Notes

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Studies on the Syntheses of Benzoheterocyclic Compounds. VI.[1] Diphenide and Its Methoxyl Derivatives

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The preceding paper[1] reported that monomethyl esters of diphenic acid and its tetramethoxyl derivatives as the starting materials for these title compounds were prepared in excellent yield by methanolysis of the corresponding diphenic anhydrides.

This paper reports that diphenide (5,7-dihydrodibenz[*c*,*e*]oxepin-5(7H)-one) (Ia) and its new methoxyl derivatives, were prepared by two different methods to test their biological activities. The first method was the intramolecular Cannizzaro reaction of diphenaldehyde (IIa) and its methoxyl derivatives, and the second was the partial reduction of diphenic acid derivatives with sodium borohydride.

Examples of the conversion of dialdehydes to the corresponding lactones or alcohol acids by an intramolecular Cannizzaro reaction have been reported; *o*-phthalaldehyde,[3] naphthalene-2,3-dicarboxaldehyde,[4] polygodial,[5] and IIa.[6] Recently, Sturrock, *et al.*[7] found that IIa yielded Ia when heated in dilute sodium hydroxide containing a small amount of ethanol to facilitate contact. However, Matarasso–Tchiroukhine[8] reported that 4,4′,5,5′-tetramethoxydiphenaldehyde (IIb) did not undergo this reaction in aqueous potassium hydroxide solution and suggested that the reaction was prevented by the presence of methoxyl groups.

To investigate this suggestion[8] about the effect of methoxyl groups in IIb and to obtain diphenide derivatives (I), Cannizzaro reaction of IIb and the other methoxyl derivatives, 5,5′,6,6′-tetramethoxydiphenaldehyde (IId),[9,10] and 5,5′-dimethoxydiphenaldehyde (IIc)[11] were carried out.

The aldehyde (IIb) when heated in 6% ethanolic or even in 15% aqueous potassium hydroxide gave a good yield of 2′-hydroxymethyl-4,4′,5,5′-tetramethoxy-2-biphenylcarboxylic acid (IIIb), mp 152—153.5°. The structure of IIIb was confirmed by its conversion to the esters, IV and V, and to the lactone (Ib); methylation of IIIb with diazomethane yielded the corresponding methyl ester (IV), mp 126—128°, which in turn was treated with acetic anhydride and pyridine to afford methyl 2′-acetoxymethyl-4,4′,5,5′-tetramethoxy-2-biphenylcarboxy-

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[1] Part V: S. Kobayashi and M. Azekawa, *Annual Reports of The Faculty of Pharmaceutical Sciences Tokushima Univ.* (Japan), **18**, 11 (1969).

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[3] J. Thiele and O. Gunther, *Ann.*, **347**, 106 (1906).

[4] K. Yagi, *Mem. Inst. Sci. Ind. Research Osaka Univ.*, **8**, 200 (1951).

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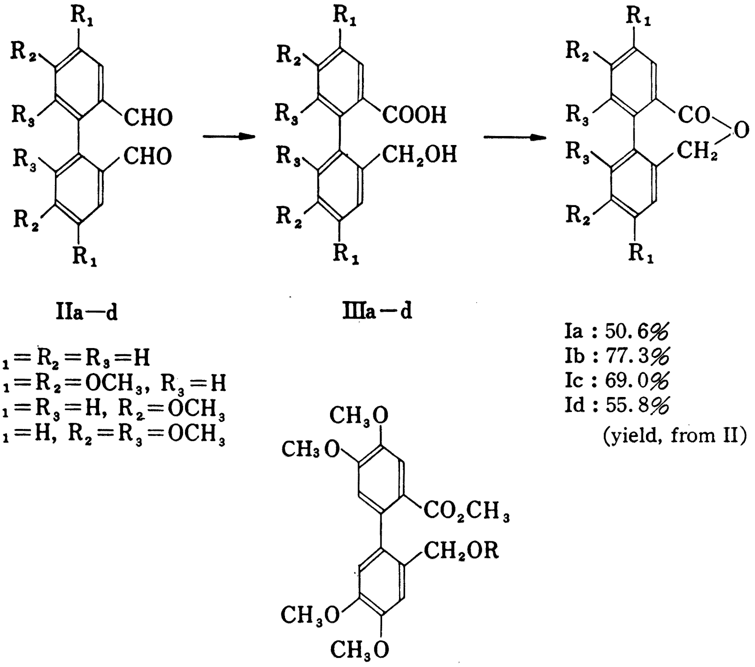
[10] *a*) T. Kametani, K. Fukumoto, and T. Nakano, *Yakugaku Zasshi*, **82**, 1307 (1962); *b*) M. Nilsson, *Acta Chem. Scand.*, **12**, 1830 (1958).

[11] J. Koizumi, S. Kobayashi, and S. Uyeo, *Chem. Pharm. Bull.* (Tokyo), **12**, 696 (1964).



IIa—d

a : $R_1=R_2=R_3=H$
b : $R_1=R_2=OCH_3$, $R_3=H$
c : $R_1=R_3=H$, $R_2=OCH_3$
d : $R_1=H$, $R_2=R_3=OCH_3$

IIIa—d

Ia : 50.6%
Ib : 77.3%
Ic : 69.0%
Id : 55.8%
(yield, from II)

IV : R=H
V : R=$COCH_3$

Chart 1

late (V), mp 106—109°. Lactonization of IIIb to 2,3,9,10-tetramethoxydiphenide (Ib) was achieved by heating IIIb *in vacuo* at 150° for 7 hr or in excellent yield by refluxing it in benzene in the presence of a small amount of hydrochloric acid.

The Cannizzaro reaction of IId with 5% ethanolic potassium hydroxide gave a good yield of 2'-hydroxymethyl-5,5',6,6'-tetramethoxy-2-biphenylcarboxylic acid (IIId), mp 145—146.5°, which was cyclized with benzene–hydrochloric acid to 1,2,10,11-tetramethoxydiphenide (Id).

In the case of IIc, the reaction was achieved with 5% ethanolic potassium or barium hydroxide followed by treatment of the resulting product with hydrochloric acid to afford 2,10-dimethoxydiphenide (Ic). The alcohol acid (IIIc), mp 123—124°, was obtained by hydrolysis of Ic.

These facts show that in contrast to results[8] reported about IIb, the methoxyl groups in the compounds, IIb—d, do not inhibit the intramolecular Cannizzaro reaction and the reactions proceed very smoothly to give normal products in good yield. In the case of IIb, Matarasso–Tchiroukhine[8] seems to have mistaken the product (Ib) for the starting material (IIb), because of the similarity in their melting points.

The preparation of Ia by partial reduction of diphenic anhydride (VIa) and the monomethyl ester (VIIa) of diphenic acid (VIIIa) with lithium aluminum hydride has been reported;[12] diphenide (Ia) was obtained from VIa and VIIa in yields of 11.4 and 60.5%, respectively.

We performed the partial reduction of VIIIa *via* its dichloride (IXa) with sodium borohydride by the procedure used for the reduction of phthalic acid dichloride.[13] Method A

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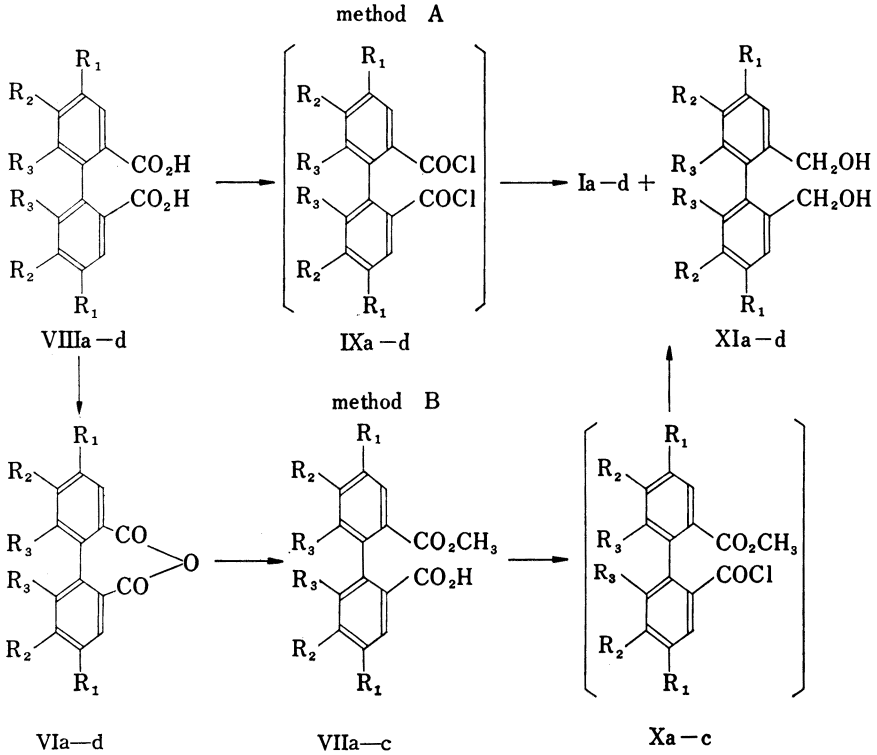
[12] R. Madeja, *Poznan Towarz. Przyjaciol Nauk, Wydzial Mat.-Przyrod., Prace Komisji Mat.-Przyrod.*, **10**, 17 (1965) [*C. A.*, **64**, 3404h (1966)].

[13] S.W. Chaikin and W.G. Brown, *J. Am. Chem. Soc.*, **71**, 122 (1949).



a : $R_1=R_2=R_3=H$
b : $R_1=R_2=OCH_3$, $R_3=H$
c : $R_1=R_3=H$, $R_2=OCH_3$
d : $R_1=H$, $R_2=R_3=OCH_3$

Chart 2

(Chart 2) gave a 48.1% yield of Ia from VIIIa and is superior to the method[12] of reduction of VIa with lithium aluminum hydride.

To compare Medeja's other method[12] (VIIa→Ia) with method A, the over-all yield of Ia from VIIIa was calculated from the yields of VIa and VIIa reported in our previous paper[1] and the 60.5% yield of Ia reported by Medeja.[12] A value of 50.6% was obtained which is almost equal to the 48.1% yield of Ia obtained by method A. Therefore, in this case, sodium borohydride was more effective as a reducing agent than lithium aluminum hydride.

According to Chaikin, *et al.*,[13] 2′-methoxycarbonyl-2-biphenylcarboxylic acid chloride (Xa), derived from VIIIa in excellent yield,[1] seems to be a more suitable starting material for the reduction than the dichloride (IXa).

In fact, Ia was obtained quantitatively by reduction of Xa with sodium borohydride in dioxane. Therefore, method B (VIIIa→VIa→VIIa→Xa→Ia) is a better method for preparation of Ia than method A (VIIIa→IXa→Ia).

Methods A and B can be used for 4,4′,5,5′-tetramethoxydiphenic acid (VIIIb)[1] and 5,5′-dimethoxydiphenic acid (VIIIc).[14] But attempts to obtain 5,5′,6,6′-tetramethoxydiphenic anhydride (VId)[15] in a pure state from the corresponding acid (VIIId) were unsuccessful, so the diphenide (Id) could only be prepared by Method A.

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[14] *a*) G.H. Beaven, D.M. Hall, M.S. Lesslie, E.E. Turner, and G.R. Bird, *J. Chem. Soc.*, **1954**, 131; *b*) R. Adams and N. Kornblum, *J. Am. Chem. Soc.*, **63**, 188 (1941); *c*) L.F. Fieser, *J. Am. Chem. Soc.*, **51**, 2471 (1929).

[15] B.M. Bogosslowski and W.S. Krassnowa, *Chem. J. Ser. A. J. Allg. Chem.*, **7**, 1543 (1937); *Chem. Zentr.*, II, **1937**, 4135.

Partial reduction with sodium borohydride in method B gave the desired diphenides (I) in good yields, together with small amounts of the diols (XI), but reduction in method A afforded relatively more of the diols (XI) than of the diphenides (I). These facts are consistent with the report[13] that the low reactivity with sodium borohydride is advantageous for selective reduction of an acid chloride group in the presence of an ester group. With VIIIa—c, method B is the better for preparation of the diphenides, Ia—c.

The structures Ia—d, of the corresponding diphenides were confirmed by the identity of the corresponding diphenides, prepared by the two different methods described above. Furthermore, their structures were supported by the molecular peaks in their mass spectra, which indicated that they were not lactide-type compounds, but lactones.

Compounds Ia—d gave a strong band at 1380±5 cm^{-1}, while compounds IIIa—d and XIa—d had no absorption peak in this region. This seems to be a characteristic band due to the methylene twisting and wagging vibrations in diphenides Ia—d.

Experimental[16]

Formation of Diphenide (Ia)——We reported previously that 5,6-dimethoxy-2′-formyl-2-biphenylcarboxylic acid (XII) was obtained by Ullmann condensation[9] of methyl 2-bromoveratrate with 2-iodobenzaldehyde, followed by hydrolysis of the resulting crude products with 6% EtOH–$Ba(OH)_2$. The hydrolysis gave the desired acid (XII) and a neutral substance (130 mg, mp 116—129°), which was recrystallized from ether to afford white plates, mp 131—133.5°. *Anal.* Calcd. for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.74; H, 4.82. IR cm^{-1} (KBr): $\nu_{C=O}$ 1705; δ_{CH_2} 1380. Mass Spectrum *m/e*: 210(M^+). NMR $\delta(CDCl_3)$: 5.00 (2H, singlet, $-CH_2-$), 7.38—7.67 (7H, multiplet, aromatic protons), 7.78—8.05 (1H, multiplet, aromatic proton). From its spectral characters, elemental analysis, and the similarity of its melting point to that reported in the literature,[6,7] the substance seemed to be diphenide (Ia). To confirm this, the Cannizzaro reaction of diphenaldehyde[17] was carried out as follows.

2′-Hydroxymethyl-2-biphenylcarboxylic Acid (IIIa)——A mixture of IIa (215 mg) and 5% EtOH–KOH (20 ml) was refluxed for 1 hr. After removal of EtOH and addition of water, the alkaline solution was washed with ether and benzene, acidified with conc.HCl, and extracted with ether. The extracts were washed with water and dried, and concentrated to give white crystals (65 mg, 27.9%). White plates, mp 142—145°, were obtained on recrystallization from acetone–petr. ether (reported mp 146,[6] mp 141°[7]). *Anal.* Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.52; H, 5.33. IR cm^{-1} (KBr): $\nu_{C=O}$ 1675; ν_{OH} 3300.

Diphenide (Ia)——A mixture of IIIa (1.05 g), benzene (40 ml), and 10% HCl (2 drops) was refluxed for 1.5 hr. The solvent was evaporated off to give 0.79 g (81.7%) of white needles, mp 127–132°, which were recrystallized from benzene-petr. ether as white plates, mp 130—132° (reported mp 132°,[6] mp 134.5—135.5°[7]). *Anal.* Calcd. for $C_{14}H_{10}O_2$: C, 79.98; H, 4.79. Found: C, 79.86; H, 4.83. In the second run, involving the Cannizzaro reaction of IIa (1.58 g) and direct lactonization, white plates of Ia were obtained in a yield of 0.80 g (50.6%). The neutral substance was established to be Ia by direct comparison with an authentic sample obtained in this way from IIa.

2′-Hydroxymethyl-4,4′,5,5′-tetramethoxy-2-biphenylcarboxylic Acid (IIIb)——A crude sample of IIIb (82 mg, 69.5%), prepared from IIb (112 mg) and 6% EtOH–KOH (28 ml) by a similar method to that described for preparation of IIIa, was recrystallized from acetone–petr. benzine as white needles, mp 152—153.5°. *Anal.* Calcd. for $C_{18}H_{20}O_7$: C, 62.07; H, 5.79. Found: C, 62.30; H, 5.78. IR cm^{-1} (KBr): $\nu_{C=O}$ 1720, 1700; ν_{OH} 3460. In the second run, 15% KOH (10 ml) was used instead of 6% EtOH–KOH and the crude product (288 mg) was obtained from IIb (500 mg), together with unchanged IIb (210 mg). The yield was 94.1% based on the amount of IIb reacted.

Methyl 2′-Hydroxymethyl-4,4′,5,5′-tetramethoxy-2-biphenylcarboxylate (IV)——A mixture of IIIb (280 mg) and diazomethane (from 1.5 g of nitrosomethylurea and 7 ml of 50% KOH) in dry ether (18 ml) was allowed to stand overnight at room temperature. Evaporation of the ether and recrystallization of the residue (188 mg, 64.6%) from ether gave colorless plates, mp 126—128.5°. *Anal.* Calcd. for $C_{19}H_{22}O_7$: C, 62.97; H, 6.12. Found: C, 62.82; H, 6.14. IR cm^{-1} (KBr): $\nu_{C=O}$ 1718; ν_{OH} 3485.

Methyl 2′-Acetoxymethyl-4,4′,5,5′-tetramethoxy-2-biphenylcarboxylate (V)——A mixture of IV (100 mg), Ac_2O (0.9 ml) and dry pyridine (2.3 ml) was stood at room temperature for 23 hr. Then water was added

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16) All melting points are uncorrected. IR spectra were taken on Hitachi EPI-G2 and EPI-2, NMR spectra on Varian A-60 using TMS as an internal standard, and mass spectra on Hitachi RMU-6E.

17) *a*) R.G.R. Bacon and W.S. Lindsay, *J. Chem. Soc.*, **1958**, 1375; *b*) W.S. Rapson and R.G. Shuttleworth, *ibid.*, **1941**, 487.

and the mixture was extracted with ether. The extracts were washed successively with 10% HCl, 5% Na_2CO_3 and water, dried and evaporated to give white crystals (86 mg, 76.8%), mp 103—109°. These were recrystallized from ether to afford white prisms, mp 106—109°. *Anal.* Calcd. for $C_{21}H_{24}O_8$: C, 62.37; H, 5.98. Found: C, 62.14; H, 5.98. IR cm^{-1} (KBr): $\nu_{C=O}$ 1728, 1696.

2,3,9,10-Tetramethoxydiphenide (Ib)——Treatment of a mixture of IIIb (100 mg), benzene (7 ml) and conc. HCl (1 drop) in the same way as that described for preparation Ia gave white needles (78 mg, 82.1%), mp 212—214° (from benzene–petr. benzine). *Anal.* Calcd. for $C_{18}H_{18}O_6$: C, 65.44; H, 5.49. Found: C, 65.60; H, 5.58. IR cm^{-1} (KBr): $\nu_{C=O}$ 1688, δ_{CH_2} 1377. Mass Spectrum *m/e*: 330 (M+).

5,5′-Dimethoxy-2′-hydroxymethyl-2-biphenylcarboxylic Acid (IIIc)——A lactone (Ic) (70 mg) was heated with 7% EtOH–KOH (3 ml) for 2 hr. Crude crystals (55 mg, 73.3%) of IIIc were obtained from the mixture in the usual way and recrystallized from acetone–petr. ether to afford white needles, mp 123—124°. *Anal.* Calcd. for $C_{16}H_{16}O_5$: C, 66.66;H, 5.59. Found: C, 66.66; H, 5.82. IR cm^{-1} (KBr); $\nu_{C=O}$ 1685; ν_{OH} 3410.

2,10-Dimethoxydiphenide (Ic)——A mixture of IIc (2.0 g) and 5% EtOH–KOH (100 ml) was refluxed for 1 hr. After removal of the solvent and addition of water, the alkaline solution was washed with ether, made acidic with conc. HCl (8.5 ml), and heated at 80°. The solution was extracted with ether and chromatographied in benzene on acid-washed alumina to give white crystals (1.38 g, 69.0%). mp 140—142.5°. The crude product was recrystallized from ether as white needles, mp 142—143.5°. *Anal.* Calco. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.59; H, 5.37. IR cm^{-1} (KBr): $\nu_{C=O}$ 1695; δ_{CH_2} 1380. Mass Spectrum *m/e*: 270 (M+). In the second run, the same product (20 mg, 64.5%) was obtained by treatment of IIIc (33 mg) with benzene–1% HCl in the same way as in preparation of Ia.

2′-Hydroxymethyl-5,5′,6,6′-tetramethoxy-2-biphenylcarboxylic Acid (IIId)——Following the same procedure used in preparation of IIIa, IId (100 mg) was refluxed with 5% EtOH–KOH (20 ml) for 1 hr. The resulting oily residue was triturated with ether to give colorless prisms (83 mg, 79.0%),mp 145—146.5°(from ether). *Anal.* Calcd. for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found: C, 61.64; H, 5.79. IR cm^{-1} (KBr): $\nu_{C=O}$ 1680; ν_{CH} 3410.

1,2,10,11-Tetramethoxydiphenide (Id)——Following a similar procedure to that described for Ia, IIId (54 mg) was treated with benzene (10 ml) and conc.HCl (5 drops) to afford white crystals (36 mg, 70.6%), mp 164—166°, which were recrystallized from acetone–petr.ether as colorless needles, mp 165.5—166°. *Anal.* Calcd. for $C_{18}H_{18}O_6$: C, 65.44; H, 5.49. Found: C, 65.27; H, 5.55. IR cm^{-1} (KBr): $\nu_{C=O}$ 1700; δ_{CH_2} 1375. Mass Spectrum *m/e*: 330 (M+).

Diphenide (Ia)——Method A: A solution of VIIIa (1.20 g) in dry ether (100 ml) was mixed with $SOCl_2$ (4 ml) and pyridine (0.3 ml), and heated at 45° for 1 hr. The pyridine–HCl precipitated was removed by decantation and the solution was evaporated to dryness. $NaBH_4$ (607 mg) in dioxane (30 ml) was added to the chloride (IXa) in dioxane (14 ml) at room temperature and the mixture was heated on a water-bath for 12 min. After removal of the solvent, the residue was heated with 7% EtOH–KOH (80 ml) for 1 hr. Then the concentrated alkaline solution was washed with ether to obtain 285 mg (26.9%) of the corresponding diol (XIa), mp 100—107.5°. The crude diol formed white needles, mp 111—112°, on recrystallization from petr. ether (reported mp 109—109.8°,[18a)] mp 112°,[17a)] mp 112—113°, [18b)]). *Anal.* Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.76; H, 6.74. IR cm^{-1} (KBr): ν_{OH} 3350, 3250

The alkaline solution separated from the XIa solution in etehr was made acidic with conc. HCl and heated on a water-bath for 10 min. The acidic solution was extracted with ether and the extracts were washed with 2% Na_2CO_3 and water to afford white cubes (0.50 g, 48.1%) of Ia, mp 132—133° (from ether). Found: C, 79.85; H, 5.06.

Method B: 2′-Methoxycarbonyl-2-biphenylcarboxylic Acid (VIIa): This was obtained by methanolysis of VIa as reported in our previous paper.[1)]

Diphenide (Ia): Following the same procedure used in preparation of VIIIa in method A, a mixture of VIIa (1.03 g), dry ether (30 ml), $SOCl_2$ (5 ml), and pyridine (0.1 ml) was refluxed for 3 hr. The resulting acid chloride (Xa) was heated in dioxane (30 ml) with $NaBH_4$ (250 mg) at 100° for 10 min and the crude reduction products were refluxed with 15% EtOH–KOH (60 ml) for 1 hr. The diol (XIa) (23 mg, 2.7%) was thus obtained as white cubes, mp 108—109°. The acidic fraction, separated from XIa was heated at 100° for 15 min and Ia (727 mg, 86.0%) was obtained as colorless prisms, mp 131—133° (from ether). The over-all yield from VIIIa was 71.8%. Found C, 79.90; H, 4.76. The products obtained by methods A and B were identical with a sample prepared from IIa.

2,3,9,10-Tetramethoxydiphenide (Ib)——Method A: The diphenide (Ib) was obtained from VIIIb by the same procedure used in method A for preparation of Ia, except that chlorination was achieved with $(COCl)_2$ instead of $SOCl_2$–pyridine. A mixture of VIIIb (45 mg) and $(COCl)_2$ (1.8 ml) was allowed to stand at room temperature for 2 hr and then heated at 65—68° for a further 2 hr. The acid chloride (IXb) thus obtained in dioxane (7 ml) was reduced with $NaBH_4$ (80 mg) in dioxane (2 ml). Hydrolysis of the reduction products with 10% EtOH–KOH (2 ml) gave 7 mg (16.7%) of XIb, mp 117—119° (reported[8)] mp 128° as the

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18) *a*) J.O. Hawthorne, E.L. Mihelic, M.S. Morgan, and M.H. Wilt, *J. Org. Chem.*, **28**, 2831 (1963); *b*) D.M. Hall, M.S. Lesslie, and E.E. Turner, *Nature*, **163**, 537 (1949).

1/2 H_2O hydrate, mp 136—137° as the anhydrate). After lactonization of the acidic fraction, separated from XIb, Ib (8 mg, 19.5%) was obtained as white cubes, mp 208—211° (from benzene). The diol (XIb) and the lactone (Ib) were found to be identical with the respective samples prepared from VIIIb by Method B by the mixed melting point test.

Method B: 2′-Methoxycarbonyl-4,4′,5,5′-tetramethoxy-2-biphenylcarboxylic Acid (VIIb): This was obtained by methanolysis of VIb as reported in our previous paper.[1]

2,3,9,10-Tetramethoxydiphenide (Ib): Ib was prepared from VIIb using the same procedure used for preparation of Ib in method A. Chlorination of the acid (VIIb) (50 mg) with $(COCl)_2$ (0.7 ml), reduction of the acid chloride (Xb) in dioxane (7 ml) with $NaBH_4$ (75 mg) in dioxane (1 ml), and hydrolysis of the reduction products gave 7 mg (15.9%) of XIb as white plates, mp 117—119° (from benzene). *Anal.* Calcd. for $C_{18}H_{22}O_6 \cdot 3/4\ H_2O$: C, 63.82; H, 6.69. Found: C, 63.57; H, 6.98. IR cm^{-1} (KBr): ν_{OH} 3260. Lactonization of the acidic fraction separated from XIb gave Ib (30 mg, 68.2%) as white cubes, mp 211.5—213.5° (from benzene). The over-all yield from VIIIb was 56.5%. Found: C, 65.63; H, 5.58. The lactone (Ib) obtained by Method B was identical with a sample prepared from IIb by the Cannizzaro reaction.

2,10-Dimethoxydiphenide (Ic)——Method A: Ic was prepared by the same procedure used for preparation of Ib in method A. Chlorination of VIIIc (64 mg) with $(COCl)_2$ (3 ml), reduction of the acid chloride (IXc) in dioxane (5 ml) with $NaBH_4$ (35 mg) in dioxane (5 ml), and hydrolysis of the crude reduction products thus obtained with 15% EtOH-KOH (50 ml) gave a diol (XIc) (18 mg, 31.0%) as white cubes, mp 104—105° (from ether). *Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.06; H, 6.63. IR cm^{-1} (KBr): ν_{OH} 3250, 3165. The diol was shown to be identical with a sample obtained from VIIIc by method B by the mixed melting point test and comparison of the IR. Lactonization of the acidic fraction separated from XIc gave 19 mg (33.3%) of Ic as white needles, mp 140.5—141.5° (from ether). Found: C, 70.92; H, 5.16. This was identical with samples of Ic obtained by the Cannizzaro reaction and method B.

Method B: 5,5′-Dimethoxy-2′-methoxycarbonyl-2-biphenylcarboxylic Acid (VIIc): The acid (VIIIc) (500 mg) in Ac_2O (2.5 ml) was refluxed for 2 hr. On concentration of the reaction mixture, white cubes of VIc, mp 169—171.5°, were obtained and directly refluxed with dry MeOH (20 ml) for 4 hr to afford white cubes (458 mg) of VIIc, mp 189.5—191.5° (from acetone). The over-all yield from VIIIc was 87.6%. *Anal.* Calcd. for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.54; H, 5.14. IR cm^{-1} (KBr): $\nu_{C=O}$ 1715 (ester), 1680, 1660 (acid). The elemental analysis and IR data of VIc are as follows. *Anal.* Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.26. Found: C, 67.54; H, 4.33. IR cm^{-1} (KBr): $\nu_{C=O}$ 1750, 1725.

2,10-Dimethoxydiphenide (Ic): Following a similar prodecure to that described for preparation of Ib by Method B, Ic was obtained as follows. Chlorination of VIIc (90 mg) with $(COCl)_2$ (1.2 ml), reduction of Xc (79mg) in dioxane (6 ml) with $NaBH_4$ (80 mg) in dioxane (3 ml), and hydrolysis of the resulting reduction products with 10% EtOH-KOH (30 ml) gave 10 mg (19.3%) of XIc as white needles, mp 104.5—105.5° (from ether). Found: C, 70.13; H, 6.69. Lactonization of the acidic fraction separated from XIc gave 30 mg of Ic as white needles, mp 141—141.5° (from ether). Found: C, 70.83; H, 5.16. The over-all yields from VIIIc and VIIc were 51.5 and 58.8%, respectively.' The acid (VIIIc) (29 mg) apparently formed by hydrolysis of VIIc was obtained together with Ic.

1,2,10,11-Tetramethoxydiphenide (Id)——Method A: Following the procedure described for preparation of Ib by method A Id was prepared in the following way. Chlorination of VIIId[9,19] (100 mg) with $(COCl)_2$ (1.3 ml), reduction of the acid chloride (IXd) in dioxane (2.5 ml) with $NaBH_4$ (75 mg) in dioxane (2 ml), and hydrolysis of the resulting reduction products with 10% EtOH-KOH (4 ml) afforded a new diol (XId) (55 mg, 59.8%) as white cubes, mp 131—132° (from benzene-petr. ether). *Anal.* Calcd. for $C_{18}H_{22}O_6$: C, 64.65; H, 6.63. Found: C, 64.23; H, 6.51. IR cm^{-1} (KBr): ν_{OH} 3250. Lactonization of the acidic fraction, separated from XId gave a crude product (14 mg, 15.4%) of Id, mp 155—160°, which was recrystallized from acetone-petr. ether as white prisms, mp 160—162°. Found: C, 65.21; H. 5.50. The compound was shown to be identical with a sample prepared from IId by the mixed melting point test and IR comparison.

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[19] H. Kondo and T. Watanabe, *Itsuu Kenkyusho Nempo*, 1, 3 (1950).