Mild electrophilic trifluoromethylation of secondary and primary aryl- and alkylphosphines using hypervalent iodine(III)-CF_3 reagents.

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Experimental Part

Contents

1.1 General Remarks

Techniques: All manipulations were carried out using oven dried (150 °C) glassware with magnetic stirring under an inert atmosphere of argon or in a dry box under an atmosphere of dinitrogen. Unless explicitly indicated the solvents were freshly distilled from an appropriate drying agent and degassed if necessary (by 3 freeze-pump-thaw cycles): THF, Et_2O from Na/benzophenone; pentane from Na/benzophenone/diglyme; MeOH, DCM, MeCN from CaH_2; toluene from Na. [D_2]-DCM was bulb-to-bulb distilled from CaH_2 and degassed by three freeze-pump-taw cycles; $CDCl_3$ used as received without further purification.

Neutral aluminum oxide activity I was purchased from *ICN Biomedicals GmbH* and silica gel 60 (230 – 400 mesh) from *Fluka*. TLC-plates were obtained from *Merck* (silica gel 60 F_{254}, aluminum oxide 60 F_{254}). Solvents for FC or TLC were of puriss p.a. grade: MeOH, $CHCl_3$, EtOAc, or of technical grade: TBME, pentane, hexanes, cyclohexane. TLC stains were

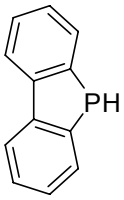
prepared according to literature methods ($KMnO_4$ and cerium-ammonium molybdate stains) [1].

Analytics: **Melting points** were measured on a *Griffin* melting point apparatus. Temperatures are given in degrees Celsius (°C) and are uncorrected. **NMR spectra** were recorded on *Bruker* AC-200 (^{1}H: 200.13, ^{13}C: 50.32, ^{19}F: 188.31, ^{31}P: 81.01), DPX-250 (^{1}H: 250.13, ^{13}C: 62.90, ^{31}P: 101.25), DPX-300 (^{1}H: 300.13, ^{13}C: 75.47, ^{19}F: 282.40, ^{31}P:121.49), DPX-400 (^{1}H: 400.13, ^{13}C: 100.61, ^{19}F: 376.50, ^{31}P: 161.98), or DPX-500 (^{1}H: 500.23, ^{13}C: 125.78, ^{31}P: 202.50) instruments operating at the denoted spectrometer frequency given in mega Hertz (MHz) for the specified nucleus. The samples were measured as solutions in the stated solvent at ambient temperature in non-spinning mode if not mentioned otherwise. To specify the signal multiplicity, the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet and m = multiplet. Shifts δ are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as an external standard for ^{1}H and ^{13}C NMR spectra and calibrated against the solvent residual peak [2]. For ^{19}F NMR spectra, $CFCl_3$ and for ^{31}P spectra H_3PO_4 (85%), respectively, were used as external standards. Coupling constants J are given in Hertz (Hz). **Infrared spectra** were recorded on a *Perkin Elmer* BX II spectrometer (neat). Relative intensities are abbreviated as w = weak, m = medium, s = strong and br. indicates a broad resonance. IR-bands $\tilde{\nu}$ are given in reciprocal wave numbers (cm^{-1}). **HPLC** analyses were run on either an *Agilent* Series 1100 (detector: DAD) or on a *Hewlett Packard* 1050 (detector: MWD) at three different wave lengths (210, 230, 254 nm) using the specified column (OD-H, length: 25 cm, inner diameter: 4.6 mm, particle size: 5 µm), flow rate of the solvent (mL/min), ratio of hexanes/*i*-PrOH, and sample injection volume (µL; sample concentration approximately 1 mg/mL). Retention times t_R are stated in minutes (min). **High resolution mass-spectra** were measured by the *MS-Service des Labors für organische Chemie, ETH Zürich*. Fragment signals are given in mass per charge number (m/z). **Elemental analyses** were carried out by the *Mikroelementanalytisches Laboratorium der ETH Zürich*. The content of the specified element is expressed in percent (%).

Chemicals: Already reported compounds are assigned their corresponding CAS number if available. Commercially available compounds were used as received without any further purification unless stated otherwise. Dicylohexylphosphine, and diphenylphosphine were purchased from *Abcr*; *N*,*N*,*N*',*N*'-tetramethylethylenediamine, *P*,*P*-dichlorophenylphosphine, diphenyl(trimethylsilyl)phosphine from *Aldrich*; *n*-butyl lithium solution from *Fluka*, respectively. Di-(*p*-tolyl)phosphine, phenylphosphine, and cyclohexylphosphine were

purchased from *Strem*. Di-*o*-tolylphosphine, and dinaphthalen-2-ylphosphine [3] were synthesized as reported in the literature. *rac*-(2-Methoxyphenyl)(phenyl)phosphine was accessed following a modified preparation from the literature [4].

1.2 Phosphines

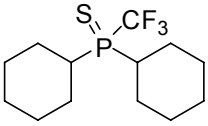


5*H*-Benzo[*b*]phosphindole (5) [5]. TMEDA (*N*,*N*,*N*',*N*'-tetramethylethylene diamine, 10.8 mL, 71.6 mmol, 2.3 eq.) was added to a cooled (ice/H_2O) solution of *n*-BuLi (44.5 mL, 71.2 mmol, 2.3 eq.; 1.6 M in hexanes) in a 250 mL Schlenk-balloon by means of a syringe. To the resulting yellow, cloudy reaction mixture was added after 30 min of stirring in the cooling bath biphenyl (5.0 g, 30.42 mmol) in a single portion as a solid. The cooling bath was removed and the reaction mixture was stirred at ambient temperature for 72 h. The red reaction mixture was cooled (ice/H_2O) and *P*,*P*-dichlorophenylphosphine (4.9 mL, 36.1 mmol, 1.2 eq.) was added by means of a syringe. The reaction mixture was allowed to warm up slowly over night (17 h) to ambient temperature and was treated with aqueous HCl (20 mL, 6 M) followed by H_2O (20 mL) and Et_2O (60 mL). The aqueous phase was extracted twice with DCM. The combined organic phases were dried over Na_2SO_4, filtered and evaporated to dryness to give an oily residue which was subjected to FC (silica gel 60, hexane/DCM 1:0 → hexane/DCM 1:2) to yield 5-phenyl-5*H*-benzo[*b*]phosphindole (2.57 g, 9.87 mmol, 32%) as white crystals.

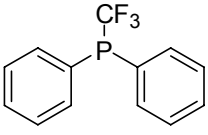
5-Phenyl-5*H*-benzo[*b*]phosphindole (2.00 g, 7.68 mmol) and lithium turnings (0.7 g, 100 mmol) were placed in a 50 mL Schlenk-tube and THF (10 mL) was added. The dark reaction mixture was stirred for 4.5 h and was then decanted by means of a cannula. The remaining Li turnings were washed with further THF (5 mL). To this dark solution was added degassed H_2O (1.5 mL) followed by degassed AcOH (0.4 mL) to give a yellowish suspension. All volatiles were removed under vacuum and the residual, waxy solid was filtered through a plug of aluminum oxide using DCM. After evaporation to dryness the residual solid was taken up in pentane and filtered over a pad of glass wool. After removal of the volatiles and drying in vacuo 5*H*-benzo[*b*]phosphindole (1.25 g, 6.79 mmol, 88%; overall yield: 28%) was obtained as a white crystalline solid. ^{1}H NMR (200 MHz, [D_2]-DCM, 25 °C, TMS): δ = 5.40 (d, ^1J(H,P) = 200.5 Hz, 1H; P*H*), 7.43 – 7.74 (m, 4H; C$H_{arom.}$), 7.90 – 8.08 ppm (m, 4H; C$H_{arom.}$); ^{13}C{^{1}H} NMR (50 MHz, [D_2]-DCM, 25 °C, TMS): δ = 121.5 (s; *C*H), 127.3 (d, J(C,P) = 7.8 Hz; *C*H), 128.4 (s; *C*H), 130.5 (d, J(C,P) = 21.6 Hz, *C*H), 137.4 (d, J(C,P) = 3.3 Hz; *C*), 145.2 ppm (d, J(C,P) = 1.2 Hz; *C*); ^{31}P{^{1}H} NMR (81 MHz, [D_2]-DCM, 25 °C, H_3PO_4): δ = –67.7

ppm (s; PH); ^{31}P NMR (81 MHz, [D$_2$]-DCM, 25 °C, H_3PO_4): δ = –67.7 ppm (dm, ^1J(P,H) = 200.4 Hz; PH); CAS 244-87-1.

1.3 Trifluoromethylation of Secondary Phosphines



Dicyclohexyl(trifluoromethyl)phosphine sulfide (6). Dicylohexylphosphine (0.22 mL, 1.087 mmol) was added dropwise by means of a syringe to a cooled (–78 °C, *i*-PrOH/CO_2(s)) solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (395 mg, 1.197 mmol, 1.1 eq.) in DCM (6.0 mL). The clear solution was stirred and kept in the cooling bath over night (23.5 h) to reach ambient temperature slowly. Solid sulfur (53 mg, 1.66 mmol, 1.5 eq.) was added to this clear colorless solution and the reaction mixture was stirred for 18.5 h at ambient temperature to give a slightly yellow, clear solution. All volatiles were removed under vacuum and the remaining solid was subjected to FC (silica gel 60, cyclohexane → cyclohexane/TBME 20:1). The desired product (189 mg, 0.565 mmol, 52%) was obtained as a colorless, viscous oil. R_f = 0.32 (hexanes/EtOAc 20:1); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.17 − 1.33 (m, 6H; CH_2), 1.40 − 1.56 (m, 4H; CH_2), 1.71 (m, 2H; CH_2), 1.86 − 1.98 (m, 8H; CH_2), 2.12 (m, 2H; C*H*); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 25 °C, TMS): δ = 25.0 (d, J(C,P) = 1.3 Hz; *C*H$_2$), 25.4 (d, J(C,P) = 1.8 Hz; *C*H$_2$), 25.8 (d, J(C,P) = 2.8 Hz; *C*H$_2$), 26.2 (d, J(C,P) = 1.4 Hz; *C*H$_2$), 26.4 (*C*H$_2$), 36.2 (d, ^1J(C,P) = 45.2 Hz; *C*HP), 123.9 ppm (dq, ^1J(C,F) = 322.5 Hz, ^1J(C,P) = 87.5 Hz; *C*F$_3$); ^{19}F NMR (188 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –62.7 ppm (d, ^2J(F,P) = 65.5 Hz, ^1J(C,F) = 322.2 Hz, calculated from ^{13}C satellites; CF_3); ^{31}P{^{1}H} NMR (101 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = 69.1 ppm (q, ^2J(P,F) = 65.4 Hz; P(S)CF_3); IR (neat): $\tilde{\nu}$ = 2931 (m), 2854 (m), 1449 (m), 1348 (w), 1292 (w), 1272 (w), 1217 (w), 1184 (m), 1168 (s), 1132 (m), 1107 (s), 1084 (w), 1039 (w), 1001 (w), 917 (w), 888 (w), 850 (m), 820 (w), 763 (s), 744 (w), 736 (w), 728 (w), 648 cm^{-1} (s); HRMS (EI): m/z: calcd for $C_{13}H_{22}F_3PS$: 298.1126 ([M]$^+$); found: 298.1126 ([M]$^+$).



Diphenyl(trifluoromethyl)phosphine (7). *Method A:* Diphenylphosphine (0.19 mL, 1.092 mmol) was added dropwise by means of a syringe to a cooled (–78 °C, *i*-PrOH/CO_2(s)-bath/cryostat) solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (390 mg, 1.180 mmol, 1.1 eq.) in DCM (4.0 mL). The clear solution was stirred and kept in the cooling bath for 48 h. Then it was warmed to reach ambient temperature. All volatiles were removed under vacuum and the remaining

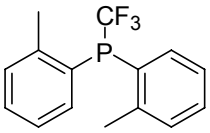
clear, colorless oil was subjected to FC (silica gel 60, cyclohexane). The desired product **7** (204 mg, 0.803 mmol, 74%) was obtained as a colorless oil.

Method B: A solution of diphenyl(trimethylsilyl)phosphine (267 µL, 1.043 mmol; tech grade) in DCM (3 mL) was added dropwise by means of a syringe to a cooled (–78 °C, *i*-PrOH/CO_2(s)) solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (355 mg, 1.075 mmol, 1.03 eq.) in DCM (1.0 mL). The syringe was rinsed with DCM (1 mL). The yellow, clear solution was kept in the cooling-bath and allowed to warm to ambient temperature over night (15 h). TLC showed complete consumption of starting material. All volatiles were removed under vacuum and the residual yellowish oil was subjected to FC (silica gel 60, hexanes). The desired product **7** (182 mg, 0.716 mmol, 69%) was obtained as a colorless oil.

Method C: To a suspension of 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (316 mg, 1.000 mmol) in DCM (3.5 mL) was added a solution of diphenylphosphine (174 µL, 1.000 mmol) in DCM (1 mL) at ambient temperature by means of a syringe. Additional DCM (0.5 mL) was used to rinse. After 5 min all solids had dissolved and after another 10 min a white precipitate began to form. After 22 h all volatiles were removed in vacuo and the reminder was subjected to FC (silica gel 60, hexanes) to yield the title compound **7** (0.198 mg, 0.779 mmol, 78%).

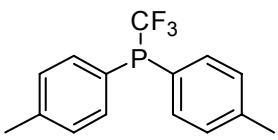
Method D: A mixture of 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (64 mg, 0.203 mmol) and trifluoromethylbenzene (25 µL, 0.204 mmol) in [D_2]-DCM (0.5 mL) in an NMR-tube was treated with diphenyl(trimethylsilyl)phosphine (51 µL, 0.199 mmol) at ambient temperature. The tube was sealed and vigorously shaken and gave a clear solution. Conversion to product after 24 h was estimated to amount to 92% based on the comparison of the ratio of the integrals of the product signal to the signal of the internal standard $PhCF_3$ in the ^{19}F NMR spectrum. R_f = 0.50 (hexanes/EtOAc 20:1); ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.43 − 7.53 (m, 6H; *m*- and *p*-C$H_{arom.}$), 7.65 ppm (m, 4H; *o*-C$H_{arom.}$); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 128.8 (d, ^3J(C,P) = 7.8 Hz; *m*-*C*H), 129.5 (dq, ^1J(C,P) = 10.0 Hz, ^3J(C,F) = 3.2 Hz; *C*), 130.4 (*p*-*C*H), 130.9 (dq, ^1J(C,F) = 320.1 Hz, ^1J(C,P) = 29.7 Hz; *C*F_3), 134.0 ppm (dq, ^2J(C,P) = 20.6 Hz, ^4J(C,F) = 1.1 Hz; *o*-*C*H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –55.0 ppm (d, ^2J(F,P) = 73.0 Hz, ^1J(F,C) = 319.4 Hz, calculated from ^{13}C satellites; CF_3); ^{31}P NMR (121 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = 2.8 ppm (q, ^2J(P,F) = 73.5 Hz; PCF_3); IR (neat): $\tilde{\nu}$ = 3060 (w), 1588 (w), 1483 (w), 1436 (m), 1386 (w), 1328 (w), 1244 (w), 1148 (s), 1093 (s), 1028 (m), 1000 (m), 970 (w), 916 (w), 882 (w),

849 (w), 741 (s), 691 (s), 618 cm^{-1} (w); HRMS (EI): m/z: calcd for $C_{13}H_{10}F_3P$: 254.0467 ($[M]^+$); found: 254.0464 ($[M]^+$); CAS 1605-56-7.



Di-*o*-tolyl(trifluoromethyl)phosphine (8). *Method A:* A solution of di-*o*-tolylphosphine (223 mg, 0.937 mmol) in DCM (2 mL) was added dropwise by means of a syringe to a cooled (–70 °C, cryostat) solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (406 mg, 1.230 mmol, 1.3 eq.) in DCM (1.0 mL). The syringe was rinsed with further DCM (0.5 mL). The clear solution was stirred and kept in the cooling bath for 15.5 h. Then it was slowly warmed to reach ambient temperature and stirred for 3 h. All volatiles were removed under vacuum and the remaining clear, colorless oil was subjected to FC (silica gel 60, cyclohexane). The desired product **8** (132 mg, 0.468 mmol, 50%) was obtained as a colorless oil.

Method B: To 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (340 mg, 1.076 mmol) in DCM (3 mL) was added a solution of di-*o*-tolylphosphine (228 mg, 1.064 mmol) in DCM (1 mL) by means of a syringe. Further DCM (1 mL) was used to rinse. After 14 h stirring at ambient temperature the mixture was evaporated to dryness in vacuo and the reminder was subjected to FC (silica gel 60, hexanes) to yield the desired product (146 mg, 0.515 mmol, 48%). R_f = 0.31 (hexanes); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.51 (unresolved d, ^4J(H,P) = 0.9 Hz, 6H; CH_3), 7.24 − 7.31 (m, 4H; C$H_{arom.}$), 7.39 (m, 2H; C$H_{arom.}$), 7.51 ppm (m, 2H; C$H_{arom.}$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.3 (unresolved dd, ^3J(C,P) = 23.2 Hz; CH$_3$), 126.3 (d, J(C,P) = 1.1 Hz; CH), 128.4 (dq, ^1J(C,P) = 9,7 Hz, ^3J(C,F) = 2.5 Hz; CP), 130.3 (CH), 130.7 (d, J(C,P) = 5.7 Hz; CH), 131.7 (dq, ^1J(C,F) = 319.8 Hz, ^1J(C,P) = 28.8 Hz; CF$_3$), 133.2 (unresolved m; CH), 143.1 ppm (unresolved dd, ^2J(C,P) = 29.0 Hz; CCH$_3$); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –53.4 ppm (d, ^2J(F,P) = 75.4 Hz, ^1J(F,C) = 319.7 Hz, calculated from ^{13}C satellites; CF_3); ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = 14.0 ppm (q, ^2J(P,F) = 75.6 Hz; PCF_3); IR (neat): $\tilde{\nu}$ = 3059 (w), 2975 (w), 1592 (w), 1472 (m), 1451 (m), 1381 (w), 1282 (w), 1202 (w), 1150 (s), 1132 (m), 1090 (s), 1032 (m), 867 (w), 800 (w), 746 (s), 714 (s), 682 (w), 672 cm^{-1} (w).

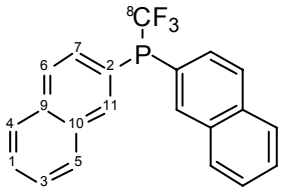


Di *p*-tolyl(trifluoromethyl)phosphine (9). *Method A:* A solution of di-*p*-tolylphosphine (105 mg = 100 µL, 0.490 mmol) in DCM (3 mL) was added by means of a syringe-pump over the course of 45 min in a dropwise fashion to a cooled solution (–5 °C, ice/H2O/acetone) of 1-trifluoromethyl-1,3-

dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (166 mg, 0.503 mmol) in DCM (1 mL). The solution was stirred for further 1.5 h at 0 °C. All volatiles were removed under vacuum and the residual slightly yellow oil was subjected to FC (silica gel 60, cyclohexane) to yield the title compound as a clear, yellowish oil (91.3 mg, 0.323 mmol, 66%).

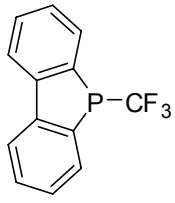
Method B: Di-*p*-tolylphosphine (97 µL, 0.475 mmol) was added by means of an Eppendorf-pipette in one portion to a cooled solution (–78 °C, *i*-PrOH/CO_2(s)) of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (162 mg, 0.491 mmol) in DCM (4 mL). The solution was stirred for further 3 h at –78 °C and warmed up to ambient temperature over the course of 30 min and stirred for 1 h. All volatiles were removed under vacuum and the residual, slightly yellow oil was subjected to FC (silica gel 60, cyclohexane) to yield the title compound as a clear, yellowish oil (94.0 mg, 0.333 mmol, 70%).

Method C: To 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (317 mg, 1.003 mmol) in DCM (3.5 mL) was added a solution of di-*p*-tolylphosphine (204 µL, 1.000 mmol) in DCM (1 mL) by means of a syringe. Further DCM (0.5 mL) was used to rinse. After 1 h of stirring at ambient temperature all volatiles were removed in vacuo and the remaining residue was subjected to FC (silica gel 60, hexanes/EtOAc 20:1) to yield the title compound (219 mg, 0.775 mmol, 78%). R_f = 0.26 (hexanes); UV/VIS: λ = 256 nm: visible, λ = 366 nm: negative; $KMnO_4$-stain: yellow spot on violet background; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.45 (s, 6H; CH_3), 7.30 (m, 4H; C$H_{arom.}$ *ortho* to CH_3), 7.57 ppm (m, 4H; C$H_{arom.}$ *ortho* to P); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.3 (d, ^5J(C, P) = 0.5 Hz; *C*H_3), 126.1 (dq, ^1J(C, P) = 8.6 Hz, ^3J(C, F) = 3.3 Hz; *C*P), 129.6 (d, ^3J(C, P) = 8.0 Hz; *C*H$_{arom.}$ *ortho* to CH_3), 131.0 (dq, ^1J(C, F) = 320.3 Hz, ^1J(C, P) = 30.5 Hz; *C*F_3), 134.0 (dq, ^2J(C, P) = 20.9 Hz, ^4J(C, F) = 1.1 Hz; *C*H$_{arom.}$ *ortho* to P), 140.7 ppm (*C*CH_3); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –55.4 ppm (d, ^2J(F, P) = 72.9 Hz, ^1J(F, C) = 320.4 Hz, calculated from ^{13}C satellites; CF_3); ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = 1.4 ppm (q, ^2J(P, F) = 72.9 Hz); IR (neat): $\tilde{\nu}$ = 3020 (w), 2976 (w), 2922 (w), 2866 (w), 1598 (m), 1499 (m), 1446 (w), 1399 (w), 1310 (w), 1188 (m), 1149 (s), 1095 (s), 1088 (s), 1039 (m), 1019 (m), 966 (w), 946 (w), 840 (w), 802 (s), 709 (m), 642 (m), 630 (m), 616 cm^{-1} (m); HRMS (EI): m/z: calcd for $C_{15}H_{14}F_3$: 282.0785 ([M]$^+$), 213.0828 ([M – CF_3]$^+$); found: 282.0781 ([M]$^+$), 213.0827 ([M – CF_3]$^+$); elemental analysis calcd (%) for $C_{15}H_{14}F_3P$ (282.24): C 63.83, H 5.00, P 10.97; found: C 63.72, H 5.03, P10.89.



Dinaphthalen-2-yl(trifluoromethyl)phosphine (10). *Method A:* A solution of dinaphthalen-2-ylphosphine (286 mg, 1.00 mmol) in DCM (3 mL) was added dropwise by means of a cannula to a cooled (–70 °C, cryostat) solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (375 mg, 1.14 mmol, 1.1 eq.) in DCM (1.0 mL). The cannula was rinsed with further DCM (1.0 mL). After 5 min the solution turned into a white suspension. The reaction mixture was stirred for 1.5 h at –70 °C, then slowly warmed up to ambient temperature by turning off the cooling, and after 24 h all volatiles were removed under vacuum. FC (silica gel 60, cyclohexane/EtOAc 1:0 → 20:1) yielded the title compound **10** (187 mg, 0.53 mmol, 53%) as a white crystalline solid.

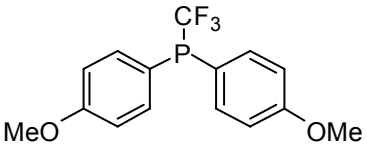
Method B: To 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (167.5 mg, 0.530 mmol) in DCM (0.5 mL) was added a solution of dinaphthalen-2-ylphosphine (150.0 mg, 0.524 mmol) in DCM (1 mL) by means of a syringe. Additional DCM (1 mL) was used to rinse and the reaction mixture was stirred for 2 h at ambient temperature. After evaporation to dryness the remaining material was subjected to FC (silica gel 60, cyclohexane/EtOAc 20:1) to yield the title product (107.8 mg, 0.304 mmol, 58%). R_f = 0.12 (hexanes); M.p. 95 – 96 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.59 (m, 4H; C^1*H*, C^3*H*), 7.70 (t, ^3J(H,H) = 7.3 Hz, 2H; C^7*H*), 7.91 (m, 6H; C^4*H*, C^5*H*, C^6*H*), 8.23 ppm (d, ^3J(H,H) = 10.5 Hz, 2H; C^{11}*H*); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$, 25 °C, TMS): δ = 127.2 (*C*^{1}H), 127.4 (dq, ^1J(C,P) = 10.2 Hz, ^3J(C,F) = 3.1 Hz; *C*^{2}), 128.1 (*C*^{3}H), 128.3 (*C*^{4}H), 128.8 (*C*^{5}H), 129.1 (d, ^3J(C,P) = 6.2 Hz; *C*^{6}H), 129.4 (d, ^2J(C,P) = 14.2 Hz; *C*^{7}H), 131.5 (dq, ^1J(C,P) = 320.6 Hz, ^1J(C,P) = 30.3 Hz; *C*^{8}F$_3$), 133.6 (d, ^4J(C,P) = 10.3 Hz; *C*^{9}), 134.5 (*C*^{10}), 136.3 ppm (d, ^2J(C,P) = 27.5 Hz; *C*^{11}H); ^{19}F NMR (376 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –54.3 ppm (d, ^2J(F,P) = 72.7 Hz, ^1J(F,C) = 320.6 Hz, calculated from ^{13}C satellites; CF_3); ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = 5.3 ppm (q, ^2J(P,F) = 72.9 Hz; P); IR (neat): $\tilde{\nu}$ = 3053 (w), 1586 (w), 1499 (w), 1358 (w), 1341 (w), 1274 (w), 1151 (s), 1100 (s), 1088 (s), 1078 (s), 1016 (m), 985 (w), 970 (w), 962 (m), 954 (w), 944 (w), 914 (w), 903 (m), 869 (m), 828 (m), 815 (s), 771 (m), 745 (s), 646 (m), 637 (m), 605 cm^{-1} (w); HRMS (EI): m/z: calcd for $C_{21}H_{14}F_3P$: 354.0785 ([M]$^+$), 285.0828 ([M]$^+$ – CF_3); found: 354.0784 ([M]$^+$), 285.0821 ([M]$^+$ – CF_3).



5-(Trifluoromethyl)-5*H*-benzo[*b*]phosphindole (11). *Method A:* A solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (340 mg, 1.030 mmol, 1.0 eq.) in DCM (1.0 mL) was added dropwise by means of a

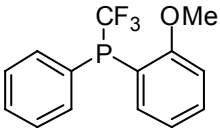
syringe to a cooled (–55 to –60 °C, cryostat) solution of 5*H*-benzo[*b*]phosphindole (**5**) (184 mg, 1.021 mmol) in DCM (3 mL). The syringe was rinsed with further DCM (1.0 mL). The clear solution was stirred and kept in the cooling bath for 24 h. Then it was allowed to reach ambient temperature and all volatiles were removed under vacuum and the remaining clear, slightly yellow oil was subjected to FC (silica gel 60, pentane). The desired product **11** (114 mg, 0.452 mmol, 44%) was obtained as a clear, colorless oil which crystallized as long colorless needles upon standing.

Method B: To a mixture of 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (343 mg, 1.085 mmol) in DCM (3.5 mL) was added a solution of 5*H*-benzo[*b*]phosphindole (**5**) (190 mg, 1.032 mmol) in DCM (1 mL) by means of a syringe. Further DCM (0.5 mL) was used to rinse. After 1.5 h stirring at ambient temperature the reaction mixture was taken to dryness in vacuo and the residue was subjected to FC (silica gel 60, hexanes) to yield the title compound (107.6 mg, 0.427 mmol, 41%). R_f = 0.28 (pentane), UV/VIS: 256 nm (gray spot), 366 nm (fluorescent blue spot); $KMnO_4$-stain: light orange brown spot on purple background; cerium-molybdate-stain: negative; M.p. 59.5 – 60.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.44 (m, 2H; C$H_{arom.}$), 7.56 (m, 2H; C$H_{arom.}$), 7.87 – 7.94 ppm (m, 4H; C$H_{arom.}$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 121.6 (d, ^3J(C,P) = 0.7 Hz; *C*H), 128.3 (d, ^2J(C,P) = 7.8 Hz; *C*H), 130.3 (dq, ^1J(C,P) = 38.6 Hz, ^1J(C,F) = 321.0 Hz; *C*F_3), 130.7 (*C*H), 131.4 (d, ^3J(C,P) = 22.6 Hz; *C*H), 132.7 (m; *C*P), 145.9 ppm (d, ^2J(C,P) = 1.7 Hz; *C*); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –57.6 ppm (d, ^2J(F,P) = 69.2 Hz, ^1J(F,C) = 321.1 Hz, calculated from ^{13}C satellites; CF_3); ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = –9.3 ppm (q, ^2J(P,F) = 69.2 Hz; PCF_3); IR (neat): $\tilde{\nu}$ = 3050 (w), 1591 (w), 1471 (w), 1437 (m), 1264 (w), 1161 (m), 1144 (m), 1120 (s), 1092 (s), 1062 (s), 1029 (m), 984 (m), 949 (m), 883 (m), 788 (w), 758 (s), 751 (s), 740 (s), 719 (s), 696 (m), 618 cm^{-1} (m); HRMS (EI): m/z: calcd for $C_{13}H_8F_3P$: 252.0310 ([M]$^+$); found: 252.0310 ([M]$^+$); elemental analysis calcd (%) for $C_{13}H_8F_3P$ (252.18): C 61.92, H 3.20, P 12.28; found: C 61.54, H 3.29, P 11.82.



Bis(4-methoxyphenyl)(trifluoromethyl)phosphine (12). *Method A:* A solution of di-(4-methoxyphenyl)phosphine (246 mg, 1.0 mmol) in DCM (2 mL) was added dropwise to a cooled solution (–78 °C, *i*-PrOH/CO_2(s)) of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (362 mg, 1.10 mmol, 1.1 eq.) in DCM (1.0 mL). The reaction mixture was left in the cooling-bath and allowed to warm up to ambient temperature over night. All volatiles were removed under vacuum and the residue was subjected to FC (silica gel 60, cyclohexane/EtOAc 20:1). The title compound **12** was isolated as a colorless waxy solid with an undefined melting point (182.0 mg, 0.579 mmol, 58%).

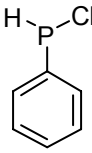
Method B: To a mixture of 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (316 mg, 1.000 mmol) in DCM (3.5 mL) was added di-(4-methoxyphenyl)phosphine (255 mg, 1.040 mmol) dissolved in DCM (1 mL) by means of a syringe at ambient temperature. Further DCM (0.5 mL) was used to rinse and the mixture was stirred for 5 h at ambient temperature. After evaporation to dryness in vacuo and FC (silica gel 60, hexanes/EtOAc 20:1) the product was isolated as a colorless solid (114 mg, 0.363 mmol, 36%). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.87 (s, 6H; CH_3), 7.00 (d, J = 8.8 Hz, 4H; C$H_{arom.}$), 7.58 ppm (t, J = 8.4 Hz, 4H; C$H_{arom.}$); ^{13}C{^{1}H} NMR (63 MHz, $CDCl_3$, 25 °C, TMS): δ = 55.3 (*C*H$_3$), 114.6 (d, J(C,P) = 8.9 Hz; *C*H$_{arom.}$), 120.4 (dq, ^1J(C,P) = 6.5 Hz, ^3J(C,F) = 3.3 Hz; *C*P), 131.1 (dq, ^1J(C,P) = 30.3 Hz, ^1J(C,F) = 320.5 Hz; *C*F$_3$); 135.7 (d, J(C,P) = 22.3 Hz; *C*H$_{arom.}$), 161.5 ppm (*C*OCH$_3$); ^{19}F NMR (188 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –56.2 ppm (d, ^2J(F,P) = 73.3 Hz; CF_3); ^{31}P{^{1}H} NMR (101 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = –0.4 ppm (q, ^2J(P,F) = 73.3 Hz; PCF_3); HRMS (EI): m/z: calcd for $C_{15}H_{14}F_3O_2P$: 314.0678 ([M]$^+$); found: 314.0677 ([M]$^+$).



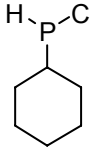
***rac*-(2-Methoxyphenyl)(phenyl)(trifluoromethyl)phosphine (13).** A solution of *rac*-(2-methoxyphenyl)(phenyl)phosphine (334 mg, 1.546 mmol) in DCM (2 mL) was added dropwise to a cooled (–78 °C, *i*-PrOH/CO_2(s)) solution of 1-trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole (**2**) (536 mg, 1.623 mmol, 1.05 eq.) in DCM (4.0 mL). Further DCM (2 mL) was used to rinse. The reaction mixture was stirred with cooling for 3 h and then allowed to warm to ambient temperature over the course of 30 min and kept at that temperature for 1 h. After evaporation of all volatile components the residue was subjected to FC (silica gel 60, hexanes/EtOAc 20:1) to give the title compound *rac*-**13** as a colorless oil (276 mg, 0.972 mmol, 63%). The racemic product mixture *rac*-**13** could be separated by chiral HPLC (Diacel CHIRALPACK

OD-H, 0.4 mL/min, hexan, 5 µL, t_R=24.7, 27.0 min) and preparative chiral HPLC. R_f = 0.28 (hexanes); $[\alpha]_D^{20}$= 61.42 ± 0.30 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.77 (s, 3H; OC*H*$_3$), 6.95 (dd, *J*(H,H) = 8.3 Hz, *J*(H,H) = 5.3 Hz, 1H; C*H*$_{arom.}$), 7.07 (t, *J*(H,H) = 7.5 Hz, 1H; C*H*$_{arom.}$), 7.46 (m, 5H; C*H*$_{arom.}$), 7.57 ppm (t, *J*(H,H) = 7.8 Hz, 1H; C*H*$_{arom.}$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 55.8 (O*C*H$_3$), 111.0 (*C*H), 118.4 (dq, ^{1}*J*(C,P) = 9.8 Hz, ^{3}*J*(C,F) = 3.2 Hz; *C*P), 121.5 (d, *J*(C,P) = 1.1 Hz; *C*H), 128.6 (d, *J*(C,P) = 8.2 Hz; *C*H), 129.9 (dq, ^{1}*J*(C,P) = 10.6 Hz, ^{3}*J*(C,F) = 3.0 Hz; *C*P), 130.3 (d, *J*(C,P) = 0.7 Hz; *C*H), 131.3 (dq, ^{1}*J*(C,F) = 320.5 Hz, ^{1}*J*(C,P) = 31.0 Hz; *C*F$_3$), 131.9 (*C*H), 133.3 (q, ^{4}*J*(C,F) = 1.7 Hz; *C*H), 134.2 (dd, ^{2}*J*(C,P) = 21.6 Hz, ^{4}*J*(C,F) = 0.7 Hz; *C*H), 161.7 ppm (d, ^{2}*J*(C,P) = 16.1 Hz; *C*OCH$_3$); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, $CFCl_3$): δ = –54.2 ppm (d, ^{2}*J*(F,P) = 72.9 Hz; CF_3); ^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$, 25 °C, H_3PO_4): δ = –6.7 ppm (q, ^{2}*J*(P,F) = 72.8 Hz; PCF_3); HRMS (EI): m/z: calcd for $C_{13}H_{12}F_3OP$: 284.0572 ($[M]^+$); found: 284.0572 ($[M]^+$);

1.4 Trifluoromethylation of Primary Phosphines



Phenyl(trifluoromethyl)phosphine (14). To a mixture of 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (63.5 mg, 0.201 mmol) and trifluoromethylbenzene (24.5 µL, 0.200 mmol) in [D_2]-DCM (0.5 mL) in an NMR-tube was added phenylphosphine (22.0 µL, 0.200 mmol) by means of an Eppendorf pipette. The tube was closed and vigorously shaken at ambient temperature. After one hour the starting materials had been found to be consumed, based on ^{19}F- and ^{31}P{^{1}H} NMR spectroscopy and the conversion to product **14** was estimated to amount to 84% based on the comparison of the ratio of the integrals of the product signal to the signal of the internal standard $PhCF_3$ in the ^{19}F NMR spectrum. ^{19}F NMR (282 MHz, [D_2]-DCM, 25 °C, $CFCl_3$): δ = –52.2 ppm (dd, ^{2}*J*(F,P) = 57.6 Hz, ^{3}*J*(F,H) = 11.3 Hz; PCF_3); ^{31}P{^{1}H} NMR (121 MHz, [D_2]-DCM, 25 °C, H_3PO_4): δ = –40.4 ppm (q, ^{2}*J*(P,F) = 57.6 Hz; PCF_3); ^{31}P NMR (121 MHz, [D_2]-DCM, 25 °C, H_3PO_4): δ = –40.4 ppm (dqt, ^{1}*J*(P,H) = 222.3 Hz, ^{2}*J*(P,F) = 57.6 Hz, ^{3}*J*(P,H) = 8.0 Hz; PCF_3).



Cyclohexyl(trifluoromethyl)phosphine (15). To a mixture of 1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one (**1**) (63.5 mg, 0.201 mmol) and trifluoromethylbenzene (24.5 µL, 0.200 mmol) in [D_2]-DCM (0.5 mL) in an NMR-tube was added cyclohexylphosphine (26.5 µL, 0.200 mmol) by means of an Eppendorf

pipette. The tube was closed and vigorously shaken at ambient temperature. After one hour the starting materials had been found to be consumed based on ^{19}F- and ^{31}P{^{1}H} NMR spectroscopy and the conversion to product **15** and its protonated form $CyP(CF_3)H_2^+$ (**15**H^+) were estimated to amount to 19% and 35% based on the comparison of the ratio of the integrals of the product signals to the signal of the internal standard $PhCF_3$ in the ^{19}F NMR spectrum. **15**: ^{19}F NMR (282 MHz, [D$_2$]-DCM, 25 °C, $CFCl_3$): δ = –48.6 ppm (dd, ^{2}J(F,P) = 49.3 Hz, ^{3}J(F,H) = 12.0 Hz; PCF_3); ^{31}P{^{1}H} NMR (121 MHz, [D$_2$]-DCM, 25 °C, H_3PO_4): δ = –37.7 ppm (q, ^{2}J(P,F) = 49.0 Hz; PCF_3); ^{31}P NMR (121 MHz, [D$_2$]-DCM, 25 °C, H_3PO_4): δ = –37.7 ppm (dq, ^{1}J(P,H) = 209.8 Hz, ^{2}J(P,F) = 49.0 Hz; PCF_3). **15**H^+: ^{19}F NMR (282 MHz, [D$_2$]-DCM, 25 °C, $CFCl_3$): δ = –42.0 ppm (dt, ^{2}J(F,P) = 45.5 Hz, ^{3}J(F,H) = 12.3 Hz; PCF_3); ^{31}P{^{1}H} NMR (121 MHz, [D$_2$]-DCM, 25 °C, H_3PO_4): δ = –123.4 ppm (q, ^{2}J(P,F) = 45.4 Hz; PCF_3); ^{31}P NMR (121 MHz, [D$_2$]-DCM, 25 °C, H_3PO_4): δ = –123.4 ppm (tq, ^{1}J(P,H) = 204.4 Hz, ^{2}J(P,F) = 45.4 Hz; PCF_3).

1.5 Literature

[1] see for example: http://www.ux1.eiu.edu/~cfthb/research/handbook/TLCstains.htm.

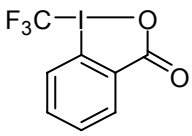
[2] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512 – 7515.

[3] a) A. L. Casalnuovo, T. V. RajanBabu, T. A. Ayers, T. H. Warren, *J. Am. Chem. Soc.* **1994**, *116*, 9869 – 9882; b) W. Kuchen, H. Buchwald, *Chem. Ber.* **1958**, *91*, 2871 – 2877.

[4] A. Togni, C. Breutel, M. C. Soares, N. Zanetti, T. Gerfin, V. Gramlich, F. Spindler, G. Rihs, *Inorg. Chim. Acta* **1994**, *222*, 213 – 224.

[5] a) W. Neugebauer, A. J. Kos, P. von Ragué Schleyer, *J. Organomet. Chem.* **1982**, *228*, 107 – 118; b) E. H. Braye, I. Caplier, R. Saussez, *Tetrahedron* **1971**, *27*, 5523 – 5537; c) E. Durán, D. Velasco, F. López-Calahorra, *Heterocycles* **2002**, *57*, 825 – 855.

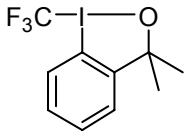
1, 1-Trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one



Chemical Formula: $C_8H_4F_3IO_2$

Molecular Weight: 316.02 g mol^{-1}

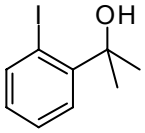
2, 1-Trifluoromethyl-1,3-dihydro-3,3-dimethyl-1,2-benziodoxole



Chemical Formula: $C_{10}H_{10}F_3IO$

Molecular Weight: 330.09 g mol^{-1}

3, 2-(2-Iodophenyl)propan-2-ol



Chemical Formula: $C_9H_{11}IO$

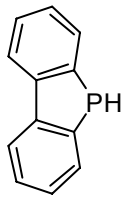
Molecular Weight: 262.09 g mol^{-1}

4, 2-Iodobenzoic acid

Chemical Formula: $C_7H_5IO_2$

Molecular Weight: 248.02 g mol^{-1}

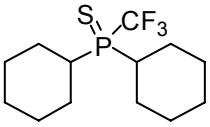
5, 5*H*-benzo[*b*]phosphindole



Chemical Formula: $C_{12}H_9P$

Molecular Weight: 184.17 g mol^{-1}

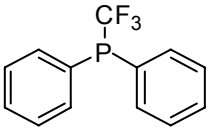
6, dicyclohexyl(trifluoromethyl)phosphine sulphide



Chemical Formula: $C_{13}H_{22}F_3PS$

Molecular Weight: 298.35 g mol^{-1}

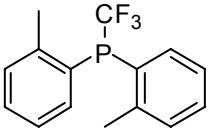
7, diphenyl(trifluoromethyl)phosphine



Chemical Formula: $C_{13}H_{10}F_3P$

Molecular Weight: 254.19 g mol^{-1}

8, di *o*-tolyl(trifluoromethyl)phosphine



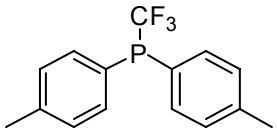
Chemical Formula: $C_{15}H_{14}F_3P$

Molecular Weight: 282.24 g mol^{-1}

9, di *p*-tolyl(trifluoromethyl)phosphine

Chemical Formula: $C_{15}H_{14}F_3P$

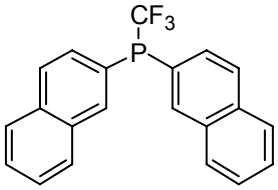
Molecular Weight: 282.24 g mol^{-1}



10, dinaphthalen-2-yl(trifluoromethyl)phosphine

Chemical Formula: $C_{21}H_{14}F_3P$

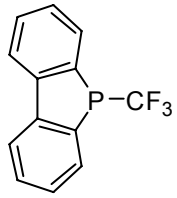
Molecular Weight: 354.30 g mol^{-1}



11, 5-(trifluoromethyl)-5*H*-benzo[*b*]phosphindole

Chemical Formula: $C_{13}H_8F_3P$

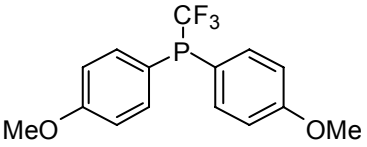
Molecular Weight: 252.17 g mol^{-1}



12, bis(4-methoxyphenyl)(trifluoromethyl)phosphine

Chemical Formula: $C_{15}H_{14}F_3O_2P$

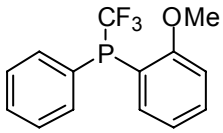
Molecular Weight: 314.24 g mol^{-1}



13, *rac*-(2-methoxyphenyl)(phenyl)(trifluoromethyl)phosphine

Chemical Formula: $C_{14}H_{12}F_3OP$

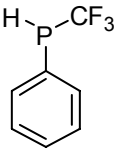
Molecular Weight: 284.21 g mol^{-1}



14, phenyl(trifluoromethyl)phosphine

Chemical Formula: $C_7H_6F_3P$

Molecular Weight: 178.09 g mol^{-1}



15, cyclohexyl(trifluoromethyl)phosphine

Chemical Formula: $C_7H_{12}F_3P$

Molecular Weight: 184.14 g mol^{-1}