Reaction of 2,6-dibenzylidenecyclohexanone with phosphorus pentachloride: triple functionalization of the isosemiquinoid system

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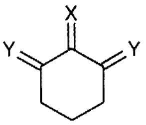
The reaction of 2,6-dibenzylidenecyclohexanone with PCl_5 occurs *via* the sequential stages of desoxychlorination and substitutional phosphorylation to form (after oxidation, methoxylation, and hydrolysis on the surface of the chromatographic SiO_2 adsorbent) organophosphorus products of the 1-(α-chloro-, α-hydroxy-, or α-alkoxy)benzyl-2-chloro-3-(α-(dimethylphosphoryl)benzylidene)cyclohex-1-ene series.

Key words: dienones, phosphorylation, desoxychlorination, methoxylation; hydrolysis, phosphorus(v) derivatives, solid-phase functionalization on the surface of chromatographic adsorbents.

The previous study of transformations of isosemiquinoid systems (**1**, X = O, Y = CHPh) has shown a possibility of single (compound **2**)[1] and double (compound **3**) functionalization of 2,6-dibenzylidenecyclohexanone (**4**) under the action of Na_2PdCl_4/Na_2CO_3 in MeOH. A nucleophile (Nu = OMe) enters the *exo*-unsaturated position accompanied by the oxidation of one or two allyl CH_2 fragments and removal of double bonds to the ring (in the latter case, the reaction is accompanied by aromatization of intermediate product **3**).



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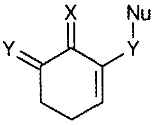

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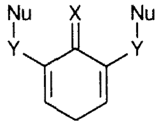

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On the other hand, it has previously[2] been shown that di- and trialkyl phosphites actively react with dienone **4** as nucleophiles by C-attack of the benzylidene atom to form phosphorane products as well as dialkyl or cyclic 2-(6-benzylidenecyclohexanone)benzyl phosphonates.

In this work, the direction of the attack of dienone **4** is found to change basically on going to electrophilic phosphorylating agent PCl_5: it is directed to the oxygen atom (*cf.* reactions of PCl_5 with other ketones[3–7]). Subsequent treatment of the reaction mixture with SO_2 and MeONa and its chromatography on SiO_2 results in the triple functionalization of molecule **4** to form organophosphorus products **5**—**7**. In addition, individual compound **8a** and a mixture of compounds **8b,c** (2 : 1 ratio) were isolated from the reaction mixture. The composition and structure of the products were confirmed by the elemental analysis and NMR, IR, and mass spectrometry data.

Formation of products **5**—**7** can be presented by the sequential desoxychlorination of dienone **4** to dichlorodiene, its substitutional phosphorylation, complete or partial methoxylation, and interphase hydrolysis on the SiO_2 surface.*

The characteristic general property of compounds **5**—**7** is the existence of two doublets of diastereotopic methoxyphosphoryl groups (A and B), multiplets of 6 protons of the central ring (1—3 ppm), singlet of the benzyl proton (6—7 ppm), and multiplet of 10 phenyl protons (7—8 ppm) in the ^{1}H NMR spectra. The mass spectra of compounds **5**—**7** contain the same peaks of the monochloro-containing ion at *m/z* 311/313 corresponding to the elimination of the nonphosphorylated

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* Compare with other examples of the use of chromatographic adsorbents for various chemical transformations of separated substances rather than for separation.[8,9]

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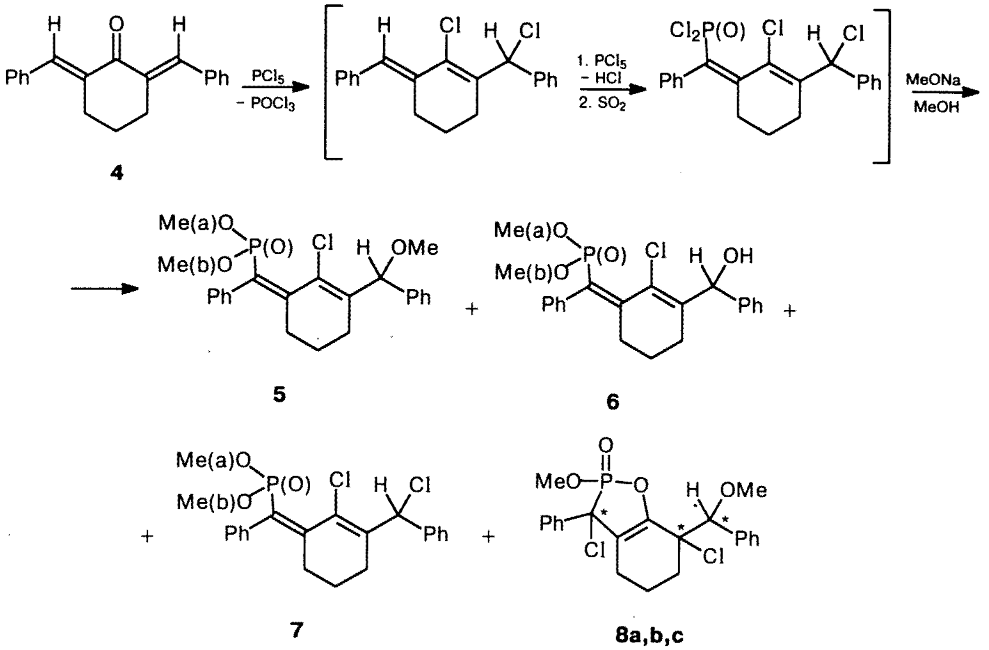
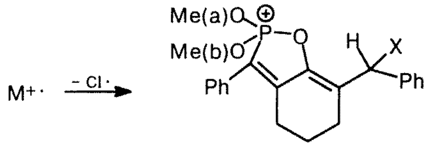
Scheme 1



benzyl fragment and ions of these fragments and the peaks of phosphonium ions $[M—Cl]^+$ with the maximum intensities.



The study of the structure and mechanism of formation of compounds **8a—c** will be published elsewhere.

Experimental

NMR spectra were recorded on Bruker WP-200SY (200 MHz) and Bruker WM-250 (250 MHz) instruments in $CDCl_3$. IR spectra of pure compounds and suspensions in Vaseline oil were recorded on a UR-20 instrument, and mass spectra were recorded on an AEI MS-30 mass spectrometer (70 eV). Silica gel and silica plates (Chemapol) were used for chromatography. Dienone **4** was prepared by the known procedure.[10] PCl_5 was purified by sublimation *in vacuo*.

Reaction of 2,6-dibenzylidenecyclohexanone (4) with PCl_5. An aqueous solution of dienone **4** (0.98 g, 3.6 mmol) in 16 mL of anhydrous C_6H_6 was added dropwise to a solution of PCl_5 (4.5 g, 21.6 mmol) in 40 mL of anhydrous C_6H_6 in an argon flow with magnetic stirring for 4 h. The mixture was kept for 45 h, 3 L of SO_2 was bubbled through, and the solution was evaporated *in vacuo* at 50 °C (1 Torr). The dry residue was dissolved in anhydrous Et_2O (20 mL) and poured with stirring into a solution of MeONa prepared by dissolution of sodium metal (1.4 g, 60 mmol) in anhydrous MeOH (90 mL). The mixture was stirred for 1.5 h at 20 °C, neutralized with an aqueous solution of NH_4Cl, and extracted with Et_2O (10×50 mL). The extract was dried over $MgSO_4$ and evaporated. The dry residue (0.56 g) was chromatographed (TLC) on silica gel Silpearl 029 (C_6H_6—EtOH (19 : 1) mixture as the eluent). The fraction with $R_f = 0.17$ was collected and repeatedly separated using a C_6H_6—Et_2O (1 : 1) mixture as the eluent. Product **6** (R_f = 0.2) was obtained. Individual compounds **5** (R_f = 0.35), **7** (R_f = 0.4), and **8a** (R_f = 0.45) and a mixture of compounds **8b,c** (2 : 1) (R_f = 0.55), which we failed to separate, were isolated by chromatography from the mixture of compounds **5** and **7** (R_f = 0.35 to 0.4).

1-(α-Methoxybenzyl)-2-chloro-3-(α-(dimethylphosphoryl)-benzylidene)cyclohex-1-ene (5) was obtained as light-yellow oil (8 mg, 5.2 % yield). ^{1}H NMR, δ: 1.45—1.78 (m, 2 H, CH_2(5), $J_{a—e}$ = 12.3 Hz); 2.0—2.2 (m, 2 H, CH_2(4)); 2.02 (dt, 1 H, CH_2(6), $J_{a—e}$ = 17.5 Hz, $J_{6—5}$ = 6.0 Hz); 2.37 (dt, 1 H, CH_2(6), $J_{a—e}$ = 17.5 Hz, $J_{6—5}$ = 6.5 Hz); 3.44 (s, 3 H, MeOC); 3.48 (d, 3 H, (A)MeOP, $J_{H—P}$ = 11.0 Hz); 3.53 (d, 3 H, (B)MeOP, $J_{H—P}$ = 10.8 Hz); 6.74 (s, 1 H, CH(a)); 7.15—7.48 (m, 10 H, Ph). ^{31}P NMR, δ: 16.5 (m, $J_{P—H}$ = 11 Hz). Mass spectrum, *m/z*, (I_{rel} (%)): 432 $[M^+]$ (0.01), 397 [M—Cl] (100), 313/311 [M—PhCHOMe] (4.5+17), 121 [PhCHOMe] (11), 105 $[PhCO^+]$ (30), 432 $[M^+]$ (0.01).

1-(α-Hydroxybenzyl)-2-chloro-3-(α-(dimethylphosphoryl)-benzylidene)cyclohex-1-ene (6) was obtained from an Et_2O—C_5H_{12} mixture after additional purification by crystallization (59 mg, 3.9 %, white crystals, m.p. 152—157 °C). Found (%): C, 62.72; H, 6.08; Cl, 9.24; P, 7.66. $C_{22}H_{24}ClO_4P$. Calculated (%): C, 63.08; H, 5.73; Cl, 8.48; P, 7.41. IR, ν/cm^{-1}: 3300 (O—H); 1240 (P=O); 1050 (P—O). ^{1}H NMR, δ: 1.45—1.80 (m, 2 H, CH_2(5), $J_{a—e}$ = 13 Hz); 1.95—2.25 (m, 3 H, CH_2(4) and CH_2(6)); 2.48 (dt, 1 H, CH_2(6), $J_{a—e}$ = 18 Hz, $J_{6—5}$ = 6.5 Hz); 3.44 (d, 3 H, (A)MeOP, $J_{H—P}$ = 10.8 Hz); 3.62 (d, 3 H, (B)MeOP, $J_{H—P}$ = 11.3 Hz); 4.73 (br.s, 1 H, OH); 6.25 (s, 1 H, CH(a)); 7.10—7.53 (m, 10 H, Ph). ^{31}P NMR, δ: 16.5 (m, J_{P-H} = 11 Hz). Mass spectrum, *m/z* (I_{rel} (%)): 420/418 [M^+] (0.8), 383 [M—Cl] (100), 313/311 [M—PhC(OH)H] (7+17), 105 [$PhCO^+$] (15).

1-(α-Chlorobenzyl)-2-chloro-3-(α-(dimethylphosphoryl)-benzylidene)cyclohex-1-ene (7) was obtained as a light-yellow oil (7 mg, 0.5 %). ^{1}H NMR, δ: 1.45—1.80 (m, 2 H, CH_2(5)), 2.02 (dt, 1 H, CH_2(6), J_{a-e} = 17.8 Hz; J_{6-5} = 6.5 Hz); 2.10 (m, 2 H, CH_2(4)); 2.40 (dt, 1 H, CH_2(6), J_{a-e} = 17.8 Hz, J_{6-5} = 6.5 Hz); 3.48 (d, 3 H, (A)MeOP, J_{H-P} = 10.8 Hz); 3.53 (d, 3 H, (B)MeOP, J_{H-P} = 10.8 Hz); 5.85 (s, 1 H, CH(a)); 7.15—7.52 (m, 10 H, Ph).

Compound 8a was purified by crystallization from an Et_2O—C_5H_{12} mixture (44 mg, 2.7 %, white crystals, m.p. 155.5—157 °C). Found (%): C, 58.35; H, 5.19; Cl, 15.23; P, 6.88. $C_{22}H_{23}Cl_2O_4P$. Calculated (%): C, 58.29; H, 5.11; Cl, 15.64; P, 6.83. IR, ν/cm^{-1}: 1260 (P=H); 1050 (P—O). ^{1}H NMR, δ: 1.70—2.40 (m, 4 H, (CH_2)); 2.65—2.95 (m, 2 H, CH_2); 3.29 (s, 3 H, MeOC); 3.42 (d, 3 H, MeOP); 5.65 (s, 1 H, CH(a)); 7.20—7.63 (m, 10 H, Ph). ^{31}P NMR, δ: 33.0 (q, J_{P-H} = 11 Hz). Mass spectrum, *m/z* (I_{rel} (%)): 452/454/456 (traces) [M^+], 416/418 [M—HCl] (87), 415/417 [M—HCl—H] (27), 381 [M—HCl—Cl] (16), 366 [M—HCl—Cl—Me] (11), 350 [M—HCl—Cl—MeO] (68), 151 ? (80), 121 [PhCHOMe] (100), 105 [PhCO] (20), 91 [C_7H_7] (33).

A mixture of compounds 8b and 8c (2 : 1) was additionally purified by crystallization from an Et_2O—C_5H_{12} mixture to give white crystals (54 mg, 3.3 %, m.p. 161—166 °C). Found (%): C, 58.26; H, 5.16; Cl, 15.38; P, 6.80. $C_{22}H_{23}Cl_2O_4P$. Calculated (%): C, 58.29; H, 5.11; Cl, 15.64; P, 6.83. IR, ν/cm^{-1}: 1255 (P=O); 1050 (P—O). ^{1}H NMR, δ: compound **8b** 1.55—2.40 (m, 4 H, $(CH_2)_2$); 2.60—2.95 (m, 2 H, CH_2); 3.20 (d, 3 H, MeOC, *J* = 0.8 Hz); 3.53 (d.d, 3 H, MeOP, J_{H-P} = 11 Hz, *J* = 1.2 Hz); 5.57 (d, 1 H, CH(a), *J* = 0.7 Hz); 7.20—7.63 (m, 10 H, Ph); compound **8c** 1.55—2.40 (m, 4 H, (CH_2)); 2.60—2.95 (m, 2 H, CH_2); 3.25 (d, 3 H, MeOC, *J* = 0.8 Hz); 3.83 (d.d, 3 H, MeOP, J_{H-P} = 11.0 Hz, *J* = 1.2 Hz); 5.69 (d, 1 H, CH(a), *J* = 0.6 Hz); 7.20—7.63 (m, 10 H, Ph). ^{31}P NMR, δ: compound **8b** 32.1 (q, J_{P-H} = 11 Hz); compound **8c** 33.1 (q, J_{P-H} = 11 Hz). Mass spectrum, *m/z* (I_{rel} (%)): 452/454/456 [M^+] (traces), 417/419 [M—Cl] (75), 416/418 [M—HCl] (23), 382 [M—2Cl] (12), 367 [M—2Cl—Me] (14), 351 [M—2Cl—OMe] (34), 350 [M—2Cl—MeOH] (8), 151? (100), 121 [PhCHOMe] (57), 105 [PhCO] (12), 91 [C_7H_7] (12).

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