Easier Preparation of 2,6-Di-*tert*-butylphenyl Derivatives[1]

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Dedicated to Professor Rolf Huisgen on the occasion of his 90th birthday

Abstract: Despite steric shielding by the 2,6-di-*tert*-butylphenyl group ('super-2,6-xylyl' = xyl*), inexpensive sodium phenolate (xyl*–ONa) reacts with dimethyl sulfate to produce only xyl*–OCH_3 (94%) with complete suppression of the alternative 4-methylation. Reductive cleavage of xyl*–OCH_3 by elemental lithium with the help of an electron carrier generates xyl*–Li, which in turn yields xyl*–CO_2H (63%). The corresponding 4-methyl-derivatives of these compounds were obtained analogously. The acid chloride xyl*–COCl (77% yield) acylates $HalMgCH_2R$ to give only xyl*–$COCH_3$ (86%) or xyl*–COEt (97%). These two ketones react with *n*-butyllithium (no carbonyl addition) and Cl–$PO(OEt)_2$ to furnish only the enol phosphates xyl*–$C(=CH_2)OPO(OEt)_2$ (84%) or xyl*–$C(=CHCH_3)OPO(OEt)_2$ (up to 70%), respectively. Only 1,2-elimination occurs when the latter two products are treated with *tert*-butyllithium, affording xyl*–C≡CH (68%) or xyl*–C≡CMe (88%), respectively.

Key words: acylation, alkynes, deoxygenation, electron transfer, ketones

The published syntheses[2–5] of compounds carrying a 3,4,5-unsubstituted 2,6-di-*tert*-butylphenyl group employ multistep routes that give yields that are not always satisfactory.[4] Our search for a short and easy pathway with fewer side-reactions revealed that 2,6-di-*tert*-butyl-4-methyl-anisole (**2b**; Scheme 1) had been observed in unpublished work[6] to break 'predominantly' its aryl–oxygen bond (rather than O–CH_3) on treatment with elemental potassium in 1,2-dimethoxyethane (DME). Using, instead, the much safer elemental lithium together with an electron carrier, we have discovered and report here how this reductive cleavage can be used for the preparation of other 2,6-di-*tert*-butylphenyl-derivatives on reasonably large scales (30 mmol or more).

A first problem arose with the preparation of pure 2,6-di-*tert*-butylanisole (**2a**) as a starting material: We found that most of the published procedures[7–11] for hydroxyl-methylation with iodomethane in alkaline solution, when applied to inexpensive, commercial 2,6-di-*tert*-butylphenol (**1a**), led to **2a** contaminated with small but significant quantities of **2b**, which could not readily be separated from **2a** by physical or chemical methods [transformation of the unwanted 4-CH_3 group of **2b** into 4-CO_2H (**2d**) or 4-CH_2CO_2H functions, with subsequent alkaline separation from **2a**, were feasible but unrewarding]. In an alternative approach, the more expensive 4-bromo-2,6-di-*tert*-butylphenol (**1c**) was converted into **2c**, which furnished **2a** upon debromination with elemental lithium in *tert*-butyl alcohol.

A surprisingly simple solution to the above 4-methylation problem was found by deprotonating **1a** with sodium hydride[12] (1.5 equiv) and adding dimethyl sulfate[12] (DMS, 1.3 equiv) instead of iodomethane, provided that the solvent diethyl ether[12] was replaced by 1,2-dimethoxyethane (the excess of sodium hydride is stable[13] towards dimethyl sulfate at r.t. and provides for the scavenging of adventitious proton sources). The crude product **2a** contained no **2b** and was pure after distillation (yield 94%).

The reductive cleavage of **2a** worked well with the blue tetrahydrofuran solution formed with elemental lithium (3.1 equiv) and 4,4′-di-*tert*-butylbiphenyl (DTBB; 0.50 equiv), whereas other suggested[14] electron carriers (biphenyl, naphthalene, 1-dimethylaminonaphthalene[15]) were less suitable. The successful conditions had to balance exhaustive formation of the emerging aryllithium compound **5a** against its protonation to give 1,3-di-*tert*-butylbenzene[16] (**6a**); therefore, the blue mixture was poured onto crushed solid carbon dioxide immediately after consumption of **2a** (90 min at r.t.). The best isolated yields (ca. 67%) were attained after taking into account an unusual phase transfer property: Because the sodium salt of the acid **4a** is soluble in both water (to give pH ~7) and diethyl ether, low-boiling petroleum ether was used instead of diethyl ether for the workup with aqueous sodium hydroxide so that the non-acidic components could be extracted and the expensive carrier DTBB easily recovered[17] (isolated yield 95%). Small amounts (up to 7%) of 2,6-di-*tert*-butylphenol (**1a**) could be detected only in the non-acidic fractions, showing that **1a** was not extracted into aqueous sodium hydroxide[18] and indicating that a corresponding amount of the lithium phenolate **3a** had been generated through the O–CH_3 cleavage of **2a**. Similar treatment of 2,6-di-*tert*-butyl-4-methylanisole[8] (**2b**) with DTBB (1 equiv) and lithium (3.2 equiv) for only one hour furnished the acid **4b** (crude yield 60%) along with a non-acidic fraction containing some phenol **1b**, which was derived from **3b**. The solid acid chloride **7** (distilled yield 77%), which was prepared from **4a** with thionyl chloride (2 equiv) and a trace of pyridine at room temperature, reacted cleanly with either methylmagnesium chloride or ethylmagnesium bromide (2 equiv in either case) at room temperature to provide ketones **8a** (86%) or **8b** (97%), respectively. Side-products could not be detected,[19] al-

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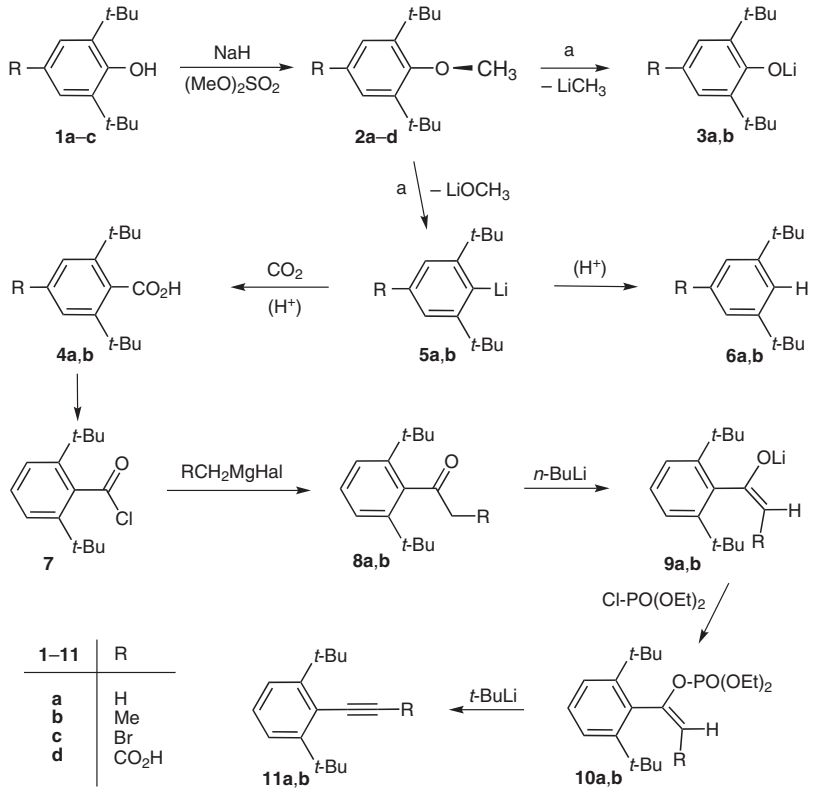

Scheme 1 *Reagents and conditions*: (a) Li (3 equiv), DTBB (0.5 equiv).

though the α-diketone 2,2′,6,6′-tetra-*tert*-butylbenzil might have been expected by analogy with reports in the literature.[20,21] In contrast, the addition of methyllithium to **7** furnished ketone **8a** along with several side-products, among which a trace of α-diketone was recognized through its two diastereotopic $C(CH_3)$ groups, which exhibited broadened[20] ^{1}H NMR signals (δ = 0.89 and 1.45 ppm at 80 MHz in CCl_4) that were close to coalescence. Not unexpectedly,[22] ketone **8a** was not produced by treatment of **5a** with acetyl chloride, which, instead, resulted in proton transfer to give **6a**.

The diethyl α-(2,6-di-*tert*-butylphenyl)vinyl phosphate (**10a**) was prepared from ketone **8a** in tetrahydrofuran with *n*-butyllithium (1.5 equiv) via enolate **9a** formation and subsequent addition of $ClPO(OEt)_2$ (2.0 equiv), with 84% yield of pure **10a** after chromatography. A similar procedure converted the ketone **8b** via the enolate **9b** into the pure *E*-isomer **10b** (ca. 66%). After numerous attempts, the most suitable base for preparing the alkyne **11a** from **10a** was found to be *tert*-butyllithium (2.5–2.7 equiv) in methyl *tert*-butoxide. This base avoids the interfering O–P cleavage reactions and furnished spontaneously crystallizing **11a** (pure yield 68%). Similarly, **10b** afforded almost pure propyne **11b** ('crude' yield 88%, no propargyl or allenyl isomer), which was also obtained from **11a** in tetrahydrofuran with *n*-butyllithium and dimethyl sulfate.

In conclusion, steric shielding appears to account for the clean course of the above reactions with small Grignard reagents, *n*-BuLi, or *t*-BuLi.

The spectroscopic equipment was described in a previous publication.[23]

2,6-Di-*tert*-butylanisole (2a)

A dry Schlenk flask (1 L) was charged with a magnetic stirring bar, NaH (15.70 g, 55% in oil), and anhydrous pentane (60 mL) under a well-ventilated hood. After stirring for 10 min, the liquid was removed with a pipette and discarded, and the washed NaH powder (calcd. 360 mmol) was covered with DME (200 mL) under a blanket of dried N_2 gas. A solution of 2,6-di-*tert*-butylphenol (**1a**; 50.04 g, 242.5 mmol) in anhydrous DME (150 mL) was added dropwise with stirring during 2 h at r.t. (CARE! Brisk evolution of H_2 gas). DMS (30.1 mL, 317 mmol) was then added within 20 min to the stirred, yellow-greenish suspension, which was stirred at r.t. for a further 2.5 h.

Residual NaH was destroyed under an N_2 atmosphere through the dropwise addition of EtOH (3 mL) and then distilled H_2O (20 mL), and unconsumed DMS was hydrolyzed by stirring overnight. The colorless sediment was dissolved within the mixture by adding aq HCl (100 mL, 100 mmol), and the two phases were separated. The aqueous layer was shaken with Et_2O (3 × 80 mL), and the combined four organic layers were washed with distilled H_2O (3 × 150 mL) until neutral, dried over $MgSO_4$, and concentrated to yield the almost pure, golden-yellow oil **2a** (54.66 g). Pure **2a** distilled at 130–132 °C/20 Torr (Lit.[12] 96 °C/0.15 Torr).

Yield: 50.02 g (94%); bright-yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42 (s, 18 H), 3.67 (s, 3 H, OCH_3), 6.96 and 7.23 (arom. AB_2 system, ^3J = 7.8 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 32.13 [2 × C(*C*H$_3$)$_3$], 35.71 [2 × *C*(CH$_3$)$_3$], 64.19 (OCH_3), 122.88 (C-4), 126.48 (C-3/-5), 143.63 (C-2/-6), 159.49 (C-1).

4-Bromo-2,6-di-*tert*-butylanisole (2c)
^{1}H NMR (80 MHz, CCl_4): δ = 1.46 (s, 18 H), 3.65 (s, 3 H, OCH_3), 7.20 (s, 2 H, *m*-ArH).

Converted into **2a** (75% yield after chromatography) with elemental Li (at least 5 equiv) in THF–*t*-BuOH (8 h at 70 °C).

3,5-Di-*tert*-butyl-4-methoxybenzoic Acid (2d)
The oxidation of **2b** with a large excess of $KMnO_4$ in refluxing aq NaOH and Aliquat 336 remained incomplete after 15 h, affording the acid **2d**.

Yield: 22% (crude); mp ~191 °C (hexane) (Lit.[11] 195–197 °C; Lit.[24] 192.5–194.5 °C).

IR (KBr): 3600–2500 (br, CO_2–H), 2966, 2873, 1692 (s), 1393, 1300, 1254, 1227, 1006 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 18 H), 3.73 (s, 3 H, OCH_3), 8.03 (s, 2 H, 2 × ArH).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 31.9 [2 × C(CH_3)$_3$], 35.9 [2 × C(CH$_3$)$_3$], 64.5 (OCH_3), 123.4 (C-1), 129.0 (C-2/-6), 144.3 (C-3/-5), 164.8 (C-4), 172.3 (CO_2H); assigned through comparison with **2a** and **4a**.

2,6-Di-*tert*-butylbenzoic Acid (4a)
Elemental Li (975 mg, 140 mmol) was hammered to flat sheets, which were cut into smaller pieces and dropped into a dried Schlenk flask (250 mL) containing anhydrous THF (75 mL) and a magnetic stirring bar under dried argon gas. After the addition of DTBB (6.05 g, 22.7 mmol), the Schlenk flask was stoppered and sonicated in an ultrasound bath at r.t. until the mixture acquired a dark-blue color (not longer than 10 min). Pure 2,6-di-*tert*-butylanisole (**2a**; 10.00 g, 45.4 mmol) was introduced within 3 min, and the contents of the stoppered flask was stirred at r.t. for 90 min (not less than 60 min) without fading of the blue color. The mixture was poured quickly onto solid CO_2 and set aside for warming up over 30 min, whereupon the larger pieces of the unconsumed lithium were taken out. The orange-colored product mixture was dissolved in low-boiling PE (50 mL) together with aq NaOH (1 M, 100 mL). The separated aqueous layer was extracted with PE (50 mL), and the combined organic layers were then shaken with aq NaOH (2 M, 50 mL), washed with distilled H_2O (50 mL), dried over $MgSO_4$, and concentrated. The remaining yellow cake (7.11 g) contained mainly DTBB along with 1,3-di-*tert*-butylbenzene[16] (**6a**; yield 30%) and some 2,6-di-*tert*-butylphenol (**1a**; yield 7%), but no anisole **2a**. This material was thoroughly mixed with MeOH, which was removed under suction, and again washed with MeOH to afford recovered pure DTBB (5.75 g, 95%).

The combined aq NaOH extracts were washed once more with PE (50 mL, to be discarded), then acidified with concd HCl and extracted with Et_2O (3 × 100 mL). The combined Et_2O extracts were washed with distilled H_2O until neutral, dried over $MgSO_4$, and evaporated to complete dryness, yielding the almost pure acid **4a**.

Yield: 6.73 g (63%); mp 171–172 °C (hexane).

IR (KBr): 3600–2400 (br, CO_2–H), 3010, 1698 (s), 1295 (s), 758 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (s, 18 H), 7.29 and 7.42 (arom. AB_2 system, ^3J = 8.1 Hz, 3 H), 11.8 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 32.16 [2 × C(CH_3)$_3$], 36.81 [2 × C(CH$_3$)$_3$], 125.11 (C-3/-5), 128.83 (C-4), 130.30 (C-1), 146.90 (C-2/-6), 179.95 (CO_2H).

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.19; H, 9.59.

Separation of **4a** from non-acidic components was also complete after extraction with one portion of aq Na_2CO_3, but incomplete with aq $NaHCO_3$. The side-product **1a** could not be extracted from Et_2O into either aq 2 M NaOH or Na_2CO_3.

Sodium 2,6-Di-*tert*-butylbenzoate
^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.34 (s, 18 H), 7.08 and 7.25 (br, arom. AB_2 system, ^3J = ~7.8 Hz, 3 H).

2,6-Di-*tert*-butyl-4-methylbenzoic Acid (4b)
Prepared as for **4a** from **2b** (3.00 g, 12.8 mmol) with DTBB (1 equiv) and Li (3.2 equiv) in 1 h.

Yield: 1.92 g (60%, crude); mp 182–184 °C (hexane).

IR (KBr): 3600–2500 (br, CO_2–H), 2968, 2916, 1697 (s), 1290 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47 (s, 18 H), 2.34 (s, 3 H, 4-CH_3), 7.22 (s, 2 H, 3-/5-H), 12.0 (br s, 1 H, CO_2H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 21.9 (4-CH_3), 32.2 [2 × C(CH_3)$_3$], 36.7 [2 × C(CH$_3$)$_3$], 125.8 (C-3/-5), 127.7 (C-1), 138.0 (C-4), 146.9 (C-2/-6), 180.4 (CO_2H).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.24; H, 9.57.

2,6-Di-*tert*-butylbenzoyl Chloride (7)
The acid **4a** (16.97 g, 72.42 mmol) was dissolved in anhydrous Et_2O (120 mL) with magnetic stirring under argon in a dried Schlenk flask (250 mL). The yellow solution became orange-colored upon the addition of $SOCl_2$ (10.52 mL, 144.8 mmol) and anhydrous pyridine (10 drops) as a catalyst. The flask was kept under anhydrous conditions at r.t. overnight without stirring. The brownish solution was separated by pipette from the resinous precipitate and concentrated (16.93 g, including residual $SOCl_2$). This material can be successfully processed further only after distillation in a wide-bore apparatus (to avoid obstruction through rapid crystallization).

Yield: 14.19 g (77%); mp 31.5–33 °C; bp 75–80 °C/0.1 mbar.

IR (Nujol): 1806 (COCl) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.48 (s, 18 H), 7.29 and 7.39 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 32.5 [2 × C(CH_3)$_3$], 37.3 [2 × C(CH$_3$)$_3$], 125.9 (C-3/-5), 129.6 (C-4), 136.0 (C-1), 144.9 (C-2/-6), 173.6 (COCl).

Anal. Calcd for $C_{15}H_{21}ClO$: C, 71.27; H, 8.37; Cl, 14.02. Found: C, 71.33; H, 8.35; Cl, 13.11.

Note: **7** will hydrolyze to **4a** within a few hours upon contact with moisture.

2,6-Di-*tert*-butylacetophenone (8a)
A dried Schlenk flask (250 mL) was charged with purified acid chloride **7** (14.19 g, 56.13 mmol), anhydrous Et_2O (120 mL), and a magnetic stirring bar under argon gas. The stirred, clear solution became turbid and began to boil gently on the dropwise addition of a THF solution of MeMgCl (37.4 mL, 112 mmol) at r.t. from a pressure-equalizing dropping funnel. Stirring was continued for 2.5 h, whereafter the mixture was poured into sat. aq NH_4Cl (300 mL). The aqueous layer was shaken with Et_2O (2 × 100 mL) and discarded. These three organic layers were combined, washed with distilled H_2O (3 × 80 mL), dried over $MgSO_4$, and evaporated to dryness, yielding the pure ketone **8a** as a yellow oil that crystallized after a few minutes.

Yield: 11.24 g (86%); mp 39–41 °C (MeOH at –18 °C).

IR (KBr): 2955, 1697 (s), 1363, 1348, 1236, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 (s, 18 H), 2.63 (s, 3 H, CH_3-α), 7.22 and 7.37 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 32.80 [qm, ^1J = 125.9 Hz, ^3J = 4.9 Hz, 2 × C(CH_3)$_3$], 36.98 [m, ^2J = 3.7 Hz, 2 × C(CH_3)$_3$], 38.23 (sharp q, ^1J = 127.3 Hz, CH_3-α), 125.66 (ddd, ^1J = 157.3 Hz, ^3J = 7.5 Hz, ^2J = +1.5 Hz, C-3/-5), 127.64 [app. dd, ^1J = 159.43 Hz, ^2J = –0.01 (± 0.03) Hz, C-4], 140.26 (tdq, ^3J = 6.78 Hz, ^4J = –1.65 Hz, ^3J = +0.89 Hz, C-1), 145.17 [dm, ^3J = 7.40 Hz to 4-H, ^2J = +1.13 Hz to 3-H or 5-H, ^4J = –1.20 Hz to 5-H or 3-H, ^3J = 3.68 Hz to 2-C(CH_3)$_3$ or 6-C(CH_3)$_3$, C-2/-6], 210.89 (qtd, ^2J = –5.57 Hz, ^4J = ±1.13 Hz, ^5J = –0.01 Hz, C=O); assigned through the following selective {^{1}H} decoupling experiments: {3-/4-/5-H} → C=O as a sharp quartet with ^2J = 5.6 Hz, C-1 as a br singlet (^3J q unresolved), C-2/-6 as a sharp decet; {CH_3-α} → C=O as a triplet with ^4J = 1.1 Hz, C-1 as a triple-doublet with ^3J = 6.7 Hz and ^4J = 1.5 Hz; signs and values of the long-range couplings were determined through computer simulation.

Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.77; H, 10.32.

2,6-Di-*tert*-butylpropiophenone (8b)

Purified acid chloride **7** (1.43 g, 5.66 mmol) in anhydrous THF (24 mL) was stirred magnetically under argon gas in a dried Schlenk flask (100 mL) during the dropwise addition of a THF solution of EtMgBr (11.3 mmol, 11.3 mL) within 15 min. The darkening mixture became hot and was stirred for 2 h at r.t., then poured into iced aq NH_4Cl (50 mL) and shaken with Et_2O (3 × 25 mL). The combined organic extracts were washed with distilled H_2O (2 × 40 mL), dried over Na_2SO_4, and evaporated to dryness, affording the uncontaminated ketone **8b**.

Yield: 1.36 g (97%); yellow, very viscous liquid (later a waxy solid, mp 46–48 °C); bp 85–90 °C (bath temp)/0.1 mbar.

IR (film): 2970, 1708 (s), 1474, 1457, 1364, 1203, 945, 741 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (t, ^3J = 7.0 Hz, 3 H, CH_3-β), 1.33 (s, 18 H), 2.85 (q, ^3J = 7.0 Hz, 2 H, CH_2-α), 7.22 and 7.35 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 7.16 (qt, ^1J = 127.4 Hz, ^2J = 3.7 Hz, CH_3-β), 32.74 [qsept, ^1J = 126.1 Hz, ^3J = 4.9 Hz, 2 × C(CH_3)$_3$], 37.11 [m, ^2J = 3.7 Hz, 2 × C(CH_3)$_3$], 42.73 (tq, ^1J = 124.1 Hz, ^2J = 4.4 Hz, CH_2-α), 125.73 (dd, ^1J = 158.0 Hz, ^3J = 7.4 Hz, C-3/-5), 127.56 (dm, ^1J = 160.6 Hz, C-4), 139.76 (td, ^3J = 6.6 Hz, ^4J = 1.5 Hz, C-1), 145.40 (m, ^3J = 3.7 Hz, C-2/-6), 212.31 (m, ^3J = ~ ^2J = 4.9 Hz, C=O); assigned through the following selective {^{1}H} decoupling experiments: {3-/4-/5-H} → C=O as a sextet with ^3J = ~ ^2J = 4.8 Hz, C-1 as a singlet with linewidth = 1.2 Hz ($|^3J|$ < 0.3 Hz unresolved); {CH_2-α} → CH_3-β as a sharp quartet with ^1J = 127 Hz; {CH_3-β} → CH_2-α as a sharp triplet with ^1J = 124.1 Hz, C=O as a triple-triplet with ^2J = 4.8 Hz and ^4J = ~1.1 Hz.

Anal. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.98; H, 10.84.

Diethyl α-(2,6-Di-*tert*-butylphenyl)vinyl Phosphate (10a)

2,6-Di-*tert*-butyl acetophenone (**8a**; 11.24 g, 48.37 mmol) in anhydrous THF (225 mL) was stirred magnetically in a dry Schlenk flask (500 mL) under argon gas and cooled to –60 °C. The yellow solution turned red and the internal temperature rose to –30 °C on addition of *n*-BuLi (2.4 M in hexane, 30.25 mL, 72.6 mmol) within 5 min. After further stirring for 5 min, $ClPO(OEt)_2$ (13.94 mL, 96.68 mmol) was added at –30 °C. The mixture was warmed to r.t. and poured into aq NaOH (1 M, 200 mL). The aqueous layer was shaken with Et_2O (2 × 100 mL) and the combined three organic layers were washed with distilled H_2O (3 × 50 mL), dried over $MgSO_4$, and concentrated to give a yellow liquid containing **10a** and residual $ClPO(OEt)_2$. Chromatography in a column (diameter 35 mm) of silica gel (63–200 mesh; 60 Å; 200 g) with low-boiling PE (500 mL) and then PE–Et_2O (4:1, 300 mL) removed part of the contamination. The elution rate had to be decreased very much on increasing the Et_2O concentration, so as to avoid heating and breaking of the silica gel column. The almost pure product **10a** (14.90 g, 84%) was eluted with the next 100-mL portions of PE–Et_2O (4:1, then 2:1) and Et_2O, followed by other byproducts with additional Et_2O. The analytically pure sample was obtained as a colorless oil through rechromatography.

IR (film): 2967, 2912, 1647, 1364, 1274, 1256, 1056, 1033, 993 (vs), 807 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 [td, $^3J_{HH}$ = 7.0 Hz, $^4J_{PH}$ = 1.1 Hz, 6 H, 2 × POC(CH_3)], 1.49 (s, 18 H), ~4.19 and ~4.23 (2 × m, 4 H, diastereotopic H of 2 × $POCH_2$ groups, including $^3J_{PH}$), 4.80 (dd, $^2J_{HH}$ = 2.8 Hz, $^4J_{PH}$ = 1.7 Hz, 1 H, 1 β-H *syn* to aryl), 5.42 (dd, $^2J_{HH}$ = 2.8 Hz, $^4J_{PH}$ = 0.5 Hz, 1 H, 1 β-H *anti* to aryl), 7.23 and 7.42 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 16.08 (qtd, $^1J_{CH}$ = 127.5 Hz, $^2J_{CH}$ = 2.7 Hz, $^3J_{CP}$ = 7.2 Hz, 2 × POCCH_3), 33.0 [qsept, $^1J_{CH}$ = 126 Hz, $^3J_{CH}$ = 4.8 Hz, 2 × C(CH_3)$_3$], 37.51 [m, $^2J_{CH}$ = 3.8 Hz, 2 × C(CH_3)$_3$], 64.26 (tqd, $^1J_{CH}$ = 148.5 Hz, $^2J_{CH}$ = 4.5 Hz, $^2J_{CP}$ = 6.2 Hz, 2 × $POCH_2$), 104.04 (td, $^1J_{CH}$ = 161.5 Hz, $^3J_{CP}$ = 2.2 Hz, olefinic CH_2-β), 125.34 (dm, $^1J_{CH}$ = ~158 Hz, C-3/-5), 128.46 (dm, $^1J_{CH}$ = ~159 Hz, C-4), 133.62 (m from $^3J_{CP}$ = 10.6 Hz and several differing $^3J_{CH}$, C-1), 150.36 (app. octet, $^3J_{CH}$ = 3.6 Hz, C-2/-6), 151.94 (td, $^2J_{CH}$ = 6.0 Hz, $^2J_{CP}$ = 8.9 Hz, C-α).

Anal. Calcd for $C_{20}H_{33}PO_4$: C, 65.20; H, 9.03. Found: C, 65.00; H, 8.87.

Diethyl 1-(2,6-Di-*tert*-butylphenyl)-1-propenyl Phosphate (10b)

In a procedure similar to that used for **10a**, 2,6-di-*tert*-butylpropiophenone (**8b**) was treated with *n*-BuLi (1.9 equiv) and $ClPO(OEt)_2$ (2 equiv) to give the enol phosphate **10b** (63–70% after chromatography as above).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (d, $^3J_{HH}$ = 7.1 Hz, 3 H, CH_3-γ), 1.34 [td, $^3J_{HH}$ = 7.1 Hz, $^4J_{PH}$ = 1.1 Hz, 6 H, 2 × POC(CH_3)], 1.45 (s, 18 H), ~4.18 and ~4.21 (2 m, 4 H, diastereotopic H of 2 × $POCH_2$ groups, including $^3J_{PH}$), 5.60 (qd, $^3J_{HH}$ = 7.1 Hz, $^4J_{PH}$ = 0.7 Hz,[25] 1 H, 1 β-H anti to aryl), 7.24 and 7.43 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 15.39 (qd, $^1J_{CH}$ = 127.3 Hz, $^2J_{CH}$ = 1.4 Hz, CH_3-γ), 16.11 (qtd, $^1J_{CH}$ = 127.3 Hz, $^2J_{CH}$ = 2.6 Hz, $^3J_{CP}$ = 7.2 Hz, 2 × POCCH_3), 33.00 [qsept, $^1J_{CH}$ = 126 Hz, $^3J_{CH}$ = 4.9 Hz, 2 × C(CH_3)$_3$], 37.70 [m, $^2J_{CH}$ = ~3.7 Hz, 2 × C(CH_3)$_3$]), 64.07 (tqd, $^1J_{CH}$ = 148 Hz, $^2J_{CH}$ = 4.5 Hz, $^2J_{CP}$ = 6.2 Hz, 2 × $POCH_2$), 111.32 (dqd, $^1J_{CH}$ = 154.1 Hz, $^2J_{CH}$ = 7.1 Hz, $^3J_{CP}$ = 2.2 Hz, olefinic CH-β), 125.81 (dm, $^1J_{CH}$ = ~157 Hz, C-3/-5), 128.34 (dm, $^1J_{CH}$ = ~158 Hz, C-4), 130.80 (m from $^3J_{CP}$ = 10.6 Hz and several differing $^3J_{CH}$, C-1), 146.39 (unresolved, includes d, $^2J_{CH}$ = 6.0 Hz and d, $^2J_{CP}$ = 9.4 Hz, C-α), 150.73 (unresolved, includes d, $^3J_{CH}$ = 7.0 Hz to 4-H, C-2/-6); assigned through selective {^{1}H} decoupling experiments as follows: {3-/4-/5-H} → C-1 as a dd of $^3J_{CP}$ and $^3J_{CH}$ = 6.2 Hz;[25] {all CH_3} → CH-β as a dd ($^1J_{CH}$, $^3J_{CP}$), C-α as a dd ($^2J_{CH}$ = 6.0 Hz, $^2J_{CP}$), C-2/-6 as a d ($^3J_{CH}$ = 7.0 Hz), and $POCH_2$ as a td ($^1J_{CH}$, $^2J_{CP}$).

Anal. Calcd for $C_{21}H_{35}PO_4$: C, 65.95; H, 9.22. Found: C, 66.21; H, 9.23.

2,6-Di-*tert*-butylphenylacetylene (11a)

Anhydrous *t*-BuOMe (50 mL) in a dried Schlenk flask (500 mL) under argon gas was stirred magnetically during the addition of the sticky oil **10a** (14.49 g, 39.32 mmol) together with further *t*-BuOMe (150 mL). After complete dissolution and subsequent cooling to –70 °C, *t*-BuLi (1.7 M in hexane, 62.5 mL, 106.2 mmol) was added dropwise with stirring. The resulting red solution was stirred for 10 min at –70 °C and for 15 min at r.t., then poured onto iced H_2O (500

mL). The aqueous layer was shaken with Et_2O (2 × 200 mL), and the combined organic layers were washed with distilled H_2O until neutral, dried over $MgSO_4$, and evaporated to give a reddish-brown liquid (8.16 g) that was purified by chromatography on a column (diameter 35 mm) of silica gel (63–200 mesh; 60 Å; 92 g) with low-boiling PE: The first 200 mL eluted part of the hydrocarbon contaminations, followed by 220 mL with the pure product **11a** that crystallized immediately after concentration.

Yield: 5.73 g (68%); mp 39–40.5 °C (EtOH).

IR (KBr): 3264 (sharp, ≡C–H), 2963, 2912, 2870, 1584 (w), 1463, 1362, 1258, 754 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.56 (s, 18 H), 3.81 (s, 1 H, ≡C*H*), 7.20 and 7.29 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 30.32 [qsept, ^1J = 126 Hz, ^3J = 4.8 Hz, 2 × C(*C*H_3)$_3$], 36.32 [m, ^2J = 3.8 Hz, 2 × *C*(CH$_3$)$_3$], 85.91 (d, ^2J = 48.8 Hz, *C*≡CH), 92.47 (d, ^1J = 250.0 Hz, C≡*C*H), 119.43 (m, C-1), 123.60 (sharp dd, X-part of AA′X, ^1J = 159.1 Hz, ^3J = 7.6 Hz, C-3/-5), 128.03 (sharp d, ^1J = 159.8 Hz, C-4), 154.54 (m, C-2/-6).

Anal. Calcd for $C_{16}H_{22}$: C, 89.66; H, 10.35. Found: C, 89.50; H, 10.35.

1-(2,6-Di-*tert*-butylphenyl)-1-propyne (11b)

The pure enol phosphate **10b** (1.61 g, 4.21 mmol) dissolved very slowly in anhydrous *t*-BuOMe (30 mL) on magnetic stirring in a Schlenk flask (100 mL) under argon gas. The pale-yellow solution was cooled to –70 °C with stirring and turned dark-red during the dropwise addition of *t*-BuLi (1.7 M in hexane, 6.20 mL, 10.5 mmol). After further stirring for 15 min at –70 °C and for 15 min at r.t., the contents of the flask were poured onto iced H_2O (100 mL) and Et_2O (30 mL). The aqueous layer was shaken with Et_2O (2 × 50 mL), and the combined organic extracts were washed with distilled H_2O until neutral, dried over $MgSO_4$, and evaporated to dryness, affording propyne **11b** (849 mg, 88%; mp 83–88.5 °C). The analytically pure sample (white needles) had mp 90–92 °C (2 × from MeOH); bp 85–90 °C (bath temp)/0.15 mbar.

IR (KBr): 2959, 2912, 2870, 1481 (w), 1416, 1362, 1256, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.53 (s, 18 H), 2.12 (s, 3 H, CH_3-γ), 7.13 and 7.26 (arom. AB_2 system, ^3J = 8.0 Hz, 3 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 4.90 (sharp q, ^1J = 130.8 Hz, CH_3-γ), 30.23 [qsept, ^1J = 125.6 Hz, ^3J = 4.9 Hz, 2 × C(*C*H$_3$)$_3$], 36.27 [m, ^2J = 3.7 Hz, 2 × *C*(CH$_3$)$_3$], 82.17 (q, ^3J = 4.8 Hz,[26,27] *C*≡CCH$_3$), 99.69 (sharp q, ^2J = 10.8 Hz,[26,27] C≡*C*CH$_3$), 121.25 (tdq, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^4J = 1.9 Hz, C-1), 123.43 (dd, ^1J = 158.5 Hz, ^3J = 7.5 Hz, C-3/-5), 126.72 (sharp d, ^1J = 160.0 Hz, C-4), 153.16 (unresolved m, containing d ^3J = 7.3 Hz, C-2/-6); assigned through the following selective {^{1}H} decoupling experiments: {3-/4-/5-H} → C-1 as a quartet (^4J = 1.9 Hz to CH$_3$-γ); {C(C*H*$_3$)$_3$} → C-2/-6 as a doublet (^3J = 7.3 Hz to 4-H), *C*(CH$_3$)$_3$ as the X-part of AA′X with |^3J+^5J| = 3.8 Hz to 3-H and 5-H; {CH$_3$-γ} → C-α as a singlet, C-β as a singlet, C-1 as a triple doublet (^3J to 3-/5-H and ^4J = 1.5 Hz to 4-H).

Anal. Calcd for $C_{17}H_{24}$: C, 89.41; H, 10.59. Found: C, 89.52; H, 10.87.

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