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228. Masao Tomita,*[1] Tohru Kikuchi,*[1] Kiyoshi Bessho,*[1],*[2] Toshio Hori,*[1] and Yasuo Inubushi*[3] : Studies on Pilocereine and Related Compounds. III.*[4] Synthesis of 2,2′,3-Trimethoxydiphenyl Ether-4′,5- and -4′,6-dicarboxaldehyde.

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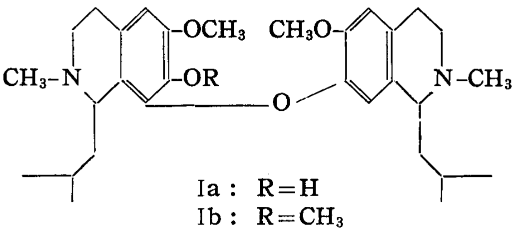
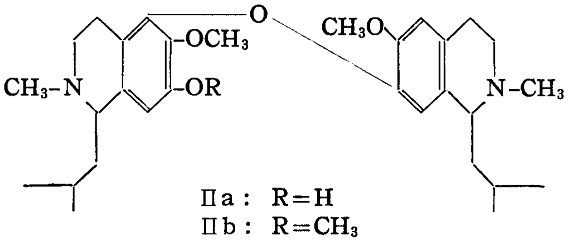
In the preceding paper,*[4] it was reported that the structure of isopilocereine should be either Ia of IIa, although the former seemed improbable since this structure had already been assigned to pilocereine and piloceredine.


Ia : R=H
Ib : R=CH_3


IIa : R=H
IIb : R=CH_3

The isomerization of pilocereine (Ia) to isopilocereine (IIa), however, seemed unlikely from our experience in alkali metal-liq. ammonia reactions of biscoclaurine alkaloids. In addition, the behaviour[1] of O-methylpilocereine (Ib) in the potassium-liq. ammonia reaction did not agree with the empirical rule on the position of cleavage. Therefore, the syntheses of Ib and IIb were undertaken to compare these compounds with O-methylpilocereine and O-methylisopilocereine, respectively. This paper presents the preparations of 2,2′,3-trimethoxydiphenyl ether, 4′,5-dicarboxaldehyde (IX) and 2,2′,3-trimethoxydiphenyl ether 4′,6-dicarboxaldehyde (XXX), which are important intermediates in the syntheses of the bases.

Preparation of IX from bromoveratrate and methyl vanillate *via* VII and VIII has been reported by Kondo, *et al.*[2] The yield was increased by improvements in several of the synthetic steps. In the preparation of IV according to the procedure described previously,[3] Wolff-Kishner reduction of 5-bromoveratraldehyde afforded III nearly quantitatively, whereas the yield in the Clemmensen reduction was only 34%. The conventional Ullmann reaction between III and creosol gave IV in a maximum yield of 30%, while condensation in pyridine solution in the presence of pulverized potassium carbonate and copper powder raised the yield to above 80%. Crystallization of IV yielded needles melting at 42~44°. In this reaction, a phenolic by-product, m.p. 131~132°, was obtained, which was probably formed by oxidative coupling of two molecules of creosol. Structure (V) was deduced for this substance from its ultraviolet spectrum, negative Gibbs reaction, and from the fact that it gave 5,5′-dimethyl-2,2′,3,3′-tetramethoxy biphenyl (VI) on methylation.

Permanganate oxidation of IV gave the diacid (VII), which was converted into the diacid chloride (VIII). Although a catalytic reduction of VIII over palladium-on-charcoal in

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*[4] Part II. This Bulletin, **11**, 1477 (1963).
1) C. Djerassi, S.K. Figdor, J.M. Bobbitt, F.X. Markley : J. Am. Chem. Soc., **79**, 2203 (1957).
2) H. Kondo, H. Kataoka, Y. Baba : Ann. Rept. ITSUU Lab. (Tokyo), **5**, 8 (1954).
3) Part I. M. Tomita, K. Bessho : Yakugaku Zasshi, **79**, 1097 (1959).

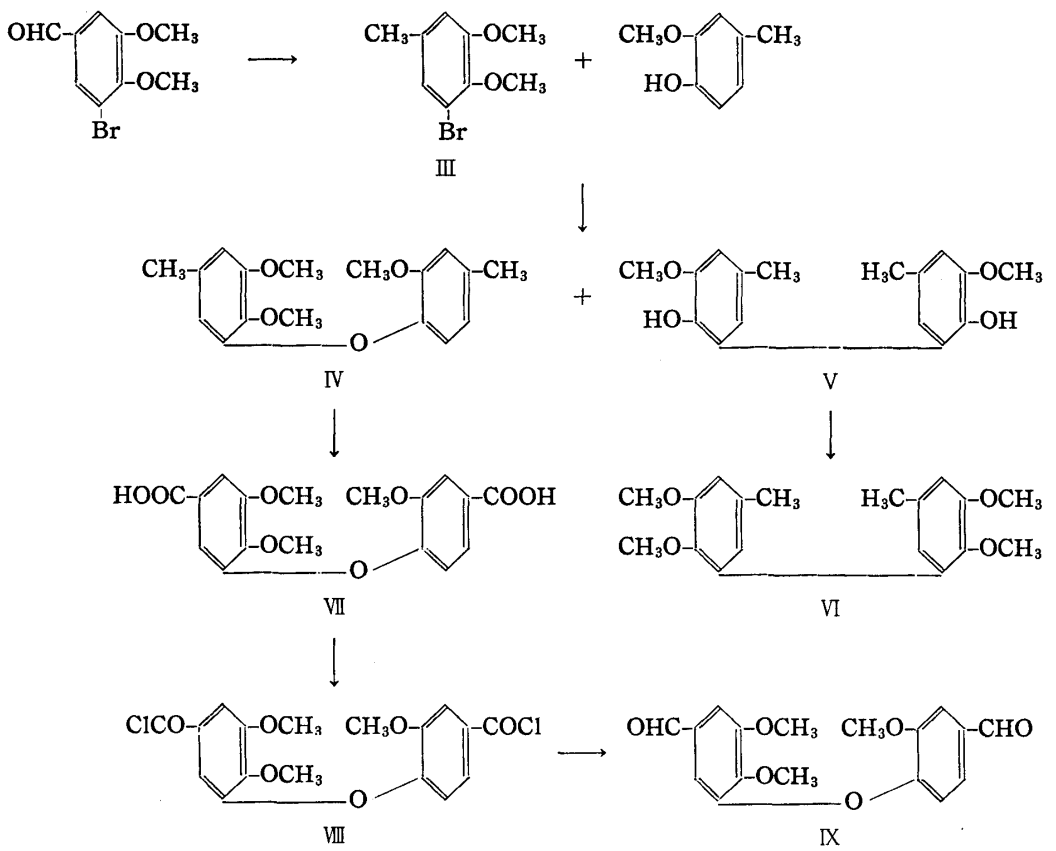

Chart 1.

the presence of N,N-dimethylaniline resulting in formation of the dialdehyde (IX) in 63% yield was reported by Kondo, *et al.*,[2] insufficient absorption of hydrogen was observed in our experiments under the same conditions. However, the conventional Rosenmund method using palladium-barium sulfate catalyst at high temperature gave the dialdehyde (IX) in 81% yield. The total yield of IX calculated on the basis of vanillin was 36%.

In the above procedures the aldehyde groups of the starting materials were reduced to methyl groups, and then oxidized to carboxylic acids and reduced to regenerate aldehyde groups. If an Ullmann condensation of two components containing aldehyde groups were possible, this procedure would save many steps. The condensations of 5-bromopiperonal (X) with vanillin (XI) and of their acetals were not achieved by Kondo, *et al.*,[4] nor the condensation ot XII with XIII by Whaley, *et al.*[5] However, Robinson and Sugasawa[6] reported that the condensation of aldehydes (XIV and XV) took place forming XVI in pyridine solution in the presence of pulverized potassium carbonate and copper powder. This encouraged us to reexamine the reaction of aldehydes. Under conditions similar to the reaction of III and creosol (described above), the possibility of condensations of 5-bromoveratraldehyde (XVII) with vanillin (XI) and also of their acetals was studied and in both cases the dialdehyde (IX) was obtained. But because of the poor yields (4% and 10%, respectively), these procedures were unsatisfactory for synthesis of IX.

Borrows, *et al.*[7] reported that aromatic halogeno-compounds or tosyloxy compounds activated by two nitro groups in the *o*- and *p*-positions reacted easily with phenol in

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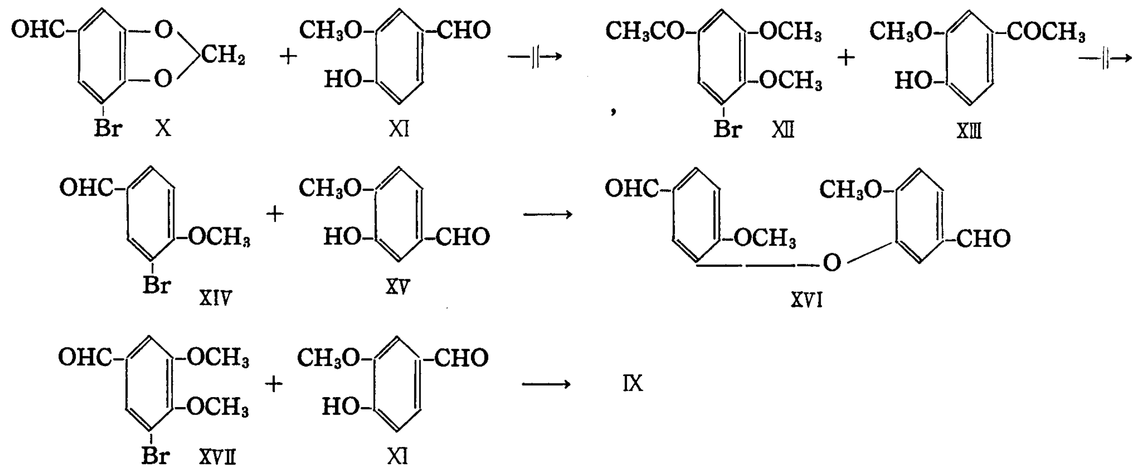
[4] H. Kondo, *et al.* : Ann. Rept. ITSUU Lab. (Tokyo), **1**, 15 (1950).

[5] W.M. Whaley, M. Meadow, W.L. Dean : J. Org. Chem., **19**, 1022 (1954).

[6] R. Robinson, S. Sugasawa : J. Chem. Soc., **1931**, 3173.

[7] E.T. Borrows, J.C. Clayton, B.A. Hems, A.G. Long : J. Chem. Soc., **1949**, S190.



pyridine solution to yield diphenyl ether derivatives. In addition, Grundon, *et al.*[8] found that the substitution of one of the nitro groups by a formyl group did not affect this reaction. They prepared nitrodiphenyl ethers by this method, which were converted into formyldiphenyl ethers by reduction of the nitro groups and deamination. The possibility of taking advantage of these highly reactive nitro-compounds for the synthesis of IX was tested. When iridinaldehyde (XVIII) was refluxed with XIX or XX in pyridine

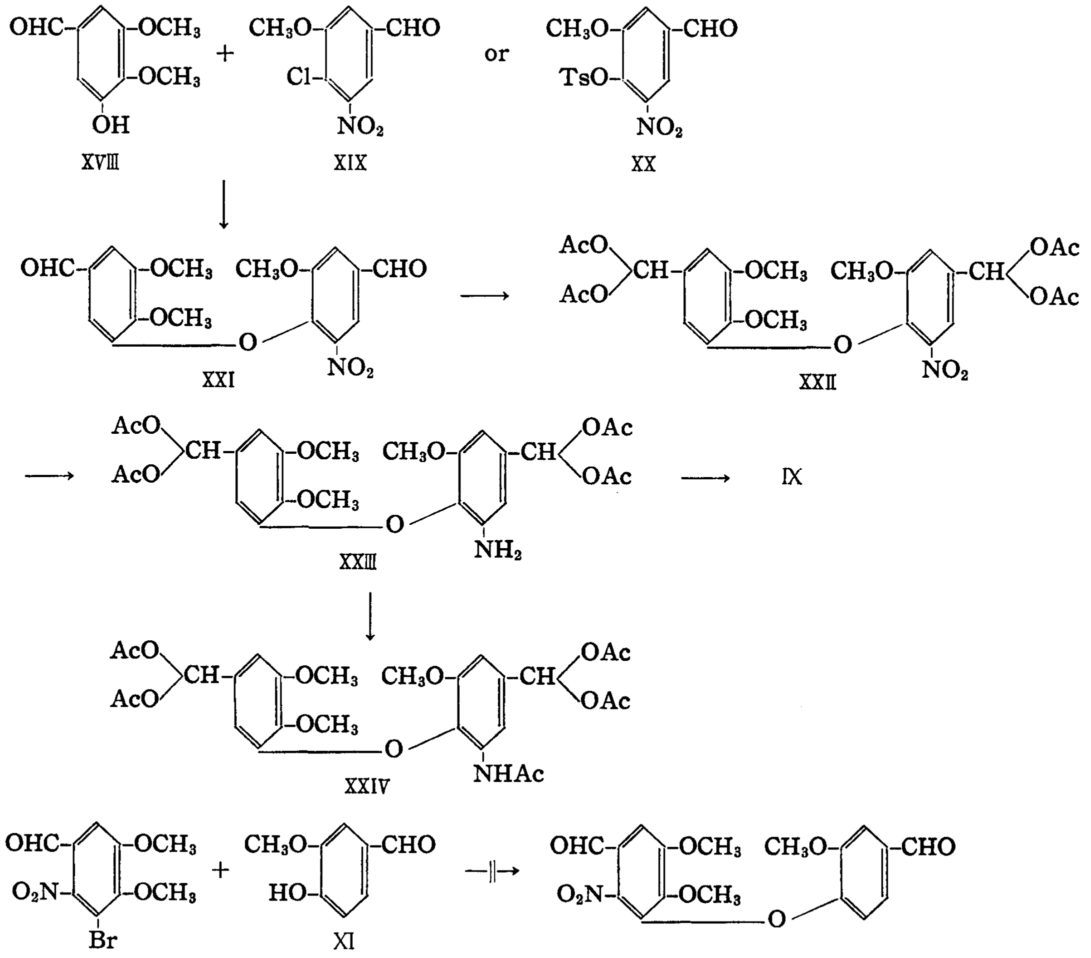


Chart 2.

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[8] M. F. Grundon, H. J. H. Perry: J. Chem. Soc., 1954, 3531.

solution, nitrodiphenyl ether (XXI), m.p. 140~141°, was obtained. Conversion of XXI into the dialdehyde (IX) *via* XXII and XXIII was achieved in good yield (70%). However, since the preparation of iridinaldehyde (XVIII) requires many steps, this method was unsuitable for synthetic use. Attempts were made also at the condensation of vanillin (XI) and 5-bromo-6-nitroveratraldehyde (XXV) which can be easily prepared. The expected diphenyl ether derivative, however, could not be obtained in this procedure and the only product was a phenol $C_8H_6O_5NBr$, m.p. 190~191°, which was considered to be a desmethylated product of XXV because it yielded XXV on methylation. In view of the unsuccessful condensation of *p*-nitrophenol tosylate with phenol reported by Borrows, *et al.*,[7] activation by only one nitro group seemed to be insufficient for this procedure.

The intermediate (XXX) for the synthesis of IIb was prepared in a similar manner to IX. 2-Bromoveratraldehyde, which had been derived from isovanillin, was reduced to XXVI. Ullmann condensation of this with creosol afforded diphenyl ether (XXVII). Permanganate oxidation of this followed by Rosenmund reduction gave the dialdehyde (XXX). The latter compound was allowed to react with nitromethane giving a nitrostyrene (XXXI), but the poor yield of this material made this synthetic route unpractical.

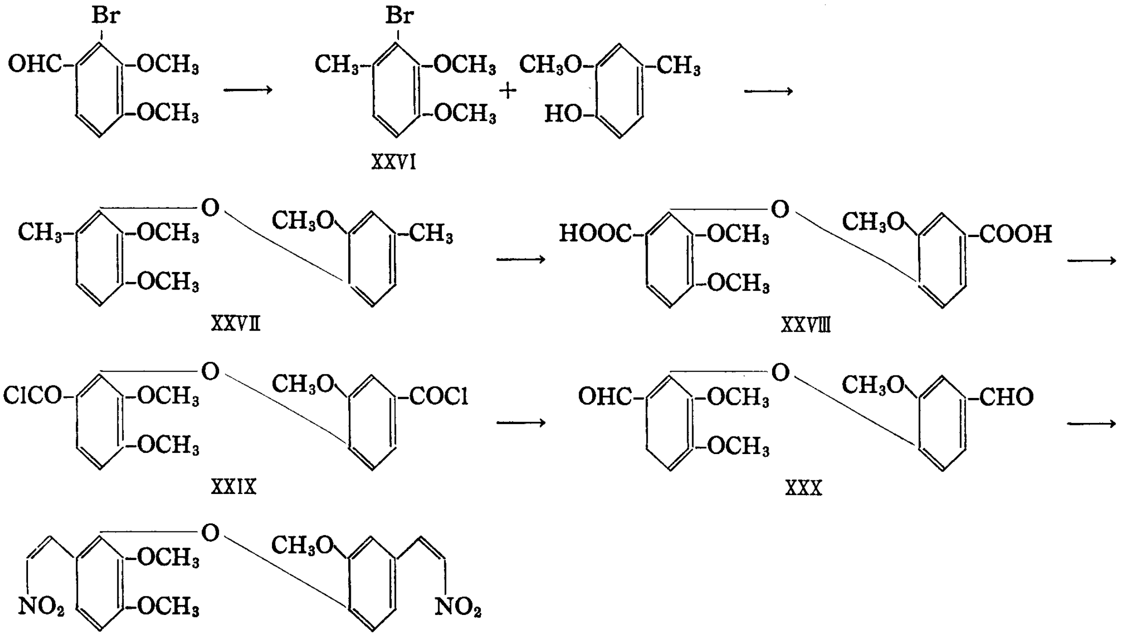

Chart 3.

Experimental*[5]

5-Bromo-3,4-dimethoxytoluene (III)——A mixture of 100 g. of 5-bromoveratraldehyde, 60 ml. of abs. EtOH, and 60 ml. of 80% hydrazine hydrate was refluxed for 30 min. To this mixture was added a solution of 15 g. of Na in abs. EtOH (280 ml.) and heated gently for 2 hr. in an oil bath at 90~100°, where vigorous effervescence was observed. Then the bath temperature was raised to 140° and heating was continued for additional 3 hr. to complete the reaction. The mixture was concentrated to about one third of its volume and after addition of 700 ml. of H_2O, the oily product was extracted with Et_2O. The Et_2O extract was washed successively with 10% KOH, 5% HCl, and 30% $NaHSO_3$ and dried over anhyd. K_2CO_3. Evaporation of this ethereal solution left an oily product, which was purified by distillation yielding 88.5 g. of a colorless oil, b.p$_1$ 112~115° (95%). (rec.[9] b.p$_8$ 124~126).

4′,5-Dimethyl-2,2′,3-trimethoxydiphenyl Ether (IV)——i) The Ullmann reaction of 33.5 g. of III with K salt prepared from 20 g. of creosol was carried out in the presence of Cu powder. After the usual treatment, the product was distilled under reduced pressure to give 12.5 g. of a colorless oil (b.p$_2$ 172~174°) which gradually crystallized as needles, m.p. 42~44° (27%). (rec.[10] b.p$_3$ 188~189°). *Anal.*

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*[5] All melting points are uncorrected.

[9] M. Tomita: Yakugaku Zasshi, 54, 885 (1934).

Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found : C, 70.68; H, 7.29.

ii) A mixture of 100 g. of Ⅲ, 70 g. of creosol, 20 g. of Cu powder, 100 g. of pulverized anhyd. K_2CO_3, and 200 ml. of anhyd. pyridine was refluxed for 15 hr. with vigorous stirring in an oil bath at 155°. Then the reaction mixture was filtered and the residue was washed with pyridine. The combined filtrates were evaporated under reduced pressure and the residue was taken up in Et_2O. The Et_2O solution was filtered, washed with 10% KOH, dried over anhyd. K_2CO_3, and evaporated. Distillation of the residue under reduced pressure gave 17 g. of a fore-run (the starting material and the demsethylated product) and 102 g. of Ⅳ, $b.p_3$ 183~184°, which crystallized gradually sa colorless needles, m.p. 42~44° (82%).

Alkaline washings were acidified with HCl and extracted with Et_2O. The solvent was evaporated, and the residue was distilled under reduced pressure to give 12 g. of recovered creosol ($b.p_1$ 67°). When the distillation residue was treated with MeOH, a crystalline, phenolic product was obtained. Recrystallizations from benzene gave 1.5 g. of colorless plates, m.p. 131~132°. *Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61; $2CH_3O$, 22.6. Found : C, 70.16, 70.19; H, 6.72, 6.77; CH_3O, 22.7, 22.8. UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε) : 252 (4.04), 293 (3.81).

Treatment of this substance (300 mg.) with diazomethane and recrystallization from hexane gave its O,O-dimethyl ether (310 mg.) as colorless plates, m.p. 100~101°, which was identified with the synthetic specimen (described later) of 5,5′-dimethyl-2,2′3,3′-tetramethoxybiphenyl (Ⅵ) by mixed melting point and IR comparison (in Nujol). *Anal.* Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.30; $4CH_3O$, 41.2. Found: C, 71.43; H, 7.52; CH_3O, 41.1. UV : $\lambda_{\max}^{\mathrm{EtOH}}$ 282 mμ (log ε 3.58).

Another 300 mg. portion of the phenolic product was acetylated with Ac_2O and AcONa affording 350 mg. of the diacetyl compound. Recrystallization from EtOH gave colorless prisms, m.p. 163~164°. *Anal.* Calcd. for $C_{20}H_{22}O_6$: C, 67.02; H, 6.19. Found : C, 66.82; H, 6.22.

5,5′-Dimethyl-2,2′,3,3′-tetramethoxybiphenyl (VI)——In a glass tube was placed a mixture of 2.0 g. of Ⅲ and 2.0 g. of Cu powder and additional 4.0 g. of Cu powder was superposed on it. This was heated in an oil bath, the temperature of which was slowly raised from 230° to 290° over a period of 4 hr. After cooling, the product was extracted with Me_2CO, dried over anhyd. K_2CO_3, and evaporated to leave 1.6 g. of an orange-colored oil. A low-boiling material was removed by distillation ($b.p_1$ 100~105°) and the residue was chromatographed on Al_2O_3 (1×10 cm.). After 0.57 g. of an oily material had been eluted with hexane, continued elution with hexane and with benzene afforded 0.25 g. of a crystalline material, which was recrystallized from hexane as colorless plates, m.p. 100~101°. *Anal.* Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found : C, 71.77; H, 7.46. UV : $\lambda_{\max}^{\mathrm{EtOH}}$ 282 mμ (log ε 3.58).

4′,5-Dicarboxy-2,2′,3-trimethoxydiphenyl Ether (VII)——Permanganate oxidation of 80 g. of Ⅳ in a hot pyridine-H_2O mixture (3:1) yielded 62 g. of the diacid (Ⅶ), m.p. 244~246°, (64%). (rec.[11] m.p. 238~243°).

4′,5-Bis(chlorocarbonyl)-2,2′,3-trimethoxydiphenyl Ether (VIII)——A mixture of 25 g. of Ⅶ and 50 ml. of $SOCl_2$ was refluxed for 3 hr. Recrystallization of the product from dry benzene-Et_2O gave 26 g. of Ⅷ as colorless plates, m.p. 97~99°, (95%). (rec.[2] m.p. 83~85°). *Anal.* Calcd. for $C_{17}H_{14}O_6Cl_2$: C, 53.00; H, 3.67. Found : C, 53.15; H, 3.84.

4′,5-Diformyl-2,2′,3-trimethoxy-6′-nitrodiphenyl Ether (XXI)——i) A mixture of 600 mg. of iridinaldehyde (XVIII)[12] and 600 mg. of 3-methoxy-4-chloro-5-nitrobenzaldehyde (XIX)[8] was dissolved in 3 ml. of dry pyridine and refluxed in an oil bath at 140° for 1.5 hr. The reaction mixture was poured into 30 ml. of ice water causing the precipitation of a gummy product, which crystallized on treatment with Et_2O and was recrystallized from EtOH-Et_2O to give 510 mg. of colorless octahedrons, m.p. 140~141°, (51%). *Anal.* Calcd. for $C_{17}H_{15}O_8N$: C, 56.51; H, 4.18; N, 3.88. Found : C, 56.25; H, 4.19; N, 3.76.

In another experiment where 200 mg. of finely pulverized anhyd. K_2CO_3 was added to the reaction mixture, the yield of the product was 760 mg. (75%).

ii) When 500 mg. of XVIII and 800 mg. of 5-nitrovanillin tosylate (XX)[8] were allowed to react in 3 ml. of dry pyridine in the same manner as described in i), there was obtained 360 mg. of XXI, m.p. 140~141°, (44%).

Addition of 200 mg. of pulverized anhyd. K_2CO_3 to the reaction mixture raised the yield to 390 mg. (47%).

6′-Nitro-4′,5-bis(diacetoxymethyl)-2,2′,3-trimethoxydiphenyl Ether (XXII)——To 600 mg. of XXI was added Ac_2O containing 1 drop of conc. H_2SO_4. The mixture was left at room temperature for 1 hr., then poured into ice water and the oily product was extracted with Et_2O. The Et_2O extracts were washed with 10% K_2CO_3, dried over anhyd. $MgSO_4$, and evaporated. The residue crystallized on treatment with MeOH-Et_2O to yield 890 mg. of colorless octahedrons, m.p. 127~128°, (95%). *Anal.* Calcd. for $C_{25}H_{27}O_{14}N$: C, 53.10; H, 4.82. Found : C, 52.85; H, 4.97.

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10) M. Tomita : Yakugaku Zasshi, **56**, 814 (1936).
11) H. Kondo, M. Satomi, T. Ikeda : Ann. Rept. ITSUU Lab. (Tokyo), **2**, 13 (1951).
12) J. R. Crowder, M. F. Grundon, J. R. Lewis : J. Chem. Soc., **1958**, 2142.

4′,5-Diformyl-2,2′,3-trimethoxydiphenyl Ether (IX). i) Rosenmund Reduction of VIII——In a 100 ml. three necked flask were placed 30 ml. of dry toluene, 5.00 g. of the acid chloride (VIII) and 1.00 g. of 5% Pd-$BaSO_4$ catalyst and heated in an oil bath at 105°. A stream of H_2 was passed in bubbles into the vigorously stirred mixture while hydrogen chloride formed in the reaction was titrated with 0.2*N* NaOH (indicator: phenolphthalein). After 4 hr., formation of hydrogen chloride ceased with 118 ml. of 0.2*N* NaOH being consumed (calcd.: 130 ml.). The catalyst was removed by filtration and the solvent was distilled off under reduced pressure. Vacuum distillation of the residue gave 3.58 g. of a colorless oil ($b.p_{2\times10^{-4}}$ 200°, bath temp.) which solidified upon treatment with a small amount of Et_2O. Recrystallization from Me_2CO-Et_2O yielded 3.35 g. of colorless pillars, m.p. 101~102°, (81%). (rec.[2] m.p. 104~105°).

ii) Condensation of 5-Bromoveratraldehyde (XVII) with Vanillin (XI)——A mixture of 3.0 g. of XVII, 4.0 g. of XI, 3.0 g. of finely pulverized anhyd. K_2CO_3, 0.6 g. of Cu powder, and 40 ml. of dry pyridine was refluxed for 2 hr. with stirring. After cooling, the reaction mixture was filtered and evaporated. The residue was dissolved in benzene and the solution was washed with 10% KOH, dried over anhyd. K_2CO_3, and evaporated. When the residue was submitted to vacuum distillation, the distillate (2×10^{-4} mm. Hg, at 200°, bath temp.) (150 mg.) crystallized on treatment with Et_2O as pillars, m.p. 98~99°, (4%).

From the alkaline washings, 2.1 g. of vanillin (XI) was recovered.

iii) Condensation between Acetals——To a solution of 10 g. of XVII-diethyl acetal and 8.0 g. of XI-diethyl acetal in 15 ml. of dry pyridine was added a finely pulverized mixture of 0.5 g. of Cu, 8 g. of K_2CO_3, and 0.5 g. of KI and heated at 155° for 20 hr. with vigorous stirring. Then the reaction mixture was filtered, and the residue was washed with pyridine. The combined filtrates were evaporated, and the residue was dissolved in Et_2O. The Et_2O solution was washed with 10% KOH, dried over anhyd. $MgSO_4$, and evaporated. After removal of a low-boiling substance ($b.p_3$ 135~138°), the distillation residue was chromatographed on Al_2O_3 (1×10 cm.) with Et_2O to yield 2.5 g. of an oily material, which was heated with 20% HCl (30 ml.) for 30 min. in a boiling water bath. Extraction with benzene and distillation under reduced pressure gave 0.45 g. of veratraldehyde ($b.p_{0.4}$ 140~160°, m.p. 52~54°) and a colorless oil which came out at 150~160° (1×10^{-4} mm. Hg). The latter crystallized on treatment with Et_2O yielding 0.99 g. of IX as colorless pillars, m.p. 98~100°, (10%).

iv) Preparation from XXII——The nitro compound (XXII) (1.12 g.) dissolved in MeOH was hydrogenated in the presence of Pd-C catalyst (prepared from 15 ml. of 1% $PdCl_2$ and 200 mg. of carbon and previously equilibrated with H_2). In a period of 4 hr., 130.4 ml. of H_2 was absorbed (Calcd.: 142 ml.). The catalyst was filtered off and evaporation of the filtrate left 1.18 g. of oily amine (XXIII).

A 200 mg. portion of this amine was treated with 3 ml. of Ac_2O containing 1 drop of conc. H_2SO_4 for 5 min. in a water bath at 50°. The acetyl compound (XXIV) was recrystallized from MeOH-Et_2O to yield 170 mg. of colorless plates, m.p. 143~144°. *Anal.* Calcd. for $C_{27}H_{31}O_{13}N$: C, 56.15; H, 5.41. Found: C, 56.45; H, 5.50.

To an ice-cooled solution of 580 mg. of the amine (XXIII) in 2 ml. of AcOH and 2 ml. of 10% H_2SO_4 was added dropwise a solution of 100 mg. of $NaNO_2$ in 0.5 ml. of H_2O over a period of 20 min., and the mixture was stirred for 4 hr. Then a supernatant solution of $NaH_2PO_3\cdot H_2O$ (5.0 g.) in 5 ml. of 50% H_2SO_4 was added over a period of 10 min., where gentle effervescence was observed. The reaction mixture was kept in a refrigerator overnight and extracted with Et_2O after addition of 20 ml. of H_2O. The oily product obtained from the Et_2O extract was distilled in vacuum. The distillate at 180° (1×10^{-4} mm. Hg) crystallized as colorless pillars, IX, m.p. 95~97°. The yield was 230 mg. (72% calcd. based on XXII).

Unsuccessful Reaction between 5-Bromo-6-nitroveratraldehyde (XXV) and Vanillin (XI)——A mixture of 1.0 g. of XXV,[13] 0.6 g. of vanillin (XI), and 3 ml. of dry pyridine was refluxed for 1.5 hr. The reaction mixture was poured into 50 ml. of ice water and acidification with HCl caused a yellow product to precipitate. The precipitate (950 mg.) was taken up in AcOEt and fractionated in the usual manner. The only substance obtained from the non-phenolic fraction was 80 mg. of unchanged XXV, m.p. 145~146°. Fractional recrystallizations of the phenolic fraction gave 320 mg. of recovered vanillin (XI) and 540 mg. of a crystalline product. The latter was recrystallized from MeOH as colorless needles, m.p. 190~191°. *Anal.* Calcd. for $C_8H_6O_5NBr$: C, 34.81; H, 2.20; N, 5.08; Br, 28.94. Found: C, 34.77, 34.66; H, 2.31, 2.22; N, 5.34; Br, 28.92.

The K salt of this phenolic product was recrystallized from MeOH as yellow needles, m.p. >250°, a portion (100 mg.) of which was refluxed with MeI (4 ml.) and MeOH (4 ml.) for 4 hr. After evaporation, the residue was partitioned into benzene and 10% NaOH. The benzene solution afforded 20 mg. of cream-yellow needles, m.p. 145~146°, which showed no depression of the melting point on admixture with XXV. From the alkaline layer, 50 mg. of the unchanged material, m.p. 190~191°, was recovered.

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[13] T. G. H. Jones, R. Robinson: J. Chem. Soc., **111**, 903 (1917); L. C. Raiford, R. P. Perry: J. Org. Chem., **7**, 354 (1942).

The reaction of XXV with XI in the presence of K_2CO_3 powder was also attempted without success.

2-Bromo-3,4-dimethoxytoluene (XXVI)——Wolff-Kishner reduction of 50 g. of 2-bromoveratraldehyde was carried out in a similar manner to the reduction of 5-bromo-compound described above and 45 g. of XXVI was obtained as a colorless oil, b.p$_{0.5}$ 82~84°, (95%). *Anal.* Calcd. for $C_9H_{11}O_2Br$: C, 46.77; H, 4.80; Br, 34.59. Found : C, 46.96; H, 4.84; Br, 34.34.

4′,6-Dimethyl-2,2′,3-trimethoxydiphenyl Ether (XXVII)——A mixture of 33.7 g. of XXVI, K salt of creosol (prepared from 20.1 g. of creosol), and 1 g. of Cu powder was heated with stirring at 160~170° for 2 hr. and then at 180~190° for 2 hr., while additional 1 g. of Cu powder was added in portions. The Et_2O extract of the reaction product was washed with 5% NaOH, dried over anhyd. K_2CO_3, and evaporated. The residue was distilled under reduced pressure to give a fore-run (b.p$_{0.5}$ 80~90°) and an oily product (b.p$_{0.5}$ 130~150°). Repeated distillation of the latter afforded XXVII as a cream-colored oil (b.p$_{0.5}$ 145°). The yield was 4 g. (10%). *Anal.* Calcd. for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found : C, 70.56; H, 6.88.

4′,6-Dicarboxy-2,2′,3-trimethoxydiphenyl Ether (XXVIII)——Permanganate oxidation of 10.2 g. of XXVII in 200 ml. of a pyridine-H_2O mixture (1:1) heated in a boiling water bath gave the diacid (XXVIII), which was recrystallized from Me_2CO-Et_2O to yield 7 g. of colorless pillars, m.p. 207~209°, (57%). *Anal.* Calcd. for $C_{17}H_{16}O_8$: C, 58.62; H, 4.63. Found : C, 58.87; H, 4.54.

4′,6-Bis(chlorocarbonyl)-2,2′,3-trimethoxydiphenyl Ether (XXIX)——The diacid chloride (XXIX) was obtained by refluxing 4.75 g. of XXVIII with $SOCl_2$ for 1 hr. and recrystallized from benzene-dry Et_2O yielding 4.5 g. of colorless prisms, m.p. 106~108°. (89%). *Anal.* Calcd. for $C_{17}H_{14}O_6Cl_2$: C, 53.00; H, 3.67; Cl, 18.41. Found : C, 53.27; H, 3.81; Cl, 18.34.

4′,6-Diformyl-2,2′,3-trimethoxydiphenyl Ether (XXX)——In the presence of 5% Pd-$BaSO_4$ (300 mg.), 2.02 g. of XXIX in dry toluene was hydrogenated as described above for the preparation of IX. In a period of 3.5 hr., 47.5 ml. of 0.2*N* NaOH was consumed (Calcd. : 48.3 ml.). The product was chromatographed on Al_2O_3 (0.7 × 3.5 cm.) with benzene and submitted to vacuum distillation. The dialdehyde (XXX) (1.4 g.) was obtained as a pale yellow oil (b.p$_{3\times10^{-4}}$ 160~180°, bath temp.), (84%).

Semicarbazone : Recrystallized from MeOH. Colorless needles, m.p. 205~215° (decomp.). *Anal.* Calcd. for $C_{19}H_{22}O_6N_6\cdot\frac{1}{2}H_2O$: C, 51.93; H, 5.28. Found : C, 51.80, 51.81; H, 5.39, 5.41.

4′,6-Bis(2-nitrovinyl)-2,2′,3-trimethoxydiphenyl Ether (XXXI)——To an ice-cooled solution of 0.7 g. of XXX and 0.5 g. of CH_3NO_2 in 7 ml. of MeOH was added a solution of KOH (0.7 g.) in the same solvent with stirring. After 2 hr., 5 ml. of H_2O was added, then the reaction mixture was poured into 50 ml. of ice-cooled 5% HCl. The yellow precipitate was collected by suction, dissolved in AcOEt, and the solution was dried over anhyd. $MgSO_4$. After removal of the solvent under reduced pressure, treatment of the residue with MeOH yielded 0.20 g. of the crude crystals melting at 155~165°. Two recrystallizations from Me_2CO-MeOH afforded an analytical sample as yellow needles, m.p. 171~173.5°. *Anal.* Calcd. for $C_{19}H_{18}O_8N_2$: C, 56.71; H, 4.51. Found : C, 56.49; H, 4.75.

Summary

As an important intermediate in the synthesis of Ib, several ways of preparing the dialdehyde (IX) were investigated and a considerable increase in total yield was achieved.

Synthesis of XXXI, an intermediate in the synthesis of IIb, was also examined.

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