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Facile Synthesis of 2-Aminocyclobutenylphosphonates

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Abstract—The addition of various amines to diethyl 4-chlorobut-1-yn-1-ylphosphonate produced novel biologically potent substituted diethyl 2-aminocyclobut-1-en-1-ylphosphonates in 70–83% isolated yield. This regioselective reaction was carried out at room temperature in the absence of solvent and catalyst.

Keywords: vinylphosphonates, cyclobutenes, β-aminophosphonates, amine addition.

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Cyclobutene derivatives are of particular interest as organic units not only due to their intriguing molecular skeleton suggesting specific properties such as a high ring strain and consequent enhanced electrophilicity but also because of their reactivities and importance as intermediates in organic synthesis [1–3]. They undergo electrocyclic ring-opening reaction to produce highly electron-deficient 1,3-dienes [4], thermal aromatization [5], and other transformations [6–18]. In addition, cyclobutene derivatives have wide utility as biologically active compounds [19, 20]. For instance, they possess anti-inflammatory [21–23], herbicidal [24], and antitumor activity [25]. Moreover, they showed protective properties against UV radiation [26], and other useful properties [27].

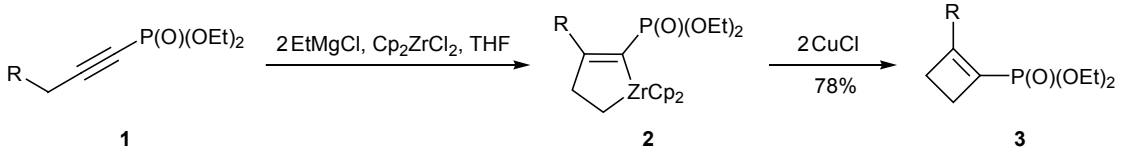
During the last few decades several methods have been developed for the preparation of polysubstituted cyclobutenes. For example, they can be obtained by photochemical [2+2]-cycloaddition of olefines and acetylenes to cyclic enones and unsaturated lactones [28–32], titanium-mediated intramolecular cyclization of bis-propargyl alcohols [33], reaction of dilithiated benzylacetylene with isothiocyanates [34], metallocupration of allenes and acetylenes [35], zirconium-mediated inter- or intramolecular cyclodimerization of alkynes [36], gold-catalyzed intermolecular reaction of terminal alkynes with alkenes [37], cycloalkylation reactions involving (4-halo-1-alkenyl)metals [38], intramolecular Wittig reaction of vinyl(triphenyl)phosphonium salt with dioxobutanoates [4], thermolysis–oxidation [39], and other reactions [40, 41].

Interestingly, the presence of a phosphonate group on the cyclobutene ring enhances its biological activity [42]. Despite that, not many methods have been yet reported for the synthesis of cyclobutenylphosphonates. Generally, they are produced from readily available halogenated cyclobutenes via Arbuzov reaction [43, 44] or by cyclizations of diazophosphonate intermediates [45–48].

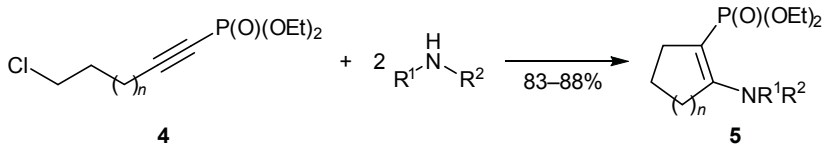
We previously synthesized cyclobutenylphosphonates by zirconation of 1-alkynylphosphonates, followed by treatment with copper(I) chloride (Scheme 1) [49]. In addition, cyclization reactions of ω-chloro-1-alkynylphosphonates with amines were also found to produce cyclic β-aminophosphonates as shown in Scheme 2 [50].

Being encouraged by these results, we focused on the reaction of amines with an alkynylphosphonate having a shorter alkynyl chain, in particular, with

Scheme 1.

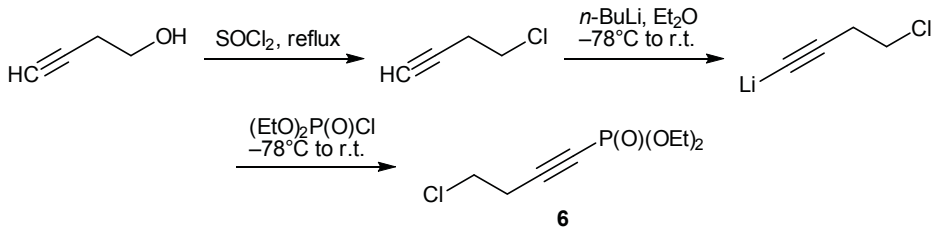


Scheme 2.

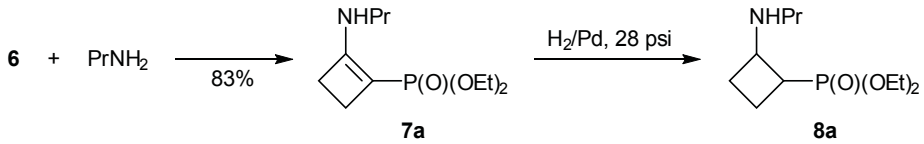


R^1, R^2 = H, Alk, Ar; n = 1, 2.

Scheme 3.



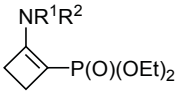
Scheme 4.



diethyl (4-chlorobut-1-yn-1-yl)phosphonate (**6**) which was successfully prepared by substituting the hydroxy group in but-3-yn-1-ol using thionyl chloride under reflux. The product was isolated by distillation, dissolved in diethyl ether, lithiated with *n*-BuLi, and reacted with diethyl chlorophosphate (Scheme 3).

We have developed an effective and facile method for the synthesis of novel cyclobutenes. 2-Aminocyclobutenylphosphonates were obtained by the addition of various amines to diethyl 4-chlorobut-1-yn-1-ylphosphonate (**6**). When the latter was allowed to react with propylamine at 25°C for 15 h, diethyl [2-(propylamino)cyclobut-1-en-1-yl]phosphonate (**7a**) was formed as the only product in 83% yield (Scheme 4). Likewise, other primary and secondary amines were reacted with phosphonate **6** under similar conditions to obtain 2-aminocyclobutenylphosphonates **7b**–**7i** which were isolated by silica gel column chromatography in good yields (70–83%; Table 1) and were characterized by NMR, GC/MS, and elemental analyses. The ^{1}H NMR spectra of **7a**–**7i** showed two broad triplets in the region δ 2.18–2.93 ppm along with vinylic carbon signals at δ_C 68.9–217.2 ppm in the ^{13}C NMR spectra. The phosphorus atom of **7** resonated in ^{31}P NMR spectra at δ_P ~30 ppm.

Table 1. Synthesis of diethyl 2-aminocyclobutenylphosphonates **7a**–**7i**



7a–**7i**

Compound no.	Amine	Yield,[a] %
7a	Propylamine	83
7b	Isopropylamine	81
7c	*tert*-Butylamine	80
7d	Benzylamine	75
7e	Aniline	73
7f	Methylamine[b]	80
7g	2-Phenylethylamine	78
7h	2-Aminoethanol	77
7i	Diisopropylamine	70

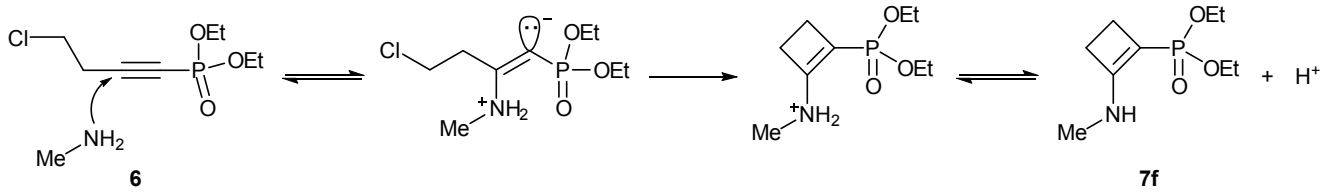
[a] Isolated yield (after silica gel chromatography); in all cases, the conversion was higher than 98% according to the GC/MS and ^{31}P NMR data.

[b] Methylamine was used as a 40% aqueous solution.

This process represents a general and facile one-pot method for the synthesis of novel oily 2-aminocyclobutenylphosphonates **7**. Compounds **7a**–**7i** are stable on exposure to air at room temperature and are soluble in most organic solvents. Apart from primary and secondary amines, the described cyclization is also tolerant to alkyl (**7a**–**7c**, **7f**, **7i**), aryl (**7d**, **7e**, **7g**), and hydroxy groups (**7h**) as shown in Table 1.

Compound **7a** was smoothly hydrogenated over Pd/C as a catalyst to afford cyclobutane derivative **8a** in a high yield. On the basis of our observations and

Scheme 5.



previous theoretical calculations, we presumed that the reaction proceeds by a stepwise mechanism where the first step involves initial addition of the amine to the triple bond to give zwitterionic intermediate, and the next steps involve cyclization followed by elimination of proton, leading to 2-aminocyclobut-1-en-1-ylphosphonates **7** [50] (Scheme 5).

In summary, novel biologically potent diethyl 2-aminocyclobut-1-en-1-ylphosphonates **7a**–**7i** were smoothly prepared by addition of amines to diethyl 4-chlorobut-1-yn-1-ylphosphonate. The reaction is facile, general, and selective, it requires neither solvent nor catalyst, and the products are formed in high yield. This makes the described reaction a convenient method for the synthesis of 2-aminocyclobutenylphosphonates with the phosphorus and nitrogen substituents linked to the neighboring double-bonded carbon atoms (β-aminophosphonates).

EXPERIMENTAL

The ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded from solutions in $CDCl_3$ on a Varian Mercury 300 spectrometer at 300, 75.5, and 121.4 MHz, respectively; the chemical shifts were measured relative to TMS (^{1}H, ^{13}C) and H_3PO_4. The mass spectra (EI) were recorded on an HP G1800A GCD GC/MS instrument using a 30-m methyl silicone column.

Diethyl (4-chlorobut-1-yn-1-yl)phosphonate (6) was prepared in our lab by refluxing but-3-yn-1-ol with thionyl chloride. The product, 4-chlorobut-1-yne, was isolated by distillation and dissolved in diethyl ether, the solution was cooled to –78°C, an equivalent amount of butyllithium was added, and the mixture was allowed to gradually warm up to room temperature. The mixture was then cooled again to –78°C, and an equivalent amount of diethyl phosphorochloridate was added. The reaction was quenched with 1 M aqueous HCl, and the product was extracted into diethyl ether, followed by evaporation of the solvent on a rotary evaporator and distillation of the residue under reduced pressure.

Diethyl [2-(propan-2-ylamino)cyclobut-1-en-1-yl]phosphonate (7a). Diethyl (4-chlorobut-1-yn-1-yl)-phosphonate (0.22 g, 1 mmol) was mixed with isopropylamine (0.07 g, 1.1 mmol) in a 10-mL round-bottom flask, and the mixture was stirred at 25°C for 15 h. The mixture was then washed with 0.1 N aqueous sodium hydroxide and extracted with methylene chloride (2×20 mL), the extract was dried over $MgSO_4$ and concentrated on a rotary evaporator, and the residue was purified by silica gel column chromatography (CH_2Cl_2–MeOH, 9 : 1). ^{1}H NMR spectrum, δ, ppm: 1.12 d [6H, J_{HH} = 6.3 Hz, CH(C**H**$_3$)$_2$], 1.26 t (6H, J_{HH} = 6.9 Hz, OCH$_2$C**H**$_3$), 2.63 br.t (2H, J_{HH} = 6.9 Hz, CH_2CH_2), 2.86 br.t (2H, J_{HH} = 7.2 Hz, CH_2CH_2), 2.92 m [1H, C**H**(CH$_3$)$_2$], 4.11 m (4H, OC**H**$_2$CH$_3$). ^{31}P NMR spectrum: δ_P 30.38 ppm. ^{13}C NMR spectrum, δ_C, ppm: 16.2 d ($^3J_{PC}$ = 6.2 Hz, OCH$_2$**C**H$_3$), 21.4 s [(**C**H$_3$)$_2$C)] 23.7 s (**C**H$_2$CP), 32.2 d ($^3J_{PC}$ = 5.8 Hz, **C**H$_2$CN), 42.8 s [**C**H(CH$_3$)$_2$], 48.8 d ($^2J_{PC}$ = 30.2 Hz, O**C**H$_2$CH$_3$), 72.9 d ($^1J_{PC}$ = 201.6 Hz, CP), 172.8 d ($^2J_{PC}$ = 20.1 Hz, CNH). Mass spectrum, *m*/*z* (I_{rel}, %): 247 (20.5), 232 (14.8), 218 (31.0), 207 (1.1), 155 (100), 144 (6.0), 104 (10.3), 91 (80.1), 77 (1.2), 65 (21.3), 41 (10.3). Found, %: C 53.58; H 9.11; N 5.50; P 12.38. $C_{11}H_{22}NO_3P$. Calculated, %: C 53.43; H 8.97; N 5.66; P 12.53.

Compounds **7b**–**7i** were synthesized in a similar way from compound **6** and the corresponding amine.

Diethyl [2-(propylamino)cyclobut-1-en-1-yl]-phosphonate (7b). ^{1}H NMR spectrum, δ, ppm: 0.84 t (3H, J_{HH} = 8.4 Hz, CH$_2$CH$_2$C**H**$_3$), 1.26 t (6H, J_{HH} = 7.5 Hz, OCH$_2$C**H**$_3$), 2.05 m (2H, C**H**$_2$CH$_3$), 2.40 br.t and 2.61 br.t (2H each, J_{HH} = 7.5 Hz, CH_2CH_2), 3.06 t (2H, J_{HH} = 6.5 Hz, NHC**H**$_2$), 4.00 m (4H, OC**H**$_2$CH$_3$). ^{31}P NMR spectrum: δ_P 28.83 ppm. ^{13}C NMR spectrum, δ_C, ppm: 11.44 s (CH$_2$**C**H$_3$), 15.9 d ($^3J_{PC}$ = 6.6 Hz, OCH$_2$**C**H$_3$), 20.3 s (**C**H$_2$CH$_3$), 20.5 s (CH_2CH_2), 43.9 s (CH_2N), 44.8 d ($^3J_{PC}$ = 33.5 Hz, **C**H$_2$CN), 60.2 d ($^2J_{PC}$ = 5.4 Hz, OCH_2), 73.0 d ($^1J_{PC}$ = 217.2 Hz, CP), 161.3 d ($^2J_{PC}$ = 21.2 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 247 (4.2), 232 (10.2), 207 (11.1), 158 (100), 144 (6.0), 133 (21.7), 104 (10.8), 85 (5.7), 43 (35.6). Found, %: C 53.66; H 9.06; N 5.54; P 12.39. $C_{11}H_{22}NO_3P$. Calculated, %: C 53.43; H 8.97; N 5.66; P 12.53.

Diethyl [2-(*tert*-butylamino)cyclobut-1-en-1-yl]-phosphonate (7c). ^{1}H NMR spectrum, δ, ppm: 1.20 s (9H, *t*-Bu), 1.26 t (6H, J_{HH} = 6.7 Hz, $OCH_2C\mathbf{H}_3$), 2.74 br.t (2H, J_{HH} = 6.5 Hz, CH_2CH_2), 2.93 br.t (2H, J_{HH} = 6.3 Hz, CH_2CH_2), 3.96 m (4H, $OC\mathbf{H}_2CH_3$). ^{31}P NMR spectrum: δ_P 27.44 ppm. ^{13}C NMR spectrum, δ_C, ppm: 16.3 d ($^3J_{PC}$ = 6.0 Hz, $OCH_2\mathbf{C}H_3$), 23.4 s (CH_2CH_2), 28.9 s [$C(\mathbf{C}H_3)$], 32.4 d ($^3J_{PC}$ = 5.7 Hz, $\mathbf{C}H_2CN$), 50.4 s [$\mathbf{C}(CH_3)$], 61.3 d ($^2J_{PC}$ = 4.6 Hz, $O\mathbf{C}H_2CH_3$), 72.2 d ($^1J_{PC}$ = 215.6 Hz, CP), 159.8 d ($^2J_{PC}$ = 19.6 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 261 (34.5), 246 (66.5), 233 (6.7), 218 (17.6), 206 (50.7), 178 (22.7), 160 (31.7), 132 (35.6), 108 (29.3), 95 (55.9), 69 (100), 57 (29.9). Found, %: C 54.97; H 9.17; N 5.51; P 11.98. $C_{12}H_{24}NO_3P$. Calculated, %: C 55.16; H 9.26; N 5.36; P 11.85.

Diethyl [2-(benzylamino)cyclobut-1-en-1-yl]-phosphonate (7d). ^{1}H NMR spectrum, δ, ppm: 1.26 t (6H, J_{HH} = 6.2 Hz, $OCH_2C\mathbf{H}_3$), 2.82 br.t and 2.92 br.t (2H each, J_{HH} = 6.9 Hz, CH_2CH_2), 3.89 s (2H, $C\mathbf{H}_2Ph$), 3.96 m (4H, $OC\mathbf{H}_2CH_3$), 7.27–7.34 m (5H, Ph). ^{31}P NMR spectrum: δ_P 28.1 ppm. ^{13}C NMR spectrum, δ_C, ppm: 15.9 d ($^3J_{PC}$ = 6.2 Hz, $OCH_2\mathbf{C}H_3$), 21.8 s (CH_2CH_2), 45.6 s ($\mathbf{C}H_2Ph$), 47.1 d ($^3J_{PC}$ = 31.7 Hz, CH_2CH_2), 60.2 d ($^2J_{PC}$ = 7.8 Hz, $O\mathbf{C}H_2CH_3$), 71.8 d ($^1J_{PC}$ = 215.6 Hz, CP), 126.6 (C_{arom}), 127.3 (C_{arom}), 128.2 (C_{arom}), 141.3 (C_{arom}), 162.4 d ($^2J_{PC}$ = 19.2 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 295 (3.9), 280 (22.1), 207 (5.3), 208 (100), 155 (3.8), 137 (8.6), 91 (70.8), 77 (18.8), 57 (13.5), 41 (15.5). Found, %: C 60.88; H 7.44; N 4.83; P 10.61. $C_{15}H_{22}NO_3P$. Calculated, %: C 61.01; H 7.51; N 4.74; P 10.49.

Diethyl (2-anilinocyclobut-1-en-1-yl)phosphonate (7e). ^{1}H NMR spectrum, δ, ppm: 1.24 t (6H, J_{HH} = 7.2 Hz, $OCH_2C\mathbf{H}_3$), 2.18 br.t (2H, J_{HH} = 6.9 Hz, CH_2CH_2), 2.81 br.t (2H, J_{HH} = 6.5 Hz, CH_2CH_2), 3.96 m (4H, $OC\mathbf{H}_2CH_3$), 7.17–7.32 (5H, Ph). ^{31}P NMR spectrum: δ_P 31.27 ppm. ^{13}C NMR spectrum, δ_C, ppm: 16.0 d ($^3J_{PC}$ = 6.0 Hz, $OCH_2\mathbf{C}H_3$), 23.4 s (CH_2CH_2), 46.4 d ($^3J_{PC}$ = 31.7 Hz, CH_2CH_2), 61.3 d ($^2J_{PC}$ = 6.2 Hz, $O\mathbf{C}H_2CH_3$), 70.2 d ($^1J_{PC}$ = 205.6 Hz, CP), 126.0 (C_{arom}), 128.3 (C_{arom}), 140.3 (C_{arom}), 160.2 d ($^2J_{PC}$ = 18.8 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 281 (6.3), 264 (12.4), 207 (1.1), 168 (100), 144 (5.8), 135 (23.7), 91 (78.5), 77 (15.4), 65 (17.7), 41 (18.9). Found, %: C 59.91; H 7.26; N 4.83; P 10.87. $C_{14}H_{20}NO_3P$. Calculated, %: C 59.78; H 7.17; N 4.98; P 11.01.

Diethyl [2-(methylamino)cyclobut-1-en-1-yl]-phosphonate (7f). ^{1}H NMR spectrum, δ, ppm: 1.25 t (6H, J_{HH} = 7.2 Hz, $OCH_2C\mathbf{H}_3$), 2.52 s (3H, CH_3), 2.70 br.t (2H, J_{HH} = 6.5 Hz, CH_2CH_2), 2.88 br.t (2H, J_{HH} = 6.3 Hz, CH_2CH_2), 4.11 m (4H, $OC\mathbf{H}_2CH_3$). ^{31}P NMR spectrum: δ_P 27.85 ppm. ^{13}C NMR spectrum, δ_C, ppm: 15.9 d ($^3J_{PC}$ = 6.2 Hz, $OCH_2C\mathbf{H}_3$), 25.7 s (CH_2CH_2), 33.6 d ($^3J_{PC}$ = 5.6 Hz, CH_2CH_2), 39.4 s (NCH_3), 62.1 d ($^2J_{PC}$ = 6.4 Hz, $O\mathbf{C}H_2CH_3$), 68.9 d ($^1J_{PC}$ = 205.2 Hz, CP), 200.3 d ($^2J_{PC}$ = 20.1 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 219 (8.5), 206 (2.1), 133 (15.1), 132 (100), 172 (50.5), 144 (6.0), 104 (10.3), 91 (80.1), 77 (1.2), 65 (21.3), 41 (10.3). Found, %: C 49.68; H 8.38; N 6.25; P 13.94. $C_9H_{18}NO_3P$. Calculated, %: C 49.31; H 8.28; N 6.39; P 14.13.

Diethyl {2-[(2-phenylethyl)amino]cyclobut-1-en-1-yl}phosphonate (7g). ^{1}H NMR spectrum, δ, ppm: 1.26 t (6H, J_{HH} = 6.9 Hz, $OCH_2C\mathbf{H}_3$), 2.68 br.t (2H, J_{HH} = 6.3 Hz, CH_2CH_2), 2.74 br.t (2H, J_{HH} = 6.7 Hz, CH_2CH_2), 2.81 br.t (2H, J_{HH} = 6.5 Hz, CH_2CH_2Ph), 2.92 br.t (2H, J_{HH} = 6.9 Hz, CH_2CH_2Ph), 3.96 m (4H, $OC\mathbf{H}_2CH_3$), 7.10–7.30 m (5H, Ph). ^{31}P NMR spectrum: δ_P 27.50 ppm. ^{13}C NMR spectrum, δ_C, ppm: 16.1 d ($^3J_{PC}$ = 6.8 Hz, $OCH_2\mathbf{C}H_3$), 27.7 s (CH_2CH_2), 38.5 d ($^3J_{PC}$ = 4.6 Hz, CH_2CH_2), 38.5 s (CH_2CH_2Ph), 42.7 s (CH_2CH_2Ph), 60.4 d ($^2J_{PC}$ = 5.7 Hz, $O\mathbf{C}H_2CH_3$), 70.2 d ($^1J_{PC}$ = 216.6 Hz, CP), 126.0 (C_{arom}), 128.2 (C_{arom}), 128.5 (C_{arom}), 139.0 (C_{arom}), 160.8 d ($^2J_{PC}$ = 19.6 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 309 (0.5), 297 (1.1), 252 (29.2), 206 (100), 178 (17.2), 160 (29.1), 132 (2.1), 105 (11.5), 104 (11.4), 91 (12.0), 77 (5.2), 57 (1.0). Found, %: C 61.94; H 7.98; N 4.67; P 9.88. $C_{16}H_{24}NO_3P$. Calculated, %: C 62.12; H 7.82; N 4.53; P 10.01.

Diethyl {2-[(2-hydroxyethyl)amino]cyclobut-1-en-1-yl}phosphonate (7h). ^{1}H NMR spectrum, δ, ppm: 1.22 t (6H, J_{HH} = 7.3 Hz, J_{PH} = 1.3 Hz, $OCH_2C\mathbf{H}_3$), 2.38 br.t (2H, J_{HH} = 7.5 Hz, CH_2CH_2), 2.57 br.t (2H, J_{HH} = 7.5 Hz, CH_2CH_2), 3.16 t (2H, J_{HH} = 7.7 Hz, CH_2CH_2OH), 3.28 t (2H, J_{HH} = 7.7 Hz, CH_2CH_2OH), 4.06 m (4H, $OC\mathbf{H}_2CH_3$). ^{31}P NMR spectrum: δ_P 27.98 ppm. ^{13}C NMR spectrum, δ_C, ppm: 16.5 d ($^3J_{PC}$ = 6.6 Hz, $OCH_2\mathbf{C}H_3$), 22.7 s (CH_2CH_2), 45.6 d ($^3J_{PC}$ = 31.1 Hz, CH_2CH_2), 48.5 s ($\mathbf{C}H_2CH_2OH$), 54.0 s ($CH_2\mathbf{C}H_2OH$), 60.4 d ($^2J_{PC}$ = 5.2 Hz, $O\mathbf{C}H_2CH_3$), 73.8 d ($^1J_{PC}$ = 211.6 Hz, CP), 160.6 d ($^2J_{PC}$ = 21.6 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 249 (2.2), 234 (8.4), 263 (15.6), 205 (13.8), 176 (10.3), 144 (100), 133 (21.7), 128 (50.5), 97 (33.5), 44 (28.4). Found, %: C 47.00; H 7.95; N 5.73; P 12.59. $C_{10}H_{20}NO_4P$. Calculated, %: C 48.19; H 8.09; N 5.62; P 12.43.

Diethyl {2-[di(propan-2-yl)amino]cyclobut-1-en-1-yl}phosphonate (7i). ^{1}H NMR spectrum, δ, ppm:

1.14 d [12H, J_{HH} = 6.2 Hz, CH(C**H**$_3$)$_2$], 1.26 t (6H, J_{HH} = 6.9 Hz, OCH$_2$C**H**$_3$), 2.68 br.t and 2.91 br.t (2H each, J_{HH} = 7.2 Hz, CH$_2$CH$_2$), 2.90 m [2H, C**H**(CH$_3$)$_2$], 4.09 m (4H, OC**H**$_2$CH$_3$). ^{31}P NMR spectrum: δ_P 30.32 ppm. ^{13}C NMR spectrum, δ_C, ppm: 16.4 d ($^3J_{PC}$ = 6.2 Hz, OCH$_2$**C**H$_3$), 22.6 s [CH(**C**H$_3$)$_2$], 23.3 s (CH$_2$CH$_2$), 32.7 d ($^3J_{PC}$ = 5.6 Hz, CH$_2$CH$_2$), 48.8 s [**C**H(CH$_3$)$_2$], 60.1 d ($^2J_{PC}$ = 5.2 Hz, O**C**H$_2$CH$_3$), 73.3 d ($^1J_{PC}$ = 200.8 Hz, CP), 168.6 d ($^2J_{PC}$ = 19.9 Hz, CN). Mass spectrum, *m*/*z* (I_{rel}, %): 289 (18.8), 274 (22.4), 259 (15.4), 246 (100), 231 (15.4), 218 (33.4), 207 (8.8), 188 (39.8), 155 (70.5), 144 (5.8), 76 (9.3), 41 (15.7). Found, %: C 57.96; H 9.66; N 4.94; P 10.8. $C_{14}H_{28}NO_3P$. Calculated, %: C 58.11; H 9.75; N 4.84; P 10.70.

Diethyl [2-(propylamino)cyclobutyl]phosphonate (8). ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, J_{HH} = 7.5 Hz), 1.31 t (6H, J_{HH} = 7.2 Hz), 1.60 m (2H), 1.92–2.40 m (5H), 2.55 br.t (2H, J_{HH} = 7.3 Hz), 2.95 m (1H), 4.10 m (4H, OC**H**$_2$CH$_3$). ^{31}P NMR spectrum: δ_P 32.66 ppm. ^{13}C NMR spectrum, δ_C, ppm: 11.4, 16.0 d ($^3J_{PC}$ = 6.3 Hz), 18.1, 21.6, 27.8, 51.2, 42.7 d ($^1J_{PC}$ = 215.6 Hz), 54, 61.2 d ($^2J_{PC}$ = 4.6 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 247 (4.2), 232 (10.2), 207 (11.1), 158 (100), 144 (6.0), 133 (21.7), 104 (10.8), 85 (5.7), 43 (35.6). Found, %: C 53.66; H 9.06; N 5.54; P 12.39. $C_{11}H_{22}NO_3P$. Calculated, %: C 53.43; H 8.97; N 5.66; P 12.53.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Moore, H.W. and Decker, O.H.W., *Chem. Rev*., 1986, vol. 86, p. 821. https://doi.org/10.1021/cr00075a006
2. Misale, A., Niyomchon, S., and Maulide, N., *Acc. Chem. Res*., 2016, vol. 49, p. 2444. https://doi.org/10.1021/acs.accounts.6b00375
3. Namyslo, J.C. and Kaufmann, D.E., *Chem. Rev*., 2003, vol. 103, p. 1485. https://doi.org/10.1021/cr010010y
4. Yavari, I. and Asghari, S., *Tetrahedron*, 1999, vol. 55, p. 11853. https://doi.org/10.1016/S0040-4020(99)00671-7
5. Bozkaya, U. and Özkan, İ., *J. Org. Chem*., 2012, vol. 77, p. 5714. https://doi.org/10.1021/jo300877w
6. Kitayama, T., Kawauchi, T., Nakamura, M., Sufi, B., Padias, A.B., and Hall, H.K., *Polymer*, 2004, vol. 45, p. 5085. https://doi.org/10.1016/j.polymer.2004.05.024
7. Chen, X.P., Sufi, B.A., Padias, A.B., and Hall, H.K., *Macromolecules*, 2002, vol. 35, p. 4277. https://doi.org/10.1021/ma012104f
8. Perrott, M.G. and Novak, B.M., *Macromolecules*, 1996, vol. 29, p. 1817. https://doi.org/10.1021/ma951516j
9. Wu, Z. and Grubbs, R.H., *Macromolecules*, 1995, vol. 28, p. 3502. https://doi.org/10.1021/ma00114a002
10. Casey, P.K. and Mathias, L.J., *Polym. Commun*., 1991, vol. 32, p. 27.
11. Hall, H.K. and Padias, A.B., *J. Polym. Sci., Part A-1: Polym. Chem*., 2003, vol. 41, p. 625. https://doi.org/10.1002/pola.10618
12. Ingham, S., Turner, R.W., and Wallace, T.W., *J. Chem. Soc., Chem. Commun*., 1985, p. 1664. https://doi.org/10.1039/C39850001664
13. Binns, F., Hayes, R., Ingham, S., Saengchantara, S.T., Turner, R.W., and Wallace, T.W., *Tetrahedron*, 1992, vol. 48, p. 515. https://doi.org/10.1016/S0040-4020(01)89013-X
14. Hayes, R., Ingham, S., Saengchantara, S.T., and Wallace, T.W., *Tetrahedron Lett*., 1991, vol. 32, p. 2953. https://doi.org/10.1016/0040-4039(91)80660-x
15. Binns, F., Hayes, R., Hodgetts, K.J., Saengchantara, S.T., Wallace, T.W., and Wallis, C.J., *Tetrahedron*, 1996, vol. 52, p. 3631. https://doi.org/10.1016/0040-4020(96)00039-7
16. Hodgetts, K.J., Saengchantara, S.T., Wallis, C.J., and Wallace, T.W., *Tetrahedron Lett*., 1993, vol. 34, p. 6321. https://doi.org/10.1016/s0040-4039(00)73742-7
17. Gourdel-Martin, M.E. and Huet, F., *Tetrahedron Lett*., 1996, vol. 37, p. 7745. https://doi.org/10.1016/0040-4039(96)01763-7
18. Youcef, R.A., Boucheron, C., Guillarme, S., Legoupy, S., Dubreuil, D., and Huet, F., *Synthesis*, 2006, p. 633. https://doi.org/10.1055/s-2006-926303
19. Dembitsky, V.M., *J. Nat. Med*., 2008, vol. 62, p. 1. https://doi.org/10.1007/s11418-007-0166-3
20. Hansen, T.V. and Stenstrøm, Y., *Organic Synthesis: Theory and Applications*, Amsterdam: Elsevier, 1996, vol. 5, p. 1. https://doi.org/10.1016/s1047-773x(01)80002-0
21. Zarghi, A. and Arfaei, S., *Iran. J. Pharm. Res*., 2011, vol. 10, p. 655.
22. Talley, J.J., *Prog. Med. Chem. Res*., 1999, vol. 36, p. 201. https://doi.org/10.1016/s0079-6468(08)70048-1

23. Praveen, P.N., Rao, E.E., and Knaus, J., *J. Pharm. Pharm. Sci*., 2008, vol. 11, p. 81. https://doi.org/10.18433/j3t886
24. Smith, S.C., Clarke, E.D., Ridley, S.M., Bartlett, D., Greenhow, D.T., Glithro, H., Klong, A.Y., Mitchell, G., and Mullier, G.W., *Pest Manage. Sci*., 2005, vol. 61, p. 16. https://doi.org/10.1002/ps.980
25. Liu, Z.Y., Wang, Y.M., Han, Y.X., Liu, L., Jin, J., Yi, H., Li, Z.R., Jiang, J.D., and Boykin, D., *Eur. J. Med. Chem*., 2013, vol. 65, p. 187. https://doi.org/10.1016/j.ejmech.2013.04.046
26. Ortuño, R., Moglioni, M., and Moltrasio, A.G., *Curr. Org. Chem.,* 2005, vol. 9, p. 237. https://doi.org/10.2174/1385272053369088
27. Sergeiko, A., Poroikov, V., Hanuš, L., and Dembitsky, V., *Open Med. Chem. J*., 2008, vol. 2, p. 26. https://doi.org/10.2174/1874104500802010026
28. Owsley, D.C. and Bloomfield, J.J., *J. Chem. Soc. C*, 1971, p. 3445. https://doi.org/10.1039/j39710003445
29. Kosugi, H., Sekiguchi, S., Sekita, R., and Uda, H., *Bull. Chem. Soc. Jpn*., 1976, vol. 7, p. 520. https://doi.org/10.1002/chin.197620094
30. Baldwin, S.W., *Organic Photochemistry*, Padwa A., Ed., New York: Marcel Dekker, 1981, vol. 5, p. 123.
31. Demuth, M., and Gamal, M., *Synthesis*, 1989, p. 145. https://doi.org/10.1055/s-1989-27181
32. Alibés, R., March, P., Figueredo, M., Font, J., Racamonde, M., Rustullet, A., Alvarez-Larena, A., Piniella, J.F., and Parella, T., *Tetrahedron Lett*., 2003, vol. 44, p. 69. https://doi.org/10.1016/s0040-4039(02)02528-5
33. Delas, C., Urabe, H., and Sato, F., *Tetrahedron Lett*., 2001, vol. 42, p. 4147. https://doi.org/10.1016/s0040-4039(01)00666-9
34. Brandsma, L., Spek, A.L., Trofimov, B.A., Tarasova, O.A., Nedolya, N.A., Afonin, A.V., and Zinshenko, S.V., *Tetrahedron Lett*., 2001, vol. 42, p. 4687. https://doi.org/10.1016/s0040-4039(01)00787-0
35. Barbero, A., Cuadrado, P., Garcıa, C.A., Rincon, J.A., and Pulido, F.J., *J. Org. Chem*., 1998, vol. 63, p. 7531. https://doi.org/10.1021/jo980874s
36. Liu, Y., Liu, M., and Song, Z., *J. Am. Chem. Soc*., 2005, vol. 127, p. 3662. https://doi.org/10.1021/ja042636m
37. López-Carrillo, V. and Echavarren, A.M., *J. Am. Chem. Soc*., 2010, vol. 132, p. 9292. https://doi.org/10.1021/ja104177w
38. Negishi E., Liu F., Choueiry D., and Mohamud M.M., *J. Org. Chem*., 1996, vol. 61, p. 8325. https://doi.org/10.1021/jo961277d
39. Perri, S.T., Dyke, H.K., and Moore, H.W., *J. Org. Chem*., 1989, vol. 54, p. 2032. https://doi.org/10.1021/jo00270a004
40. Song, Z.Q., Li, Y.X., Liu, M., Cong, L.Q., and Liu, Y.H., *Organometallics*, 2006, vol. 25, p. 5035. https://doi.org/10.1021/om060505j
41. Chen, C., Xi, C., Lai, C., Wang, R., and Hong, X., *Eur. J. Org. Chem*., 2004, p. 647. https://doi.org/10.1002/ejoc.200300485
42. Al Quntar, A.A., Srebnik, M., Terent'ev, A.O., and Dembitsky, V., *Mini-Rev. Org. Chem*., 2014, vol. 11, p. 445. https://doi.org/10.2174/1570193x1104140926170132
43. Bauer, G. and Haegele, G., *Z. Naturforsch., B: Anorg. Chem., Org. Chem*., 1979, vol. 34, p. 1252. https://doi.org/10.1515/znb-1979-0918
44. Ueda, T., Inukai, K., and Muramatsu, H., *Bull. Chem. Soc. Jpn*., 1969, vol. 42, p. 1684. https://doi.org/10.1246/bcsj.42.1684
45. Tomioka, H., Watanabe, M., Kobayashi, N., and Hirai, K., *Tetrahedron Lett*., 1990, vol. 31, p. 5061. https://doi.org/10.1016/s0040-4039(00)97806-7
46. Facklam, T., Hoffmann, K.L., and Regitz, M., *Chem. Ber*., 1987, vol. 120, p. 1397. https://doi.org/10.1002/cber.19871200817
47. Andriamiadanarivo, R., Pujol, B., Chantegrel, B., Dehayes, C., and Doutheau, A., *Tetrahedron Lett*., 1993, vol. 34, p. 7923. https://doi.org/10.1016/s0040-4039(00)61512-5
48. Darling, S.D. and Subramanian, N., *Tetrahedron Lett*., 1975, vol. 38, p. 3279. https://doi.org/10.1016/s0040-4039(00)91425-4
49. Sinelnikove, Y., Rubinstein, A., Srebnik, M., and Al Quntar, A.A., *Tetrahedron Lett*., 2009, vol. 50, p. 867. https://doi.org/10.1016/j.tetlet.2008.11.108
50. Srivastava, H.K., Al Quntar, A.A., Azab, A., Srebnik, M., and Shurki, A., *Tetrahedron*, 2009, vol. 65, p. 4389. https://doi.org/10.1016/j.tet.2009.03.053