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SYNTHESIS OF A C_3-SYMMETRIC PHOSPHA[2.2.2]CYCLOPHANE

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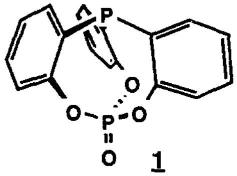
Abstract: The preparation of the C_3-symmetric monophosphine 17-phospha[2.2.2](1,3,5)-benzeno(3,3',3")triphenylmethanophane (2) is described. Its ability to coordinate to transition metals and its conformational mobility are examined.

Optically active mono- and bidentate phosphines have proven to be effective ligands in transition metal catalyzed, asymmetric syntheses.1) Recently we reported the preparation and crystal structure of the C_3-symmetric chiral monophosphine 1.2,3) As an extension of these studies, this communication describes the synthesis of the tris-bridged phospha[2.2.2]cyclophane 2 (scheme 1).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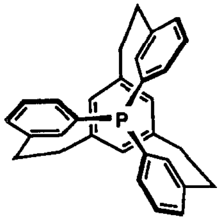
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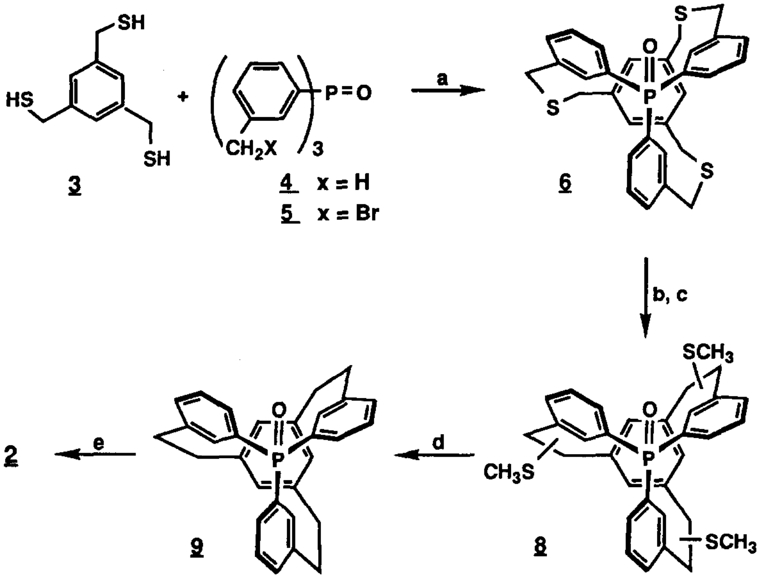
High dilution coupling 4) of the sodium salt of 1,3,5-tris(mercaptomethyl)benzene (3) 5) and phosphine oxide 5 (obtained in 98% yield with ca. 70% purity by NBS bromination of tris-(3-methylbenzene)phosphine oxide (4) 6) in CCl_4) in *tert*-butanol afforded the trithiacyclophane 6 7) in 17% yield after purification by column chromatography. Reaction with dimethoxy-carbonium fluoroborate 8) in dichloromethane provided the trisulfonium salt 7, which by treatment with sodium hydride in THF (50 - 55 °C, 4 h) underwent a Stevens rearrangement to give the tris(sulfide) 8 as a mixture of regio- and diastereoisomers (46% yield). Desulfurisation with Raney nickel (ethanol, reflux, 4 h) and reduction of the phosphine oxide 9 7) with trichlorosilane 9) (toluene, reflux, 3 h) gave, after chromatography, a 56% yield of 17-phospha[2.2.2](1,3,5)benzeno-(3,3',3")triphenylmethanophane (2) 7,10).

Scheme 1 [a]



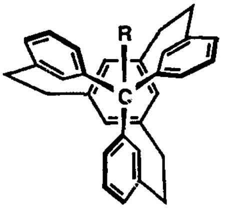
[a] (a) NaOH, *tert*-BuOH, EtOH, toluene, reflux, high dilution; (b) $CH(OCH_3)_2BF_4$, CH_2Cl_2, 22 °C, 22 h; (c) NaH, THF, 50-55 °C, 4 h; (d) Raney nickel, EtOH, reflux, 4 h; (e) Cl_3SiH, toluene, reflux, 3 h.

Nakazaki and coworkers described the synthesis of several carbon analogs (10 a-d) 12), of which some showed remarkable conformational stability. By variable temperature NMR spectral analysis they determined an energy of E_a = 15.5 kcal•mol^{-1} for the interconversion between the two enantiomeric conformations of a deuterio derivative of 10a .13) At +60 °C and at +65 °C the resonances for the methylene protons of 10a and 10b, respectively, coalesced to a sharp singlet, reflecting rapid conformational interconversion. Broad singlets for the methoxy derivative 10c and the hydrocarbon 10d could be observed only at -60 °C.

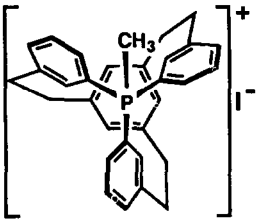
The sharp singlet for the methylene resonances in the room temperature ^1H NMR spectrum of 2 (in $CDCl_3$) reflects the relatively fast enantiomerization of the molecule on the NMR time scale.14) Variable temperature NMR experiments suggest that this exchange process is slowed significantly at about -50 °C, as illustrated by the extensive broadening of this signal. At -60 °C, separate resonances for the diastereomeric benzylic hydrogens can be detected.

The ^1H NMR spectrum of the methyl phosphonium salt 11 7) (obtained by treatment of 2 with methyl iodide in $CDCl_3$) exhibits two multiplets for the benzylic hydrogens at room temperature. Heating to +55 °C (in $CDCl_3$) does not lead to a sharpening of the signals. These coalesce at about -40 °C, giving to a broad singlet that remains unchanged upon cooling to -60 °C.

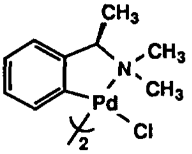
The ability of 2 to coordinate to transition metals is indicated by the characteristic downfield shift of the phosphorus resonance in the ^{31}P NMR spectrum upon complexation with 12 (2 : δ ^{31}P = -14.2 ppm; 2/ $PdCl_2$•$(PhCN)_2$ (excess) : δ ^{31}P = 30.3 ppm).



10a R = CH_3 10c R = OCH_3
10b R = Cl 10d R = H



11



12

The optically active palladium complex 12 has previously been used for the resolution of racemic tertiary phosphines.15) Treatment of 2 with 12 does lead to coordination at the metal center (2/12 : $\delta\ ^{31}P = 37.3$ ppm 7)), but no diastereomeric complexes can be distinguished by ^{31}P (room temperature) or ^1H NMR spectroscopy (room temperature to -60 °C).

The concept of C_3-symmetric phosphines is pursued by the synthesis of compounds which we hope will have greater conformational stability and which can serve as optically active ligands in transition metal-catalyzed asymmetric syntheses.

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7) **2** : ^{1}H NMR ($CDCl_3$) δ 2.80 (s, 12 H), 5.46 (d, J = 4 Hz, 3 H), 6.59 (s, 3 H), 7.13 - 7.19 (m, 3 H), 7.22 - 7.34 (m, 6 H); ^{1}H NMR (toluene - d_8) δ 2.48 - 2.53 (m, 6 H), 2.58 - 2.62 (m, 6 H), 5.61 - 5.64 (m, 3 H), 6.42 (s, 6 H), 6.89 - 6.92 (m, 3 H), 7.02 - 7.08 (m, 3 H), 7.31 - 7.38 (m, 3 H); ^{13}C {^{1}H} NMR ($CDCl_3$) δ 36.1 (t), 38.0 (t), 128.1 (d), 128.4 (dd, $|J_{CP}|$ = 13 Hz), 128.8 (d), 131.8 (dd, $|J_{CP}|$ = 38 Hz), 135.2 (d), 136.9 (d, $|J_{CP}|$ = 10 Hz), 140.2 (s), 140.8 (s); ^{31}P NMR ($CDCl_3$) δ -14.2 (upfield from H_3PO_4); mass spectrum, *m/e* 418 (M^+); exact mass spectrum for $C_{30}H_{27}P$, calcd 418.18504, found 418.18517. **6** : R_f 0.16 (silica gel, ethyl acetate); mp > 300° C; ^{1}H NMR ($CDCl_3$) δ 3.52 (s, 6 H), 3.80 (s, 6 H), 6.67 (d, J = 12 Hz, 3 H), 6.89 (s, 3 H), 7.39 - 7.49 (m, 6 H), 7.85 (dd, J = 12, 7 Hz, 3 H); ^{13}C {^{1}H} NMR ($CDCl_3$) δ 35.1 (t), 35.2 (t) 126.2 (d), 129.2 (dd, $|J_{CP}|$ = 11 Hz), 130.5 (dd, $|J_{CP}|$ = 7 Hz), 131.9 (d), 132.4 (d, $|J_{CP}|$ = 103 Hz), 132.5 (dd, $|J_{CP}|$ = 11 Hz), 138.0 (d, $|J_{CP}|$ = 13 Hz), 140.1 (s); ^{31}P NMR ($CDCl_3$) δ +25.5 (downfield from H_3PO_4); mass spectrum, *m/e* 530 (M^+); exact mass spectrum for $C_{30}H_{27}OPS_3$, calcd 530.09615, found 530.09607. **9** : R_f 0.17 (silica gel, ethyl acetate); mp > 300° C; ^{1}H NMR ($CDCl_3$) δ 2.84 (s, 12 H), 5.69 (d, J = 13 Hz, 3 H), 6.66 (s, 3 H), 7.30 - 7.33 (m, 3 H), 7.41 (ddd, J = 8, 8, 3 Hz, 3 H), 7.79 (dd, J = 12, 7 Hz, 3 H); ^{13}C {^{1}H} NMR ($CDCl_3$) δ 35.5 (t), 37.7 (t), 128.4 (d), 128.9 (dd, $|J_{CP}|$ 7 Hz), 129.3 (dd, $|J_{CP}|$ = 12 Hz), 131.9 (d), 131.9 (d, $|J_{CP}|$ = 104 Hz), 134.6 (dd, $|J_{CP}|$ = 12 Hz), 139.9 (d, $|J_{CP}|$ = 12 Hz), 140.3 (s); ^{31}p NMR ($CDCl_3$) δ +33.1 (downfield from H_3PO_4); mass spectrum, *m/e* 434 (M^+); exact mass spectrum for $C_{30}H_{27}OP$, calcd 434.17994, found 434.17996. **11** : ^{1}H NMR ($CDCl_3$ δ 2.84 - 2.88 (m, 6 H), 2.90 - 2.93 (m, 6 H), 3.27 (d, J = 13.3 Hz, 3 H), 5.72 (d, J = 14.6 Hz, 3 H), 6.64 (s, 3 H), 7.31 - 7.45 (m, 3 H), 7.56 - 7.69 (m, 3 H), 7.77 - 7.89 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 6.9 (d, $|J_{CP}|$ = 54 Hz), 35.4 (s), 37.5 (s), 118.8 (d, $|J_{CP}|$ = 89 Hz), 128.5 (s), 129.7 (d, $|J_{CP}|$ = 11 Hz), 131.3 (d, $|J_{CP}|$ = 13 Hz), 135.1 (s), 135.7 (d, $|J_{CP}|$ = 10 Hz), 140.2 (s), 142.2 (d. $|J_{CP}|$ = 12 Hz); ^{31}P NMR ($CDCl_3$) δ + 21.3 (downfield from H_3PO_4). **2/12** : ^{1}H NMR ($CDCl_3$) δ 1.75 (d, J = 7 Hz, 3 H), 2.73 (d, J = 3 Hz, 3 H), 2.79 (d, J = 2 Hz, 3 H), 2.81 (s, 12 H), 3.77 - 3.82 (m, 1 H), 5.64 (d, J = 10 Hz, 3 H), 6.35 - 6.42 (m, 1 H), 6.58 (s, 3 H), 6.76 - 6.87 (m, 1 H), 6.90 - 6.95 (m, 1 H), 7.16 - 7.28 (m, 7 H), 7.80 - 7.90 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 20.1 (s), 36.1 (s), 37.8 (s), 45.9 (s), 49.9 (s), 75.4 (s), 121.9 (s), 123.5 (s), 124.8 (s), 128.0 (s), 128.4 (d, $|J_{CP}|$ = 14 Hz), 130.5 (s), 130.8 (s), 131.5 (s), 134.3 (d, $|J_{CP}|$ = 21 Hz), 135.5 (s), 138.4 (d, $|J_{CP}|$ = 11 Hz), 140.0 (s), 140.3 (s); ^{31}P NMR ($CDCl_3$) δ +37.3 (downfield from H_3PO_4).

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