_3)_4Si$. Uv spectra were run in dichloromethane and recorded on a Perkin-Elmer Model 202 spectrophotometer. Unless otherwise mentioned, glpc analyses were performed on an F & M Model 500 gas chromatograph equipped with a thermal conductivity detector. A 7 ft × 0.25 in. column packed with 15% silicone gum rubber SE-30 on 60-80 mesh Chromosorb W was used. The terms "usual work-up" and "worked up as usual" mean that after the organic solution was washed with 3 *N* HCl or 3 *N* K_2CO_3, water, and saturated salt solution, it was dried by passage through a cone of $MgSO_4$ and the solvents were removed on a rotary evaporator. DMF, HMPA, and NMP were distilled from calcium hydride and stored over molecular sieves (Linde 4A) prior to use. TMEDA was stored over barium oxide in a desiccator. Pyridine was stored over KOH pellets. Benzene was distilled with azeotropic removal of water and then redistilled from calcium hydride prior to use. 2,2′-Bipyridine, 4,5-phenanthroline, and 2-bromo- and 2-iodobenzoic acid were obtained from the Aldrich Chemical Co. Ethoxyacetylene was obtained from the Farchan Chemical Co. Diazomethane, generated from *N*-nitroso-*N*-methylurea and 50% KOH, was used immediately after preparation.

(14) C. Schotten, *Ber.*, **21**, 2251 (1888).

(15) O. Emmerling, *Ber.*, **8**, 883 (1875).

(16) J. B. Cohen and H. S. Raper, *J. Chem. Soc.*, **85**, 1272 (1904).

(17) J. B. Cohen and S. H. C. Briggs, *J. Chem. Soc.*, **83**, 657 (1903).

(18) D. Pitre, *Farm.* (*Pavia*], **4**, 657 (1949); *Chem. Abstr.*, **44**, 4866*e* (1949).

(19) W. Gerrard and A. M. Thrush, *J. Chem. Soc.*, 741 (1952).

(20) J. H. Looker and D. N. Thatcher, *J. Org. Chem.*, **23**, 403 (1958).

(21) H. Adkins and Q. E. Thompson, *J. Amer. Chem. Soc.*, **71**, 2242 (1949).

(22) J. F. Arens and P. Modderman, *Proc. Kon. Ned. Akad. Wetensch.*, **53**, 1163 (1950); *Chem. Abstr.*, **45**, 6152 (1951); H. H. Wasserman and P. S. Wharton, *J. Amer. Chem. Soc.*, **82**, 1411 (1960).

(23) S. Reich and R. Couchet, *Helv. Chim. Acta*, **3**, 243 (1920).

(24) Venus 44-F copper from the Venus Copper Co. was used in all experiments.

(25) H. W. Underwood and E. L. Kochmann, *J. Amer. Chem. Soc.*, **45**, 3075 (1923), give mp 219°.

(26) E. B. Hunn, *J. Amer. Chem. Soc.*, **45**, 1024 (1923), gives mp 206°.

(27) F. Bell and P. H. Robinson, *J. Chem. Soc.*, 1697 (1927), give mp 233–235°.

(28) J. Meisenheimer and H. Meis, *Ber.*, **57**, 289 (1924).

(29) H. B. Hass and M. L. Bender, *J. Amer. Chem. Soc.*, **71**, 1767 (1949).

(30) L. N. Owen and M. V. S. Suttanbawa, *J. Chem. Soc.*, 3089 (1949), give mp 91°.

(31) J. J. Sudborough and K. J. Thomson, *J. Chem. Soc.*, 666 (1903), give mp 119–120° for the *E* isomer and 131–132° for the *Z* isomer.

(32) K. Freudenberg and T. Kempermann, *Justus Liebigs Ann. Chem.*, **602**, 184 (1957), give mp 116°.