Practical Synthesis of 1,1′-Binaphthyl-2-carboxylic Acids via Side Chain Oxidation of 2-Methyl-1,1′-binaphthyls

Sotaro MIYANO,* Shin-ichi OKADA, Toshiyuki SUZUKI,
Shigeru HANDA, and Harukichi HASHIMOTO
Department of Applied Chemistry, Faculty of Engineering, Tohoku University, Aramaki-Aoba, Sendai 980
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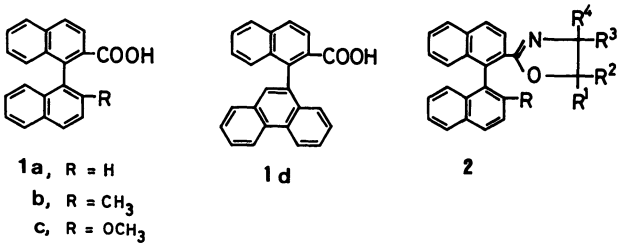
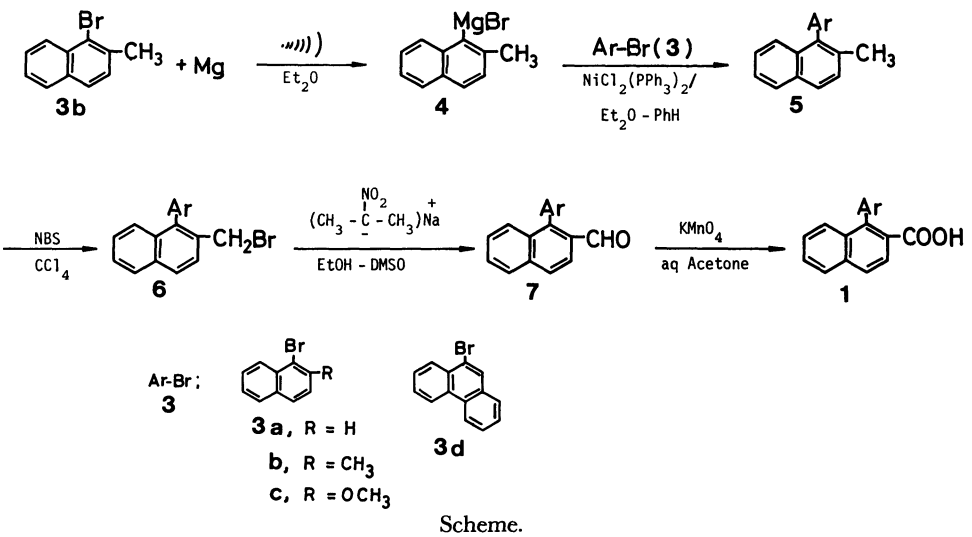
Synopsis. Four 1,1′-binaphthyl-2-carboxylic acids were obtained in 38—53% isolated yield via three-stage oxidation of 2-methyl-1,1′-binaphthyls, that is, i) NBS-bromination to benzylic bromides, ii) treatment with sodium salt of 2-nitropropane to aldehydes, and iii) $KMnO_4$-oxidation to carboxylic acids.

In the past few years, there has been an intense interest in the asymmetric reactions by means of atropisomeric binaphthyls as the chirality recognizing units.[1] The main obstacle in carrying out these reactions, however, has been the difficulty to obtain the requisite axially chiral binaphthyl skeletons.[2] In this context, 1,1′-binaphthyl-2-carboxylic acids **1** are intriguing as the starting material for elaboration of such chiral auxiliaries, considering that the carboxyl substituent should be the most helpful resort for not only optical resolutions[3] but also transformations into various functionalities.[4] Actually, Goto et al. have shown that **1b** is useful for preparation of the derivatizing agents for liquid chromatographic resolution of enantiomeric hydroxy compounds.[5] Their preparation of **1b**, however, suffered from tedious manipulations which involved the synthesis of intermediate dimethyl 1,1′-binaphthyl-2,2′-dicarboxylate. On the other hand, Meyers and Lutomski,[6] and Wilson and Cram[7] reported nucleophilic substitution of 2-oxazoline-activated 1-alkoxynaphthalenes by a naphthyl Grignard or lithium reagent to give 2-(1,1′-binaphthyl-2-yl)oxazolines **2**, which are latent binaphthyl-2-carboxylic acids. Although the procedure can be applied for the construction of axially chiral binaphthyl linkage by the use of a substrate bearing chiral alkoxyl or oxazoline group, hydrolytic regeneration of the carboxyl function from the sterically crowded **2** is not so much easy, and it is still highly-desirable to provide an alternative, operationally more simple route to **1**.

Herein we wish to report our approach to **1** which is outlined in Scheme.[8,9] Ultrasonic irradiation remarkably facilitated the reaction of **3b** with magnesium turnings in ether to form the Grignard reagent **4**. The Kumada-Tamao method[10] was successfully utilized to promote cross-coupling of **4** with bromonaphthalenes **3** to give 2-methyl-1,1′-binaphthyls **5**. The use of 1.5—1.7 molar amounts of **4** appeared to be ample excess not to leave unchanged **3**. After usual workup of the reaction, recrystallization or distillation gave pure samples of **5** (55—82% yield). The significant upfield shift of ^1H NMR of the methyl groups for **5** is consistent with the binaphthyl structure where these protons are disposed over the shielding cone of the adjacent naphthalene rings (see Experimental).

The methyl substituents of **5** were readily brominated by treatment with 1.1 equiv of *N*-bromosuccinimide (NBS) in boiling CCl_4 in the presence of a catalytic amount of benzoyl peroxide. Filtration of the precipitated succinimide from the cool reaction mixture and evaporation of the solvent left crude





Scheme.

benzylic bromides **6**, which in turn were treated with sodium salt of 2-nitropropane in DMSO–EtOH to give aldehydes **7** according to the method of Klanderman;[11] the conventional Sommelet oxidation did not work well for these bulky benzylic bromides.[12] Conversion of **7** to carboxylic acids **1** was effected by $KMnO_4$–oxidation in boiling aqueous acetone applying the method of Hall and Turner with slight modifications.[13] Pure samples of **1** were readily obtainable by recrystallization, and were characterized by elemental analysis and spectral studies.

Although the yields of **1** were moderate (38—53% based on **5**), we believe that the procedure is synthetically useful; the starting bromonaphthalenes are readily available, and any stage of the procedure does not necessarily require chromatographic purification, rendering it suitable for preparative scale synthesis of **1**.

Experimental

Materials. **3c** was prepared by treating 1-bromo-2-naphthol with NaH in DMF, followed by addition of methyl iodide and stirring overnight at room temperature, mp 85—86°C (lit,[7] mp 83—84°C). Commercial **3d** (mp 63°C) was stored over silica gel in vacuo, and **3a** was distilled before use, bp 149—152°C/16 mmHg.* **3b**[13] (bp 115—118°C/1.5 mmHg) and $NiCl_2(PPh_3)_2$[14] were prepared as described in the literature.

2-Methyl-1,1′-binaphthyls (5). The synthesis of **5d** is representative. The Grignard reagent **4** was prepared under nitrogen in a flask immersed in the water bath of an ultrasonic laboratory cleaner (53 W, 41 kHz).

To an ultrasonically irradiated mixture of magnesium turnings (7.00 g, 0.288 g-atom) in 50 ml of ether was added a solution of **3b** (37.7 g, 0.171 mol) in ether (200 ml) over 1-h period; addition of a few drops of the bromide started the reaction quite readily, which was evidenced by clouding of the ether layer with a change of the magnesium surface from dull grey to metallic. During the addition, the temperature of the water bath was allowed to rise with sonication, which kept the reaction at rapid reflux. After the addition was complete, the sonication was continued for another 2 h. The Grignard reagent was obtained as a slightly yellow slurry, which was dissolved by adding 200 ml of benzene.

The Grignard solution was transferred to another dropping funnel by means of a cannula, and then added dropwise to a magnetically stirred solution of **3d** (26.0 g, 0.101 mol) and $NiCl_2(PPh_3)_2$ (0.655 g, 1 mol% of **3d**) in 150 ml of benzene at room temperature over 1-h period. After stirred overnight at room temperature, the mixture was heated at reflux for 3 h, and then bulk of the ether was distilled off through a short Vigreux column. The cooled reaction mixture was worked up as usual.[10] Solvents were removed in vacuo, and the residue was heated up to 150°C (bath temp) at 0.1 mmHg to remove volatiles comprised mainly of 2-methylnaphthalene. The crude product was dissolved in hexane, and passed through a silica-gel pad to remove colored materials. Evaporation of the solvent and crystallization from ethanol–acetone (9:5) gave pure **5d**, 26.5 g (82%); mp 145—148.5°C; IR (KBr) 3050, 1450, 1420, 810, 740, and 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.15 (3H, s, $-CH_3$),[15] 7.0—8.1 (13H, m, Ar–H), and 8.6—8.9 (2H, m, Ar–H). Found: C, 94.39; H, 5.93%. Calcd for $C_{25}H_{18}$: C, 94.30; H, 5.70%.

5a: **4** was prepared from 2.02 g (9.14 mmol) of **3b**, allowed to react with **3a** (1.09 g, 5.27 mmol), and worked up as above. Recrystallization from hexane gave 1.11 g (79%) of **5a** which melted at 86.0—88.0°C to an opaque liquid that cleared at ca. 103°C (lit,[16] mp 120—122°C)[17]; IR (KBr) 3050, 1500, 1360, 800, 780, and 740 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.10 (3H, s, $-CH_3$) and 7.0—8.1 (13H, m, Ar–H). Found: C, 94.21; H, 6.08%. Calcd for $C_{21}H_{16}$: C, 93.99; H, 6.01%.

5b: **4** was prepared from 4.55 g (20.6 mmol) of **3b**, and then allowed to react with another 2.78 g of **3b** (12.6 mmol). Trap-to-trap distillation gave 2.17 g (61%) of **5b** as a colorless glass; bp≈200°C (bath temp)/1 mmHg (lit,[2a] 190—210°C/0.2 mmHg); ^1H NMR ($CDCl_3$) δ=1.95 (6H, s, $-CH_3\times$ 2), 6.8—8.0 (12H, m, Ar–H). Found: C, 93.21; H, 6.11%. Calcd for $C_{22}H_{18}$: C, 93.58; H, 6.42%.

5c: **4** was prepared from 2.49 g (11.3 mmol) of **3b** and allowed to react with **3c** (1.45 g, 6.12 mmol). Crystallization from hexane gave 1.00 g (55%) of **5c**; mp 118—121°C; IR (KBr) 3050, 1620, 1570, 1240, 800, and 730 cm^{-1}. ^1H NMR ($CDCl_3$) δ=2.0 (3H, s, $-CH_3$), 3.64 (3H, s, $-OCH_3$), 6.7—8.0 (12H, m, Ar–H). Found: C, 89.01; H, 6.14%. Calcd for $C_{22}H_{18}O$: C, 88.56; H, 6.08%.

Oxidation of 5 to 1,1′-Binaphthyl-2-carboxylic Acids 1. The synthesis of **1d** is representative. A mixture of **5d** (3.18 g, 10.0 mmol), NBS (1.96 g, 11.0 mmol), and benzoyl peroxide (0.1 g) in CCl_4 (70 ml) was magnetically stirred and heated at reflux for 3 h, during which almost all of **5d** had disappeared as evidenced by ^1H NMR. Precipitated succinimide was filtered off from the cool mixture, and volatiles were removed in vacuo to give crude **6d**; δ ($-CH_2Br$)/(CCl_4–$CDCl_3$)=4.09 (1H, d, J=10.3 Hz) and 4.33 (1H, d).

The bromide was dissolved in 60 ml of DMSO under nitrogen. To the stirred solution was added slowly (0.5 h) a solution prepared by adding 3.25 g (36.5 mmol) of 2-nitropropane to a sodium ethoxide in ethanol, which had been obtained by dissolving 0.58 g of sodium (25.2 mg-atom) in 35 ml of ethanol. Stirring was continued for 3 h at room temperature, and then another 3 h at 60°C. The mixture was poured into ice-water (300 ml), extracted with dichloromethane, washed successively with 2 M† HCl, 1 M Na_2CO_3, and then water, and dried over Na_2SO_4. Evaporation of the solvent in vacuo left crude **7d**; ^1H NMR ($CDCl_3$) δ=9.72 (1H, –CHO); IR (KBr) 1680 cm^{-1}.

The aldehyde was dissolved in 60 ml of acetone and heated at reflux, to which was added dropwise (0.5 h) a solution of $KMnO_4$ (2.36 g, 15.0 mmol) in 60 ml of hot water, and heating was continued for an additional 1 h. To the dark brown mixture was bubbled sulfur dioxide till it became clear accompanying deposition of white precipitate. The solid was recovered by filtration, dissolved in hot toluene (200 ml), and then filtered hot after adding small amount of activated charcoal; concentration to about a third of the volume caused crystallization of **1d** on standing, 1.84 g (53%); mp 290—291.5°C; IR (KBr) 1680 cm^{-1}. ^1H NMR (DMSO-d_6) δ=6.8—8.4 (13H, m, Ar–H), 8.6—9.1 (2H, m, Ar–H), and 12.4 (1H, br, –COOH). Found: C, 86.24; H, 4.91%. Calcd for $C_{25}H_{16}O_2$: C, 86.19; H, 4.63%.

1c: The oxidation of **5c** (9.65 g, 32.4 mmol) was carried out as above and recrystallization from water–ethanol (2:1) gave 5.64 g (53%) of **1c**; mp 258.5—260°C; IR (KBr) 1680 cm^{-1}. ^1H NMR (DMSO-d_6) δ=3.69 (3H, s, $-OCH_3$), 6.5—8.3 (12H, m, Ar–H,), and 12.2 (1H, br, –COOH). Found: C, 80.28; H, 5.06%. Calcd for $C_{22}H_{16}O_3$: C, 80.47; H, 4.91%.

1a: The oxidation of **5a** (1.86 g, 6.94 mmol) was carried out as above except that, after treatment with SO_2, ca. 1 l of 28% aqueous ammonia was added to dissolve the acid which deposited as an oil and then passed through a silica-gel pad to remove colored precipitates. The aq layer was

*1 mmHg=133.322 Pa.

† 1 M=1 mol dm^{-3}.

made acidic by adding conc HCl, and the acid was taken into ether. Evaporation of the solvent and recrystallization from water–ethanol (1:1) gave 0.78 g (38%) of **1a**; mp 200—201.5 °C (lit,[7] mp 200—201 °C); IR (KBr) 1680 cm^{-1}; ^1H NMR (DMSO-d_6) δ=6.8—8.2 (13H, m, Ar–H) and 12.4 (1H, br, –COOH). Found: C, 84.46; H, 4.67%. Calcd for $C_{21}H_{14}O_2$: C, 84.54; H, 4.73%.

1b: The oxidation of **5b** (1.00 g, 3.55 mmol) was carried out according to the procedure used for **5a**, affording 0.451 g (41%) of **1b** after recrystallization from water–ethanol (1:1); mp 228—230 °C (lit,[5] 233 °C); IR (KBr) 1670 cm^{-1}; ^1H NMR (DMSO-d_6) δ=1.98 (3H, s, $-CH_3$), 6.6—8.3 (12H, m, Ar–H), and 12.4 (1H, br, –COOH). Found: C, 84.32; H, 5.33%. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16%.

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