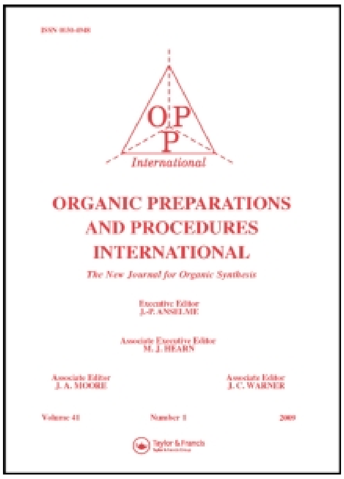

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OPPI BRIEFS

SYNTHESIS OF 1,3-bis(2-BROMOPHENYL)PROPANE

Submitted by
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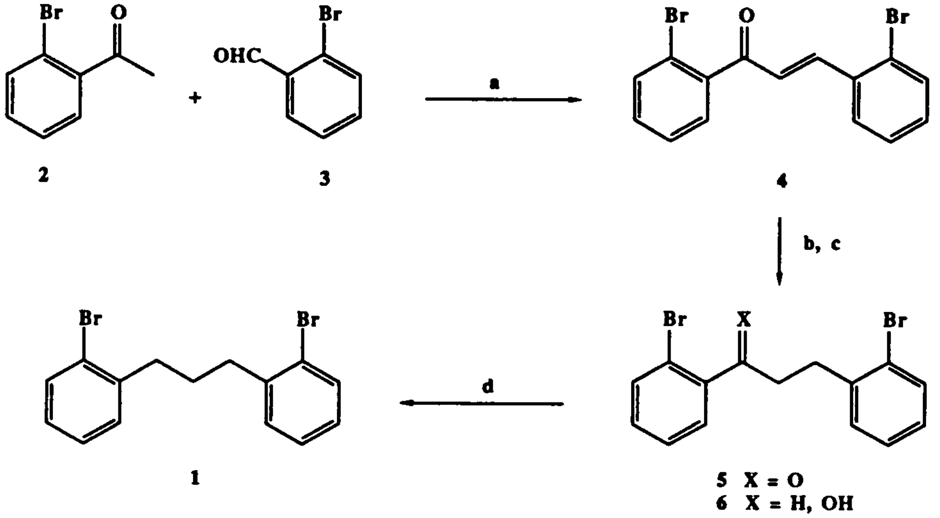
A recent synthetic study required the use of the dimetallated compound derived from 1,3-bis(2-bromophenyl)propane (1). A review of the literature revealed that this dibromide had been prepared previously and used in the synthesis of phosphine-based bidentate ligands.[1] The earlier report described the preparation of 1 by two methods, the best of which proceeded in two steps from commercial materials in 29% overall yield. This route involved reaction of 2-bromobenzyl bromide with diiron nonacarbonyl to generate 1,3-bis(2-bromophenyl)-2-propanone followed by Wolff-Kishner reduction. Our approach, outlined in the Scheme, requires four steps but gives an overall yield of 80%. The current procedure is also more cost effective and requires minimal purification of the intermediates.



a) NaOH, aq. EtOH, 98%; b) H_2 (4 atm), PtO_2, EtOAc, 40°, 92%;
c) $LiAlH_4$, Et_2O, 0°, 97%; d) 57% HI, P, reflux, 92%

The synthesis began with aldolization of 2'-bromoacetophenone (2) and 2-bromobenzaldehyde (3) to give the chalcone derivative 4 in 98% yield.[2] The conjugated double bond was reduced under 4 atm of hydrogen in ethyl acetate at 40° using platinum (IV) oxide catalyst to give 5 in 92% yield. [3] [Note: Less expensive palladium catalysts were observed to attack the aromatic halogens and, thus, could not be used for this step.] Finally, reduction of the carbonyl group with lithium aluminum hydride gave the benzylic alcohol 6 (97%) which was then deoxygenated[4,5] to 1 in 92% yield using red phosphorous in refluxing 57% aqueous hydrogen iodide.

EXPERIMENTAL SECTION

The 2'-bromoacetophenone and 2-bromobenzaldehyde were used as received from Lancaster Synthesis Ltd. All other reagents and solvents were used as received from the vendors. Reactions were monitored by TLC on silica gel plates (Analtech No. 02521) or by GC (Varian 3400 capillary GC with FI detection on a 0.1 mm X 3 m SE-30 column programmed between 100-300°). Melting points were obtained using a Fisher-Johns melting point apparatus and are uncorrected. IR spectra were determined using a PE-681 instrument and are referenced to polystyrene. ^{1}H-NMR and ^{13}C-NMR were recorded at 300 MHz and 75 MHz, respectively, using a Varian VXR-XL-300 superconducting FT instrument; chemical shifts are reported in δ units relative to internal tetramethylsilane. Mass spectra were obtained at 70 eV using a VG ZAB-2SE or a VG TS-250 instument. Elemental analyses ($\pm$ 0.4%) were performed by Galbraith Laboratories, Knoxville, TN.

1,3-Bis(2-bromophenyl)-2-propen-1-one (4).- This compound was prepared on a 62.7 mmol scale using the general procedure already published.[2] The product was isolated as described and was used without further purification. The yield was 22.4 g (62.1 mmol, 98%) of light yellow crystals, mp. 43-45°.

IR (thin film): 1660, 1608, 760 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.81 (d, 1H, J = 16.2 Hz), 7.61 (m, 3H), 7.30 (m, 5H), 7.00 (d, 1H, J = 16.2 Hz); ^{13}C-NMR ($CDCl_3$): δ 194.0, 144.6, 140.5, 134.2, 133.4, 133.1, 131.6, 131.4, 131.3, 128.1, 127.8, 127.7, 127.5, 125.8, 119.3; MS, m/e (%): 368 (M+4, 8), 366 (M+2, 17), 364 (M, 8).

Anal. Calcd for $C_{15}H_{10}Br_2O$: C, 49.18; H, 2.73. Found: C, 49.32; H, 2.88

1,3-Bis(2-bromophenyl)-1-propanone (5).- A solution of 12.0 g (32.8 mmol) of 1,3-bis(2-bromophenyl)-2-propen-1-one (4) in 100 mL of ethyl acetate was shaken with 0.25 g of PtO_2 under 4 atm of H_2 at 40° for 24 hrs.[3] [Note: The reaction was frequently incomplete at this point. When this was the case, a second charge of PtO_2 was added and the mixture was hydrogenated for an additional 24 hrs.] The crude reaction mixture was filtered through Celite and the solvent was removed under vacuum at 40° to give a brown oil. The oil was purified by flash chromatography through a 50 cm X 2.5 cm column of silica gel eluted with 5% ether in hexane. The product was isolated as a yellow oil in a yield of 11.1 g (30.2 mmol, 92%).

IR (thin film): 1692, 752 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 7.45 (dd, 2H, J = 15.0, 7.5 Hz), 7.17 (m, 5H), 6.94 (dt, 1H, J = 7.5, 2.0 Hz), 3.09 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ 201.6, 140.6, 138.9, 131.8, 131.7, 130.4, 127.3, 127.0, 126.6, 126.5, 126.3, 123.3, 117.6, 41.3, 29.5; MS, m/e (%): 370 (M+4, 3), 368 (M+2, 7), 366 (M, 3).

Anal. Calcd for $C_{15}H_{12}Br_2O$: C, 48.91; H, 3.26. Found: C, 48.72; H, 3.24

1,3-Bis(2-bromophenyl)-1-propanol (6).- To slurry of 1.12 g (29.5 mmol) of lithium aluminum hydride in 50 mL of anhydrous ether at 0° was added a 50-mL ether solution of 10.8 g (29.3 mmol) of 1,3-bis(2-bromophenyl)-1-propanone (5). The solution was warmed to 25° during 2 hrs then cautiously quenched by dropwise addition of 1 mL of water followed by 2 mL of 10% aqueous NaOH. Using Celite, the granular precipitate was removed by filtration and washed twice with 100 mL of tetrahydrofuran. The solvent was removed under vacuum at 40° using rotary evaporation. The remaining light yellow oil was placed under high vacuum (0.05 mmHg) for 2 hrs at 20° where it solidified to a soft crystalline mass. Recrystallization from hexane yielded 10.5 g (28.3 mmol, 97%) of 1,3-bis(2-bromophenyl)-1-propanol as a white powder, mp. 63.5-64.5°.

IR (thin film): 3400, 760 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.58 (m, 2H), 7.28 (m, 4 H), 7.10 (m, 2H), 5.10 (dd, 1H, J = 8.5, 3.5 Hz), 2.92 (m, 2H), 2.11 (m, 2H), 1.95 (m, 1H); ^{13}C-NMR ($CDCl_3$): δ 143.4, 141.0, 132.8, 132.7, 130.5, 128.8, 127.7, 127.6, 127.4, 127.2, 124.5, 121.9, 72.3, 37.3, 32.6; MS, m/e (%): 372 (M+4, 2), 370 (M+2, 4), 368 (M, 2).

Anal. Calcd for $C_{15}H_{14}Br_2O$: C, 48.65; H, 3.78. Found: C, 48.27; H, 3.78

1,3-bis(2-Bromophenyl)propane (1).- A mixture of 9.7 g (26.4 mmol) of 1,3-bis(2-bromophenyl)-1-propanol, 30 mL of 57% hydroidic acid (stabilized with 1.55% of hypophosphorous acid) and 2.2 g (71.0 g-atm) of red phosphorous was heated at reflux for 12 hrs, then cooled to 0° and neutralized with 10% aqueous NaOH. The red solid was removed by filtration and the filtrate was extracted with 2 X 50 mL of ether. The combined ether layers were washed with 5% sodium thiosulfate (3X), water, saturated NaCl, dried over anhydrous $MgSO_4$ and concentrated under vacuum at 40° to give a light yellow oil which crystallized on standing. Recrystallization of the crude product from 95% ethanol yielded 8.61 g (24.3 mmol, 92%) of 1,3-bis(2-bromophenyl) propane as white needles, mp. 72-73°, lit.[1] mp. 72-74°.

IR (thin film): 3070, 1610, 1575, 1450, 1400, 1040, 755 cm^{-1}; ^1H-NMR ($CDCl_3$): δ 7.55 (d, 2H, J = 7.5 Hz), 7.25 (m, 4H), 7.05 (m, 2H), 2.84 (t, 4H, J = 7.5 Hz), 1.97(m, 2 H); ^{13}C-NMR ($CDCl_3$): δ 141.3, 132.7, 130.2, 127.5, 127.3, 124.5, 35.8, 30.0; MS, m/e (%): 356 (M+4, 9), 354 (M+2, 17), 352 (M, 9).

Anal. Calcd for $C_{15}H_{14}Br_2$: C, 50.85; H, 3.95. Found: C, 50.65; H, 3.98

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