Synthesis of 4,4'-Divinyl-2,2'-bipyridine

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4,4'-Divinyl-2,2'-bipyridine (**2**) was prepared in 12% overall yield from 4,4'-dimethyl-2,2'-bipyridine (**3**) *via* a 5 step reaction sequence involving the intermediate 4,4'-R_2-2,2'-bipyridines: R = COOH, **4**; CO_2CH_3, **5**; CH_2OH, **6**; CHO, **7**. The newly synthesized compounds **2**, **6** and **7** were characterized by melting point, infrared, ^1H nmr, mass spectrometry and elemental analysis.

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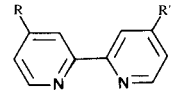
The preparation of 4-vinyl-4'-methyl-2,2'-bipyridine (**1**) was first reported by Spiro and Ghosh [1]. This compound soon became one of the most frequently used reagents for the preparation of solid phase catalysts [2,5] and electroactive polymer films [6,9]. In the latter application, it soon appeared to us and others [10] that in order to obtain layers of adequate thickness and stability it is necessary to employ monomeric metal complexes containing at least two electropolymerizable vinyl groups. Similar observations were made in a study concerning the oxidative electropolymerization of polypyridyl complexes of ruthenium(II) containing pyrrolic groups [11]. It would also be desirable to have both electropolymerizable groups on the same bipyridine ligand, since this would free up to four positions in an octahedral metal complex for substitution with other ligands necessary to tune catalytic and/or photochemical properties.

We report herein a five-step, 12% overall yield synthesis of 4,4'-divinyl-2,2'-bipyridine (**2**) from commercially available 4,4'-dimethyl-2,2'-bipyridine (**3**). This rather lengthy approach was undertaken after it became clear that simple elimination procedures, useful for the monovinyl compound **1**, produced only traces of **2**. We attributed this behavior to the high tendency of **2** to polymerize under the reaction conditions and therefore decided to prepare **2** by the use of a very mild method, such as the Wittig reaction.

In the present work compound **3** was oxidized (52%) to the diacid **4** by permanganate oxidation in dilute sulfuric acid as described by Sasse [12]. The diacid was converted into its dimethyl ester **5** by treatment with methanol and concentrated sulfuric acid in 73% yield. Reduction of the diester to the corresponding dialcohol **6** was readily accomplished (79%) by employing a large excess of sodium borohydride in ethanol; a similar facile reduction of an ester with sodium borohydride has been observed for ethyl isonicotinate [13]. Dialcohol **6** could be then oxidized smoothly (76%) to dialdehyde **7** by treatment with selenium dioxide in dioxane. A previous attempt to prepare **7** directly from **3** by selenium dioxide oxidation in dioxane only produced an aldehyde-carboxylic acid derivative **8** [14].



1 R = CH_3; R' = $CH{=}CH_2$
2 R = R' = $CH{=}CH_2$
3 R = R' = CH_3
4 R = R' = COOH
5 R = R' = $COOCH_3$
6 R = R' = CH_2OH
7 R = R' = CHO
8 R = CHO; R' = COOH

The Wittig reaction between **7** and methylenetriphenylphosphorane to give the desired divinyl product **2** was somewhat complicated by the exceptional tendency of **2** to polymerize. For example, or initial attempts to synthesize **2** from **7** produced **2** in erratic (30-40%) yield. Polymeric films were observed at the interfaces during the repeated extractions necessary for the isolation of **2** in these attempts. Subsequent preparations and manipulations of **2** were carried out in the absence of fluorescent lighting and other possible uv sources. Product work-up and purifications were performed immediately after quenching of the Wittig reaction without intermediate storage of impure sampes of **2**. Purified samples of **2** were stored in a dessicator in a cold, dark area. In this manner, pure **2** was reproducibly obtained in 54% yield. Although not investigated here, further optimization of the yield of **2** might be possible by employing decreased reaction times and/or inhibitors such as *t*-butylcatachol during product work-up. Factors such as these, as well as the reactivity of **2** in connection with the synthesis and use of metal complexes containing this ligand, form a basis for continuing research.

EXPERIMENTAL

Melting points were taken on a calibrated Büchi apparatus. The ^1H nmr spectra were recorded at 360 MHz with a Bruker WM-360 spectrometer. Infrared spectra were obtained on a Perkin-Elmer Model 683 spectrometer. Mass spectra were measured using a Model Vacuum Generators Micromass 7070E Manchester instrument. Microanalyses were performed by CIBA-Geigy, KA-Forschungzentrum, Marly 170/004, Switzerland. Dioxane (Fluka, puriss, p.a.) and tetrahydrofuran (Fluka, HPLC grade) were dried before use over sodium benzophenone ketyl. 4,4'-Dimethyl-2,2'-bipyridine (Fluka, puriss, p.a.), selenium dioxide (Merck, sublimed, for synthesis), sodium borohydride (Fluka,

purum, p.a.) as well all as the other reagents were used as received. The reactions were monitored by thin-layer chromatography carried out on 0.2 mm Merck silica gel plates (60 F_{254}). The solvents employed in the tlc were identical to those used for the preparative scale chromatographies (*vide infra*). A freshly prepared aqueous solution of ammonium iron (II) sulfate hexahydrate was used as a developing agent. The following colors were observed: dimethylbipyridine **3**, red; diacid **4**, purple; diester **5**, purple; dialcohol **6**, red; dialdehyde **7**, purple-violet; divinyl **2**, purple. E. Merck silica gel (60, particle size 0.063-0.200 mm) was used for column chromatography.

4,4'-Dicarboxy-2,2'-bipyridine (**4**).

This diacid was prepared in 52% yield from **3** by oxidation with permanganate in dilute sulfuric acid, followed by treatment of the crude product with hot dilute nitric acid, according to the procedure described by Sasse [12]. This method provides a pure product, free from 4'-methyl-2,2'-bipyridine-4-carboxylic acid, unlike the often used neutral [15,16] or alkaline [17] permanganate oxidations of **3**, first reported by Case [18].

4,4'-Dimethoxycarbonyl-2,2'-bipyridine (**5**).

The diacid **4** (10.00 g), methanol (150 ml) and concentrated sulfuric acid (20 ml) were heated under reflux for 24 hours. The reaction mixture was cooled, poured into water (300 ml) and basified to *p*H 8 with 25% sodium hydroxide. The mixture was then extracted with methylene chloride (3 x 250 ml) and the combined organic layers were dried (sodium sulfate) and evaporated to a colorless crystalline material which was recrystallized from toluene to obtain 8.16 g (73%) of **5** as colorless plates of mp 208-209° ([17], 208-210°). From the aqueous layer, there was recovered by acidification the unreacted or partially reacted diacid **4**. This material was used successfully in the production of additional **5** by this procedure.

4,4'-Bis(hydroxymethyl)-2,2'-bipyridine (**6**).

The diester **5** (8.00 g, 29.4 mmoles) was suspended in absolute ethanol (600 ml) and sodium borohydride (24.00 g, 634 mmoles) was added in one portion: The mixture was refluxed for 3 hours, cooled to room temperature, and the excess borohydride was decomposed by the addition of a saturated aqueous solution of ammonium chloride (600 ml). The ethanol was evaporated and the precipitated solids were dissolved by addition of the minimum necessary amount of water. The resulting solution was extracted five times with 600 ml portions of ethyl acetate. The extract was dried (sodium sulfate) and evaporated. The slightly pink residue was dissolved in methanol and filtered through a short silica column (methanol elution). The resulting white solid was further purified by sublimation (0.1 mm/160°). At the begining of the sublimation it was necessary to remove the condenser in order to wipe off the methanol of crystallization which separated from the solid. This procedure was repeated as needed, until all the methanol was removed. 4,4'-Bis(hydroxymethyl)-2,2'-bipyridine (**6**) was obtained as a white crystalline powder (5.00 g, 79% yield) of m.p. 171-173°; ir (potassium bromide): broad, strong band (2000-3600) with principal maximum at 3212 and additional maxima at 3065, 2889, 2830, 2736 and 2648; other peaks at 1606 (s), 1561 (m), 1460 (s), 1448 (m), 1391 (s), 1062 (s), 998 (m), 846 (m), 831 (m), 818 (s), 656 (m), 607 (m) cm^{-1}; ^1H nmr (perdeuteriomethanol): δ values, ppm 4.79 (s, CH_2, CH_2'), 7.48 (d, H_5, H_5'), 8.31 (s, H_3, H_3'), 8.63 (d, H_6, H_6') [$J_{5,6} = J_{5',6'} = 4.8$ Hz]; ms: m/e (relative intensity), 218 (4.5), 217 (34.8), M^+ 216 (100.0), 215 (100.0), 214 (7.7), 213 (7.8), 199 (9.0), 198 (8.2), 188 (9.5), 187 (71.0), 186 (90.8), 185 (37.7), 170 (8.0), 169 (24.1), 168 (8.8), 158 (11.9), 157 (14.0), 156 (9.8), 155 (9.7), 141 (5.1), 130 (7.1), 128 (7.8), 109 (5.1), 108 (17.0), 90 (6.6), 80 (12.9), 79 (7.2), 78 (15.5), 77 (5.6), 63 (11.7), 53 (9.4), 52 (8.4), 51 (19.1), 50 (5.2).

Anal. Calcd. for $C_{12}H_{12}N_2O_2$ (216.24): C, 66.65; H, 5.59; N, 12.95. Found: C, 66.69; H, 5.58; N, 12.88.

4,4'-Diformyl-2,2'-bipyridine (**7**).

A mixture of dialcohol **6** (1.00 g, 4.62 mmoles), selenium dioxide (641 mg, 5.78 mmoles) and dry dioxane (25 ml) was heated at 80° for 6 hours. The hot reaction mixture was diluted with dioxane (25 ml) and the black precipitate (elemental selenium) was removed by filtration. The precipiate was rinsed with dioxane (2 x 10 ml) and the rinsings were combined with the filtrate and evaporated. An aqueous saturated solution of sodium bicarbonate (50 ml) was added to the residue and the resulting suspension was extracted with methylene chloride (3 x 75 ml), washed with water, dried (sodium sulfate) and evaporated. The remaining solid was dissolved in a hot chloroform/tetrahydrofuran mixture (100 ml, 1:1 v/v) and applied to a jacketed silica column kept at 40°. Elution with the same chloroform/tetrahydrofuran mixture provided 861 mg of a crystalline, slightly pink solid. Recrystallization from a small amount of toluene afforded 746 mg (76%) of 4,4'-diformyl-2,2'-bipyridine (**7**) as colorless crystals of mp 194-196°; ir (potassium bromide): 3077 (w), 2863 (w), 2764 (w), 1705 (s), 1597 (m), 1558 (m), 1468 (m), 1353 (m), 1250 (m), 1199 (s), 1101 (m), 851 (s), 675 (m), cm^{-1} ^1H nmr (deuteriochloroform): δ values, ppm 7.76 (dd, H_5, $H_{5'}$), 8.87 (d, H_3, $H_{3'}$), 8.94 (d, H_6, $H_{6'}$) [$J_{3,5} = J_{3',5'} = 1.3$ Hz; $J_{5,6} = J_{5',6'} = 4.9$ Hz], 10.19 (s, CHO, CHO'); ms: m/e (relative intensity), 213 (14.1), M^+ 212 (100.0), 184 (35.1), 183 (14.8), 157 (5.0), 156 (12.5), 155 (16.1), 128 (6.5), 78 (8.1), 51 (11), 50 (5.6).

Anal. Calcd. for $C_{12}H_8N_2O_2$ (212.21): C, 67.92; H, 3.80; N, 13.20. Found: C, 68.04; H, 3.91; N, 13.12.

4,4'-Divinyl-2,2'-bipyridine (**2**).

The preparation and all manipulations involving **2** *were carried out in the absence of fluorescent lighting, sun light and other UV sources (vide supra).* A 1:1 stoichiometric mixture of methyltriphenylphosphonium bromide and sodium amide (Fluka "instant ylid" [19]; 2.20 g, 5.28 mmoles) was suspended in dry tetrahydrofuran (20 ml) and stirred for 15 minutes under argon. Dialdehyde **7** (509 mg, 2.40 mmoles) dissolved in dry tetrahydrofuran (50 ml) was added by cannula to the resulting bright yellow suspension. The color of the mixture quickly changed to a muddy gray-green. Stirring under argon was continued for 1 hour. At the end of this period the reaction mixture was quenched with water (50 ml). The resulting orange solution was extracted with methylene chloride (3 x 50 ml). The combined extract was washed with water (50 ml) and extracted with 1*M* hydrochloric acid (2 x 50 ml). The combined aqueous layers were chilled in an ice bath and neutralized (*p*H 7; some decomposition occurs if the *p*H is allowed to rise much above this value) with 10% sodium hydroxide and extracted with methylene chloride (3 x 50 ml). The combined methylene chloride extracts were washed with water (50 ml), dried (sodium sulfate), evaporated to about 10 ml and applied to a silica column. Elution with a chloroform/methanol solvent mixture (95:5 v/v) afforded a slightly yellow oil which rapidly crystallized upon pumping *in vacuo*, yield of **2**, 268 mg (54%),

white, crystalline powder of mp 66-69°; further purification by sublimation (0.1 mm/65°, 80% yield) provided a sample of mp 68-70°; ir (potassium bromide): 3095 (w), 3057 (w), 3021 (w), 1940 (w), 1874 (w), 1820 (w), 1634 (w), 1590 (s), 1549 (s), 1463 (s), 1361 (s), 1257 (m), 985 (s), 936 (s), 904 (s), 846 (s), 802 (s), 668 (m) cm^{-1}; ^1H nmr (deuteriochloroform): δ values, ppm 5.51 (d, $-C=CH_{cis}$, $-C=CH_{cis}'$), 6.08 (d, $-C=CH_{trans}$, $-C=CH_{trans}'$), 6.75 (dd, $-CH=C$, $-CH=C'$), [J_{cis} = 10.9, J_{trans} = 17.5 Hz], 7.32 (dd, H_5, $H_{5'}$), 8.39 (d, H_3, $H_{3'}$), 8.61 (d, H_6, $H_{6'}$), [$J_{3,5} = J_{3',5'}$ = 1.7, $J_{5,6} = J_{5',6'}$ = 5.1 Hz]; ms: m/e (relative intensity), 210 (1.1), 209 (14.7), M^+ 208 (100), 207 (59.3), 196 (4.5), 183 (6.4), 182 (50.0), 181 (4.8), 154 (4.8), 104 (10.6), 77 (11.3), 51 (9.8).

Anal. Calcd. for $C_{14}H_{12}N_2$ (208.26): C, 80.74; H, 5.81; N, 13.45. Found: C, 80.59; H, 5.90; N, 13.40.

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