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LETTERS TO THE EDITOR

Synthesis of Cyclohexa-1,4-dienephosphonoyl Dichlorides

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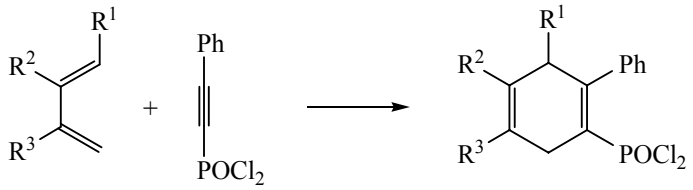
Cyclohexadiene fragment is a part of many natural compounds and synthetic drugs. Cyclohexadienes can be subjected to aromatization; therefore they can be used as reducing agents in biochemical processes [1, 2].

1,4-Cyclohexadiene and similar hydrocarbons can be prepared via the Birch reduction of aromatic hydrocarbons with metals in liquid ammonia [3]. However, this approach is limitedly applicable in the cases of functionalized derivatives. One of the convenient methods to prepare 1,4-cyclohexadiene derivatives is cycloaddition of conjugated dienes to the acetylenes containing acceptor substituents (the Diels–Alder reaction). The Diels–Alder reaction of dimethyl chloroacetylenephosphonate and tetramethyl acetylenediphosphonate with some dienes leads to formation of the phosphorus-containing 1,4-cyclohexadiene derivatives [4–6].

Aiming to obtain new phosphorus-containing cyclohexanes, we performed the Diels–Alder reaction between phenylacetylenephosphonic acid dichloride **II** and several dienes: 1,3- and 2,3-dimethyl-1,3-diene, isoprene and piperylene (**Ia**–**Id**).



Ia–**Ic** **II** **IIIa**–**IIIc**

R^1 = H, R^2 = R^3 = Me (**a**); R^1 = R^3 = H, R^2 = Me (**b**); R^1 = Me, R^2 = R^3 = H (**c**); R^1 = R^3 = Me, R^2 = H (**d**).

The reactions resulted in the corresponding substituted 1,4-cyclohexadienephosphonoyl dichlorides **IIIa**–**IIId**. The reactions of phenylacetylenephosphonic acid dichloride **II** with 1,3-dimethyl-1,3-diene, isoprene, and piperilene proceeded with low regioselectivity to give isomeric mixtures of methyl-substituted 1,4-cyclohexadienephosphonoyl dichlorides **IIIb**–**IIId** and **IVa**–**IVd**.

The reactions occurred under harsh conditions, at 140–160°C in the absence of any solvent, to form the corresponding adducts **IIIa**–**IIId**. Compounds **IIIb**–**IIId** were isolated as mixtures of isomers. The resulting compounds were viscous liquids, which were isolated by vacuum distillation. They were unstable and partially aromatized during storage.

The structures of the new phosphorus-containing carbocyclic compounds **IIIa**–**IIId** were confirmed by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy method.

General procedure for preparation of III and IV. A mixture of 0.053 mol of phenylacetylenephosphonic acid dichloride, 0.06 mol of the corresponding diene **IIa**–**IId**, and 3.5 mg of hydroquinone was placed into an ampoule. The ampoule was flushed with argon and sealed. The mixture was heated at 140–

[†] Deseased.

160°C during 10 h. The reaction products were isolated by distillation under high vacuum.

4,5-Dimethyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IIIa). Yield 78%, yellowish viscous liquid, bp 150–154°C (1 mm Hg). ^{1}H NMR spectrum, δ, ppm: 1.78 s (3H, CH_3C^4), 1.89 s (3H, CH_3C^5), 3.12 and 3.14 (2H, $C^6H^AH^B$, AB-system, $^2J_{HH}$ = $^3J_{HP}$ = 8.0 Hz), 3.21 and 3.26 (2H, $C^3H^AH^B$, AB-system, $^2J_{HH}$ 8.0 Hz), 7.34 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.47 t (1H, $C^{4'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.53 d (2H, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.85 ($\underline{CH_3}C^4$), 18.25 ($\underline{CH_3}C^5$), 34.85 d (C^3H_2, $^3J_{CP}$ 15.5 Hz), 43.65 d (C^6H_2, $^2J_{CP}$ 19.5 Hz), 122.09 (C^{meta}), 122.27 (C^{meta}), 125.46 (C^4), 127.13 (C^5), 127.23 d (C^1P, $^1J_{CP}$ 185.1 Hz), 128.67 (C^{para}), 129.04 (C^{ortho}), 140.03 d (C^{ipso}, $^3J_{CP}$ 9.4 Hz), 155.85 d (C^2, $^2J_{CP}$ 10.1 Hz). ^{31}P NMR spectrum: δ_P 33.99 ppm.

6-Methyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IIIb). Yield 73% (along with the isomer **IVb**), yellowish viscous liquid, bp 146–150°C (1 mm Hg), content in the mixture was 75%. ^{1}H NMR spectrum, δ, ppm: 0.99 d (3H, CH_3, $^3J_{HH}$ 8.0 Hz), 3.10–3.17 m (2H, C^3H_2), 3.18–3.23 m (1H, C^6H), 5.72 d (1H, C^5H, $^3J_{HH}$ 8.0 Hz), 5.81 t (1H, C^4H, $^3J_{HH}$ 8.0 Hz), 7.37 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.47 t (1H, $C^{4'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.53 d (2H, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.16 (CH_3), 28.38 d (C^3H_2, $^3J_{CP}$ 17.1 Hz), 39.46 d (C^6H, $^2J_{CP}$ 18.1 Hz), 121.32 (C^{meta}), 121.46 (C^{meta}), 127.33 d (C^1P, $^1J_{CP}$ 181.1 Hz), 128.01 br (C^{para}, C^4), 129.06 (C^{ortho}), 129.36 d (C^5 8.01 Hz), 138.86 d (C^{ipso}, $^3J_{CP}$ 10.1 Hz), 160.06 d (C^2, $^2J_{CP}$ 8.5 Hz). ^{31}P NMR spectrum: δ_P 33.60 ppm.

3-Methyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IVb). Content in the mixture was of 25%. ^{1}H NMR spectrum, δ, ppm: 1.40 d (3H, CH_3, $^3J_{HH}$ 8.0 Hz), 3.25–3.29 m (2H, C^6H_2), 3.30–3.36 m (1H, C^3H), 5.77–5.81 m (1H, C^4H), 5.84–5.89 m (1H, C^5H), 7.38 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.47 t (1H, $C^{4'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.63 d (2H, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 22.83 (CH_3), 33.57 d (C^6H_2, J_{CP} 17.1 Hz), 37.08 d (C^3H, $^2J_{CP}$ 15.1 Hz), 127.67 (C^{para}), 127.93 d (C^1P, $^1J_{CP}$ 176.1 Hz), 128.78 (C^4), 128.40 (C^{meta}), 128.90 (C^{ortho}), 140.9 d (C^5, $^3J_{CP}$ 9.05 Hz), 155.73 (C^{ipso}, $^3J_{CP}$ 18.1 Hz), 156.14 d (C^2, $^2J_{CP}$ 10.1 Hz). ^{31}P NMR spectrum: δ_P 34.39 ppm.

5-Methyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IIIc). Yield 69% (along with the isomer **IVc**), yellowish viscous liquid, bp 144–148°C (1 mm Hg), content in the mixture was of 65%. ^{1}H NMR spectrum, δ, ppm: 1.87 s (3H, CH_3), 3.07 d (2H, C^3H_2, $^3J_{HH}$ 8.0 Hz), 3.25–3.35 m (2H, C^6H_2), 5.47–5.53 m (1H, C^4H), 7.28 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.38–7.44 m (3H, $C^{4'}H_{Ar}$, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$). ^{13}C NMR spectrum, δ_C, ppm: 22.80 (CH_3), 32.87 d (C^3H_2, $^3J_{CP}$ 15.3 Hz), 38.16 d (C^6H_2, $^2J_{CP}$ 19.4), 126.80 (C^1, $^1J_{CP}$ 187.3 Hz), 127.04 (C^{meta}), 128.28 (C^{para}), 128.38 (C^{ortho}), 129.89 (C^5), 130.32 (C^4), 140.23 (C^{ipso}, $^3J_{CP}$ 9.1 Hz), 155.66 (C^2, $^2J_{CP}$ 9.1 Hz). ^{31}P NMR spectrum: δ_P 33.49.

4-Methyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IVc). Content in the mixture was of 35%. ^{1}H NMR spectrum, δ, ppm: 1.78 s (3H, CH_3), 3.07 d (2H, C^3H_2, $^3J_{HH}$ 8.0 Hz), 3.25–3.35 m (2H, C^6H_2), 5.60–5.66 m (1H, C^4H), 7.27 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.38–7.44 m (3H, $C^{4'}H_{Ar}$, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$). ^{13}C NMR spectrum, δ_C, ppm: 22.29 (CH_3), 29.48 d (C^3, $^3J_{CP}$ 16.1 Hz), .61 (C^6, $^2J_{CP}$ 19.4 Hz), 127.01 (C^1, $^1J_{CP}$ 187.8 Hz), 127.04 (C^{meta}), 128.28 (C^{para}), 128.38 (C^{ortho}), 129.89 (C^4), 130.18 (C^5), 140.13 (C^{ipso}, $^3J_{CP}$ 10.0 Hz), 155.48 (C^2, $^2J_{CP}$ 10.0 Hz). ^{31}P NMR spectrum: δ_P 33.85 ppm.

3,5-Dimethyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IIId). Yield 76% (along with the isomer **IVd**), yellowish viscous liquid, bp 149–152°C (1 mm Hg), content in the mixture was of 35%. ^{1}H NMR spectrum, δ, ppm: 1.37 d (3H, C^3CH_3, $^3J_{HH}$ 8.5 Hz), 1.84 s (3H, C^5CH_3), 3.20 s (2H, C^6H), 3.27–3.31 m (1H, C^3H), 5.67 s (1H, C^4H), 7.35 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.42 t (1H, $C^{4'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.59 d (2H, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 22.76 ($C^5\underline{C}H_3$), 22.87 ($C^3\underline{C}H_3$), 33.04 d (C^6H_2, J_{CP} 17.5 Hz), 38.16 d (C^3H, $^3J_{CP}$ 15.0 Hz), 126.42 (C^{meta}), 126.33 d (C^1P, $^1J_{CP}$ 187.1 Hz), 128.40 (C^{para}), 129.79 (C^4), 128.93 (C^{ortho}), 129.16 d (C^5, $^3J_{CP}$ 8.5 Hz), 139.10 (C^{ipso}, $^3J_{CP}$ 17.5 Hz), 156.27 d (C^2, $^2J_{CP}$ 10.0 Hz). ^{31}P NMR spectrum: δ_P 33.76 ppm.

4,6-Dimethyl-2-phenylcyclohexa-1,4-dienephosphonoyl dichloride (IVd). Content in a mixture was of 35%. ^{1}H NMR spectrum, δ, ppm: 1.02 d (3H, C^6CH_3, $^3J_{HH}$ 8.0 Hz), 1.75 s (3H, C^4CH_3), 3.10 s (2H, C^3H), 3.25–3.34 m (1H, C^6H), 5.77 s (1H, C^5H), 7.29 t (2H, $C^{3'}H_{Ar}$, $C^{5'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.45 t (1H, $C^{4'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz), 7.57 d (2H, $C^{2'}H_{Ar}$, $C^{6'}H_{Ar}$, $^3J_{HH}$ 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.93 ($C^6\underline{C}H_3$), 22.35 ($C^4\underline{C}H_3$), 29.87 (C^3H_2, $^3J_{CP}$ 16.8 Hz), 39.07 d (C^6H, $^2J_{CP}$ 17.4 Hz), 127.11 (C^{meta}), 127.15 d (C^1P, $^1J_{CP}$ 186.8 Hz), 128.28 (C^{para}), 128.40 (C^{ortho}), 129.08 (C^4), 129.92 d (C^5, $^3J_{CP}$ 8.5 Hz), 140.19 (C^{ipso}, $^3J_{CP}$ 12.5 Hz),

160.07 d (C^2, $^2J_{CP}$ 8.5 Hz). ^{31}P NMR spectrum: δ_P 33.23 ppm.

The NMR spectra in $CDCl_3$ were registered with Bruker Avance 400 spectrometer operating at 400.13 (^1H), 100.61 (^{13}C) and 161.98 (^{31}P) MHz relative to internal HMDS (^1H) or 85% H_3PO_4 (^{31}P).

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