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for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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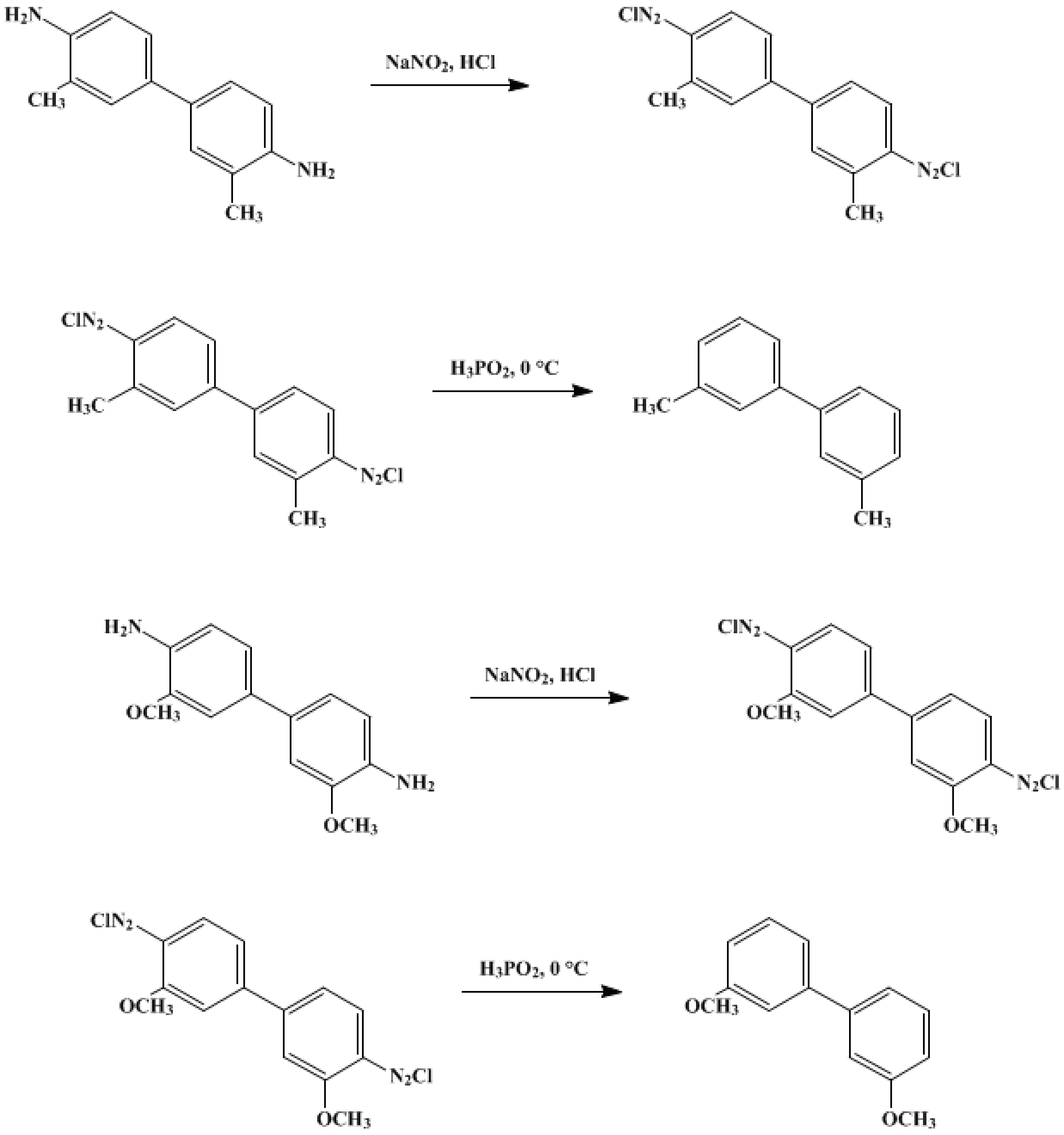
DOI:10.15227/orgsyn.021.0030

Organic Syntheses, Coll. Vol. 3, p.295 (1955); Vol. 21, p.30 (1941).

3,3'-DIMETHOXYBIPHENYL AND 3,3'-DIMETHYLBIPHENYL

[Biphenyl, 3,3'-dimethyl-, and biphenyl, 3,3'-dimethoxy-]



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1. Procedure

A. 3,3'-*Dimethoxybiphenyl*. In a 1.5-l. beaker are placed 400 ml. of water and 31 ml. of concentrated hydrochloric acid (sp. gr. 1.19). This solution is heated to boiling, the flame is removed, and 40 g. (0.16 mole) of *o*-dianisidine (Note 1) is added. The hot mixture is stirred for about 3 minutes, until only a small amount of solid remains. The beaker is then placed in an ice-salt mixture and its contents are stirred mechanically until the temperature has dropped to about 15°. At this point 35 ml. more of concentrated hydrochloric acid is added. When the temperature of the mixture has fallen to 10–13°, a solution of 23.3 g. (0.33 mole) of 97% sodium nitrite (or an equivalent amount of sodium nitrite of higher or lower purity) in 50 ml. of water is added from a dropping funnel in the course of 10–15 minutes. The contents of the beaker are then stirred for 15–20 minutes at 5–10°, and finally filtered rapidly with suction from an appreciable amount of dark material (Note 2).

The cold, clear red filtrate is now poured rapidly into a 2-l. flask containing 325 ml. of ice-cold 30% hypophosphorous acid solution (Note 3). Immediate evolution of nitrogen occurs. The flask is stoppered loosely, placed in a refrigerator for 8–10 hours, and then allowed to stand at room temperature for another 8–10 hours (Note 4). The reaction product is transferred to a 2-l. separatory funnel, and the lower dark brown layer is separated from the aqueous phase. The aqueous layer is extracted with two 125-ml. portions of ether (Note 5). The brown oil combined with the ether extracts is washed in a separatory funnel with two 30-ml. portions of 20% sodium hydroxide solution (Note 6). Separation into two layers occurs rapidly, but occasionally the aqueous phase will remain turbid for some time. The loss by discarding the turbid sodium hydroxide washings is negligible. The ether solution is dried with a minimal amount of anhydrous potassium carbonate, 5 g. usually being sufficient (Note 7).

After filtration of the ether solution from the mixture of solid potassium carbonate and dark solids which have settled out, the ether is removed by distillation on a steam cone from a 50-ml. modified Claisen flask having a 15-cm. column. Usually suction must be applied to remove the last traces of ether. The residue is distilled at 4 mm. and a bath temperature of 200°. There is a small fore-run of 1–1.5 g. of a very pale yellow liquid which distils at 155–157°. The main fraction, boiling at 157–159°, is practically colorless and weighs 19–22 g. When the temperature of the thermometer in the flask starts to drop, the bath temperature is gradually raised to 240°. In this way, 3–4 g. more of light orange-yellow dianisyl is obtained. The yield based on the three fractions is 23–27.5 g. (66–78%). The fractions usually crystallize spontaneously; if they do not crystallize, they are cooled and scratched.

The main fraction melts at 41–43° (Note 8), and the other two fractions usually melt about a degree or two lower. The product is pure enough for most purposes; it may be recrystallized from the minimal volume of ethanol necessary for solution at 45–50°. The solution is cooled to about 35°; any oil that precipitates is brought back into solution by cautious addition of ethanol. The saturated solution is seeded, allowed to cool to room temperature, and then kept in a refrigerator for at least 4 hours. In this manner, 20–21 g. of flat, colorless needles is obtained; the product melts at 42–43.5°.

B. 3,3'-*Dimethylbiphenyl*. Twenty-seven grams (0.13 mole) of *o*-tolidine (Note 9) is tetrazotized according to *Org. Syntheses* Coll. Vol. **2**, 145 (1943). It is not necessary to take the indicated precautions against a slight excess of nitrous acid. The clear orange tetrazonium solution is added to 290 ml. of 30% hypophosphorous acid (Note 10), and the mixture is allowed to stand, loosely stoppered, at room temperature for 16–18 hours (Note 11).

The reaction product is transferred to a 2-l. separatory funnel, and the red oily layer is separated from the aqueous phase. The aqueous layer is extracted once with 60 ml. of benzene. The combined red oil and benzene extract are dried with 1–5 g. of anhydrous sodium sulfate (Note 12). The benzene is removed by distillation from a 50-ml. modified Claisen flask having a 15-cm. column. The flask is heated in an oil bath to a final temperature of about 150° to ensure removal of the last traces of benzene. The residue is distilled at 3 mm. and a bath temperature of 155°. A practically colorless fore-run of 1–1.5 g. comes over from 109° to 114°. This is followed by 15.5–16 g. of a very pale lemon-yellow liquid which boils at 114–115°. When the temperature of the thermometer in the flask starts to fall the bath temperature is raised to 170°, and an additional 1–1.5 g. of light lemon-yellow material is obtained (Note 13). The total yield is 17.5–19 g. (76–82%) (Note 14) and (Note 15).

2. Notes

1. Eastman Kodak Company's technical grade, melting at 133–135°, was used.
2. Usually the pores of the filter paper become partially clogged after about half of the mixture has been filtered so that the rate of filtration is cut down considerably. In this event a fresh funnel and filter should be employed.

3. When less hypophosphorous acid solution is used, the yields are slightly lower, the product more highly colored than that obtained here, and the reaction time appreciably greater. When large amounts of a cheap amine are to be deaminated, it might be worth while to investigate the use of less hypophosphorous acid. In one run, 645 ml. of hypophosphorous acid solution was used for 40 g. of dianisidine. The yield was 29 g. (83%). With valuable amines it is probably best to use more hypophosphorous acid than is called for in these directions. Thus, in deaminating 33 g. of 2,2'-dimethyl-4,4'-diamino-5,5'-dimethoxybiphenyl, 1.2 l. of 30% hypophosphorous acid was used. There was obtained 24.5 g. (83%) of purified 2,2'-dimethyl-5,5'-dimethoxybiphenyl.

4. If the flask is permitted to stand at room temperature directly after the two solutions are mixed, the yield is a little lower than that obtained with these directions and the product is somewhat more highly colored. The entire reaction may be run at refrigerator temperature, in which event 25–30 hours should elapse before the product is worked up.

When this reaction is applied to aniline derivatives, it appears advisable to conduct it entirely at refrigerator temperature owing to lowered thermal stability of the diazonium compounds as compared to the tetrazonium salts obtained from the benzidine type.

5. If the entire reaction is carried out at refrigerator temperatures the crude product is a light-brown solid, which is best worked up by filtering with suction, dissolving in ether, and proceeding as in the regular directions.

6. When this washing is omitted, the product contains a white, alkali-soluble solid and rapidly becomes orange-brown.

7. The potassium carbonate usually retains some dianisyl. It should be washed with a little of the ether which has been removed by distillation, and these washings should be redistilled.

8. In agreement with others, the checkers obtained a product melting at 31.5–33.5°. After recrystallization from ethanol, the 3,3'-dimethoxybiphenyl melted at 33.5–35°. This low-melting form changed rapidly to the form melting at 42–43.5° when a solution or melt of the former or even the solid came in contact with a crystal of the high-melting form (obtained from the submitter).

9. Eastman Kodak Company's *o*-tolidine, m.p. 128–129°, was used.

10. Use of 175 ml. of hypophosphorous acid gave a yield of 17.8 g. (77%). The first and last fractions were turbid.

11. The yield and quality of the product are identical with those obtained by conducting the reaction at refrigerator temperature.

12. Washing the benzene solution with aqueous alkali was found to be unnecessary.

13. In spite of the slight differences in color, the three fractions have almost identical refractive indices (n_D^{20} 1.5945).

14. One run was made using 27 g. of Eastman's practical *o*-tolidine, m.p. 121–125°. The procedure employed differed from the above only in that the benzene solution was washed once with 40 ml. of 10% aqueous alkali. There was obtained 18.9 g. (82%) of a light orange-yellow liquid possessing essentially the same refractive index as the product obtained from the better grade of *o*-tolidine.

15. This method of deaminating aromatic amines appears to be of general applicability, particularly to benzidine and its derivatives. Benzidine itself has been deaminated in 60% yield. The use of hypophosphorous acid in preference to ethanol for these deaminations arises from the fact that this procedure is much simpler, the yields are higher, and the products are of better quality.

This use of hypophosphorous acid for the deamination of aromatic amines appears to have originated with Mai.[1] It has also been used for this purpose by Raiford and Oberst.[2]

3. Discussion

3,3'-Dimethoxybiphenyl has been prepared by methylating 3,3'-dihydroxybiphenyl with methyl iodide[3] or dimethyl sulfate;[4] and by deaminating tetrazotized *o*-dianisidine with alcohol.[5,6,7] The present procedure is a slight modification of Mai's directions.

3,3'-Dimethylbiphenyl can be prepared from *m*-bromotoluene[8] or *m*-iodotoluene[9] and sodium; by the action of copper powder on *m*-iodotoluene;[10] by treating 4,4'-dihydroxy-3,3'-dimethylbiphenyl with zinc dust;[11] by heating 4,4'-dichloro-3,3'-dimethylbiphenyl with hydriodic acid and phosphorus;[11] by treating *o*-toluidine with nitrous acid in alcoholic solution;[12] by the decomposition of tetrazotized *o*-toluidine with methanol or ethanol in the presence of zinc dust.[13,14] It has been prepared by reduction of *m*-bromotoluene with hydrazine hydrate, using a palladium-calcium carbonate catalyst.[15] Upon treatment of *m*-tolyllithium with oxygen, a small amount of 3,3'-dimethylbiphenyl is formed.[16]

3,3'-Dimethylbiphenyl, prepared by the general method described here, may be purified further.[17]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 412

References and Notes

1. Mai, *Ber.*, **35**, 162 (1902).
2. Raiford and Oberst, *Am. J. Pharm.*, **107**, 242 (1935) [*C. A.*, **29**, 6216 (1935)].
3. Barth, *Ann.*, **156**, 98 (1870).
4. Schultz and Kohlhaus, *Ber.*, **39**, 3343 (1906).
5. Starke, *J. prakt. Chem.*, (2) **59**, 226 (1899).
6. Haeussermann and Teichmann, *Ber.*, **27**, 2108 (1894).
7. Mascarelli and Visintin, *Gazz. chim. ital.*, **62**, 358 (1932).
8. Perrier, *Bull. soc. chim. France*, (3) **7**, 182 (1892).
9. Schultz, Rohde, and Vicari, *Ber.*, **37**, 1401 (1904); *Ann.*, **352**, 112 (1907).
10. Ullmann and Meyer, *Ann.*, **332**, 43 (1904).
11. Stolle, *Ber.*, **21**, 1096 (1888).
12. Schultz, *Ber.*, **17**, 468 (1884).
13. Winston, *Am. Chem. J.*, **31**, 128 (1904).
14. Schlenk and Brauns, *Ber.*. **48**, 666 (1915).
15. Busch, Hahn, and Mathauser, *J. prakt. Chem.*, **146**, 22 (1936).
16. Müller and Töpel, *Ber.*, **72**, 273 (1939).
17. Mills, *Nature*, **167**, 726 (1951).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

hypophosphorous acid

dianisyl

ethanol (64-17-5)

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methanol (67-56-1)

ether (60-29-7)

aniline (62-53-3)

sodium hydroxide (1310-73-2)

PHOSPHORUS (7723-14-0)

sodium sulfate (7757-82-6)

oxygen (7782-44-7)

nitrogen (7727-37-9)

sodium nitrite (7632-00-0)

nitrous acid (7782-77-6)

dimethyl sulfate (77-78-1)

copper powder (7440-50-8)

calcium carbonate (471-34-1)

zinc (7440-66-6)

sodium (13966-32-0)

palladium (7440-05-3)

hydriodic acid (10034-85-2)

Methyl iodide (74-88-4)

hydrazine hydrate (7803-57-8)

benzidine (92-87-5)

o-toluidine (95-53-4)

m-Bromotoluene (591-17-3)

m-iodotoluene (625-95-6)

3,3'-DIMETHOXYBIPHENYL,
biphenyl, 3,3'-dimethoxy- (6161-50-8)

3,3'-DIMETHYLBIPHENYL,
Biphenyl, 3,3'-dimethyl- (612-75-9)

2,2'-dimethyl-4,4'-diamino-5,5'-dimethoxybiphenyl

2,2'-dimethyl-5,5'-dimethoxybiphenyl

3,3'-dihydroxybiphenyl (612-76-0)

4,4'-dihydroxy-3,3'-dimethylbiphenyl

4,4'-dichloro-3,3'-dimethylbiphenyl

m-tolyllithium

o-TOLIDINE (119-93-7)

dianisidine,
o-dianisidine (119-90-4)