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Photocycloaddition of Enynones (4-Acylbut-1-en-3-ynes) to Alkenes

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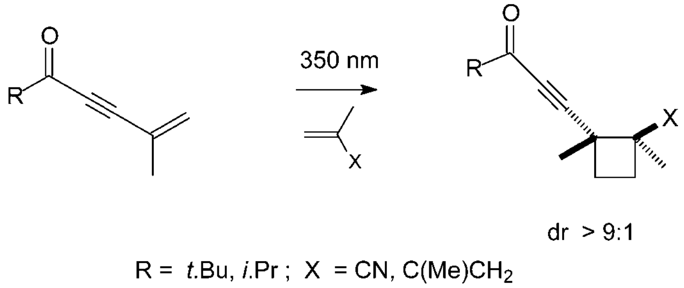
ABSTRACT



The title compounds undergo regio- and diastereoselective [2+2]-cycloaddition at the olefinic C−C bond on irradiation (350 nm) in the presence of either methacrylonitrile or 2,3-dimethylbuta-1,3-diene, affording hitherto unknown 1-cyclobutylalk-1-yn-3-ones or 1-bicyclo[4.2.0]octylalk-1-yn-3-ones, respectively.

In contrast to the thoroughly investigated photocycloaddition of (cyclic) conjugated enones to alkenes,[1] the corresponding photoreaction of (acyclic) conjugated acetylenic ketones (RC(O)C≡CR′) is less common. It has been shown that for compounds with an aliphatic alkyne moiety (R′ = alkyl) both [2+2]- and [3+2]-cycloadditions at the carbonyl group occur selectively,[2,3] whereas for phenylacetylene derivatives (R′ = aryl) cyclobutene formation becomes predominant.[4,5] Interestingly, no results on the behavior of photoexcited conjugated enynones in the presence of alkenes have been reported in the literature. Here we communicate the first results on such reactions.

Enynones **1** were synthesized according to literature procedures via Cu- or Pd-catalyzed coupling of the corresponding acyl chlorides and enynes, respectively.[6,7] Irradiation of a 0.1 M benzene solution of **1a**,**b** in the presence of a 20-fold molar excess of methacrylonitrile (**2**) affords cyclobutane-1-carbonitriles **3a**,**b** regiospecifically and diastereoselectively (9:1) and minor amounts (<10%) of **4a**,**b** with total conversion of starting material. Irradiation of the same enynones in the presence of a 20-fold molar excess of 2,3-dimethylbuta-1,3-diene (**5**) affords 1-cyclobutylpent-1-yn-4-ones **6a**,**b** selectively. Finally, irradiation of **1a**,**b** in the presence of 1-chloroacrylonitrile (**7**) affords 3:2 diastereomeric mixtures of cyclobutane-1-carbonitriles **8a**,**b** and **9a**,**b** (Scheme 1).

Enynone **1c** behaves alike in the presence of the same alkenes in affording bicyclo[4.2.0]octane derivatives **10** and **11** (17:3) with methacrylonitrile and **12** (with 2,3-dimethylbutadiene) selectively, while in the presence of chloroacrylonitrile a 5:2 mixture (diastereomers **13** and **14**) is obtained (Scheme 2). All [2+2]-photocycloadducts were isolated and purified by chromatography (SiO_2) and their

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(1) For recent reviews of enone [2+2] photocycloadditions, see: (a) Margaretha, P. In *Molecular and Supramolecular Photochemistry*; Griesbeck, A. G., Mattay, J., Eds.; Marcel Dekker: New York, 2005; Vol. 12, pp 211−238. (b) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052.

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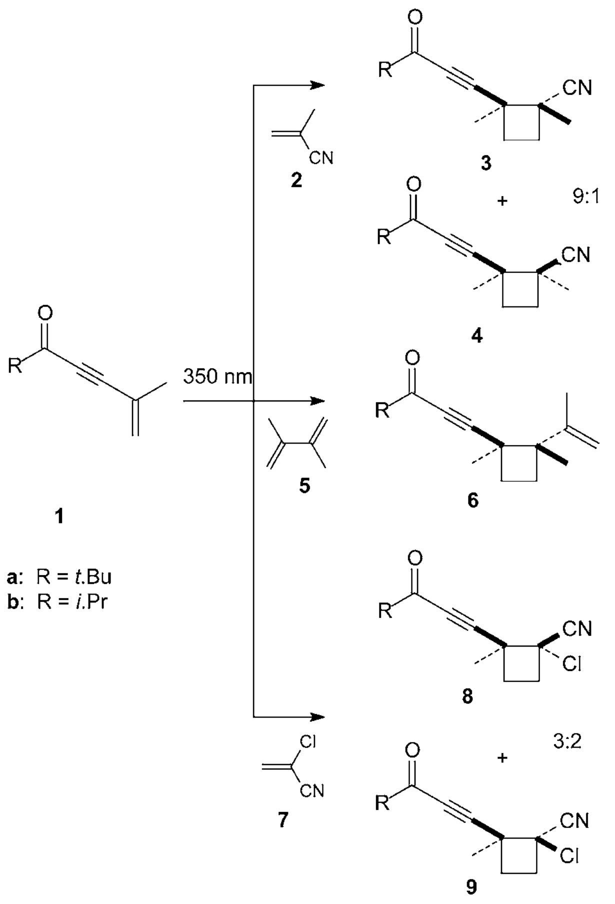
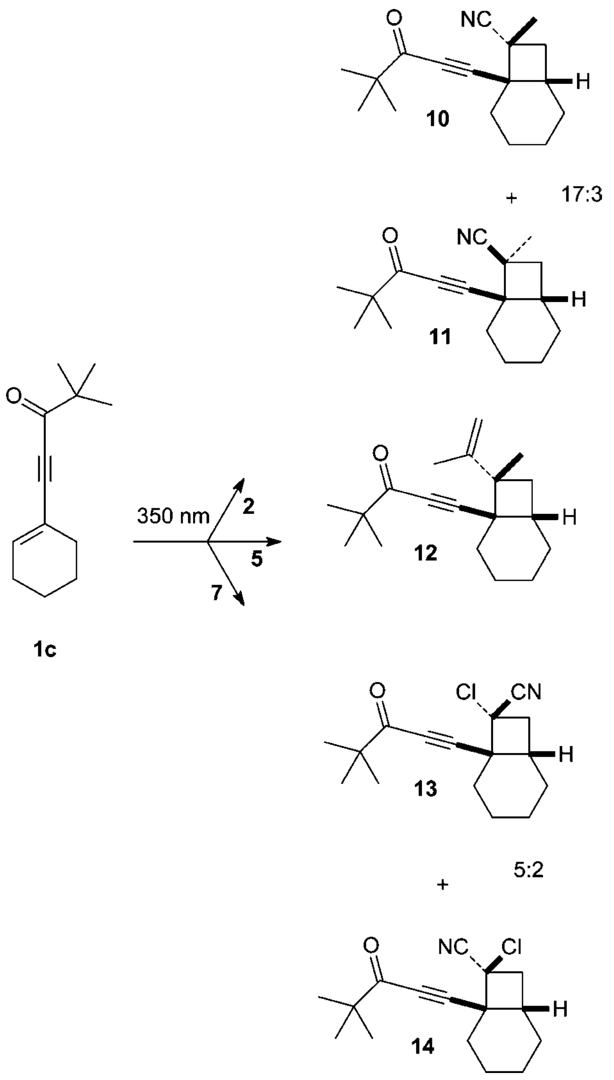
10.1021/ol902827s

Scheme 1



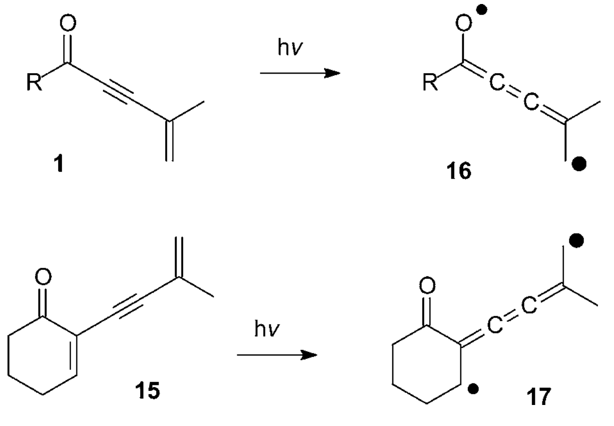
Scheme 2



structures proven by NMR (CH_2-CH_2 coupling and NOE of the methyl groups in the ^1H and acetylenic C-atoms in the ^{13}C spectrum, respectively).[8,9]

Acyclic conjugated enones do not give cyclobutanes on irradiation in the presence of alkenes due to very efficient competitive isomerization at the C=C double bond. Quite recently it has been shown that radical anions of arylenones generated by PET from suitable Ru complexes cycloadd to aliphatic Michael acceptors affording 1,2-diacylcyclobutanes.[10] The behavior of enynones **1** parallels that of cross-conjugated 2-(alkenynyl)cyclohex-2-enones **15**[11,12] in reactions with conjugated alkenes by affording cyclobutanes efficiently via chemoselective primary binding at the olefinic terminus of the enyne system. This indicates that these (triplet) excited enynones behave like cummulenic biradicals **16**/**17** exhibiting a high spin density on the enyne olefinic terminus (Scheme 3). Interestingly, both compounds **1** and **15** do not undergo photocycloadditions to “conventional” alkenes, e.g. 2,3-dimethylbut-2-ene. Alkyl radicals are known to add with much higher rates to conjugated alkenes, e.g., **2** or **5**, than to simple olefins.[13] This correlates with the

Scheme 3



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(8) **Typical preparative procedure:** Argon-degassed solutions of **1** (1 mmol) and alkene **2**, **5**, or **7** (20 mmol) in benzene (10 mL) were irradiated in a Rayonet RPR-100 photoreactor equipped with (16) 350 nm lamps for 6−9 h. After evaporation of the solvent and the excess alkene, the residue was flash chromatographed (SiO_2, CH_2Cl_2), the main products (**3a**, **3b**, and **10**) eluting before the minor products (**4a**, **4b**, and **11**), respectively All compounds are colorless liquids or oils. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 500 and 125.04 MHz, respectively. GC/MS were recorded at 70 eV.

assumption that the dissociation energy of the π bonds in the former compounds is 5−10 kcal/mol lower than that in, e.g., 2,3-dimethylbut-2-ene.[14] The observed diastereoselectivities in the reactions with methacrylonitrile or 2,3-dimethylbutadiene most probably reflect the thermodynamic control in the 1,4-cyclization of the intermediate biradical leading preferentially to trans-configurated cyclobutanes.

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(9) **3a**: R_f 0.80; 53% yield. ^{1}H NMR: δ 2.55 (ddd, 1H, H-4a, $^{3}J = 8.8$ Hz, $^{3}J = 8.8$ Hz, $^{2}J = 11.7$ Hz), 2.44 (ddd, 1H, H-3a, $^{3}J = 8.8$ Hz, $^{3}J = 8.8$ Hz, $^{2}J = 11.7$ Hz), 2.08 (ddd, 1H, H-3b, $^{3}J = 4.7$ Hz, $^{3}J = 8.8$ Hz, $^{2}J = 11.7$ Hz), 2.03 (ddd, 1H, H-4b, $^{3}J = 4.7$ Hz, $^{3}J = 8.8$ Hz, $^{2}J = 11.7$ Hz), 1.69 and 1.65 (s, 3H), 1.20 (s, 9H). ^{13}C NMR: δ 193.7 (C-3′), 121.7 (CN), 94.4 (C-1′), 91.2 (C-2′), 44.7 ($C(CH_3)_3$), 38.8 (C-1), 38.7 (C-2), 31.5 (C-3), 29.3 (C-4), 26.0 ($C(CH_3)_3$), 24.9 and 22.7 (CH_3). EI-MS [*m*/*z*] 217 (M^+, <1%), 57 (100%). **3b**: R_f 0.60; 62% yield. ^{1}H NMR: δ 2.64 (sept, 1H, H-4′, $^{3}J = 7.0$ Hz), 2.55 (ddd, 1H, H-4a, $^{3}J = 8.8$, $^{3}J = 8.8$, $^{2}J = 11.7$ Hz), 2.43 (ddd, 1H, H-3a, ^{3}J= 8.8, $^{3}J = 8.8$, $^{2}J = 11.7$ Hz), 2.08 (ddd, 1H, H-3b, $^{3}J = 4.7$ Hz, $^{3}J = 8.8$ Hz, $^{2}J = 11.7$ Hz), 2.01 (ddd, 1H, H-4b, $^{3}J = 4.7$ Hz, $^{3}J = 8.8$ Hz, $^{2}J = 11.7$ Hz), 1.69 and 1.65 (s, 3H), 1.20 (d, 6H, $^{3}J = 7.0$ Hz), ^{13}C NMR: δ 191.9 (C-3′), 121.7 (CN), 93.7 (C-1′), 83.0 (C-2′), 43.1 ($CH(CH_3)_2$), 38.4 (C-1), 38.2 (C-2), 31.2 (C-3), 29.0 (C-4), 24.8 and 22.5 (CH_3), 17.9 ($CH(CH_3)_2$). EI-MS [*m*/*z*] 203 (M^+, <1%), 93 (100%). **4a**: R_f 0.60; 5% yield. ^{1}H NMR: δ 2.59 (ddd, 1H, H-4a, $^{3}J = 3.8$ Hz, $^{3}J = 6.8$ Hz, $^{2}J = 8.8$ Hz), 2.50 (ddd, 1H, H-3a, $^{3}J = 3.8$ Hz, $^{3}J = 6.8$ Hz, $^{2}J = 8.8$ Hz), 2.12−1.99 (m, 2H, H-3b/H-4b), 1.47 and 1.42 (s, 3H), 1.26 (s, 9H). ^{13}C NMR: δ 194.0 (C-3′), 122.8 (CN), 95.5 (C-1′), 91.4 (C-2′), 44.7 ($C(CH_3)_3$), 39.5 (C-1/C-2), 31.7 (C-3), 29.6 (C-4), 26.0 ($C(CH_3)_3$), 21.2 and 19.6 (CH_3). EI-MS [*m*/*z*] 217 (M^+, <1%), 57 (100%). **4b** (data from product mixture): ^{1}H NMR: δ 2.73 (sept, 1H, H-4′, $^{3}J = 7.0$ Hz), 1.47 and 1.42 (s, 3H), 1.24 (d, 6H, $^{3}J = 7.0$ Hz). ^{13}C NMR: δ 191.3 (C-3′), 122.8 (CN), 42.1 ($CH(CH_3)_2$), 39.1 (C-1), 39.0 (C-2), 30.5 (C-3), 29.4 (C-4), 20.9 and 19.4 (CH_3), 17.6 ($CH(CH_3)_2$). EI-MS [*m*/*z*] 203 (M^+, <1%), 93 (100%). **6a**: R_f 0.78; 81% yield. ^{1}H NMR: δ 4.86 (br s, 1H, H-2″a), 4.85 (t, 1H, H-2″b, $^{4}J = 1.3$ Hz), 2.44−2.33 (m, 2H, H-3a/H-4a), 1.70−1.57 (m, 2H, H-3b/H-4b), 1.66, 1.42 and 1.29 (s, 3H), 1.21 (s, 9H). ^{13}C NMR: δ 194.4 (C-3′), 148.8 (C-1″), 110.6 (C-2″), 99.7 (C-1′), 80.6 (C-2′), 49.9 (C-1′), 44.5 ($C(CH_3)_3$), 37.3 (C-2), 30.0 (C-3), 27.4 (C-4), 26.2 ($C(CH_3)_3$), 24.5, 22.5 and 18.7 (CH_3). EI-MS [*m*/*z*] 232 (M^+, 1%), 82 (100%). **6b**: R_f 0.71; 62% yield. ^{1}H NMR: δ 4.86 (s, 1H, H-2″a), 4.67 (s, 1H, H-2″b), 2.64 (sep, 1H, H-4′, $^{3}J = 6.9$ Hz), 2.38−2.29 (m, 2H, H-3a/H-4a), 1.72−1.54 (m, 2H, H-3b/H-4b), 1.66, 1.43 and 1.29 (s, 3H), 1.21 (d, 6H, $^{3}J = 7.0$ Hz). ^{13}C NMR: δ 191.5 (C-3), 148.7 (C-1″), 110.6 (C-2″), 99.4 (C-1′), 81.5 (C-2′), 49.7 (C-1), 43.2 ($CH(CH_3)_2$), 37.3 (C-2), 30.0 (C-4), 27.4 (C-3), 24.3, 22.4 and 18.7 (CH_3), 18.1 ($CH(CH_3)_2$). EI-MS [*m*/*z*] 218 (M^+, <1%), 82 (100%). **8a** (data from product mixture): R_f 0.70. ^{1}H NMR: δ 2.96−2.85 (m, 1H, H-4a), 2.72−2.61 (m, 1H, H-4b), 2.71−2.58 (m, 1H, H-3a), 2.28−2.17 (m, 1H, H-3b), 1.72 (s, 3H), 1.23 (s, 9H). ^{13}C NMR: δ 193.6 (C-3′), 116.8 (CN), 91.8 (C-1′), 91.4 (C-2′), 56.9 (C-1), 45.8 (C-2), 44.8 ($C(CH_3)_3$), 35.7 (C-3), 35.4 (C-4), 25.9 (C(CH3)), 24.6 (CH_3). EI-MS [*m*/*z*] 181 ($M^+ - 56$, <1%), 57 (100%). **9a** (data from product mixture): R_f 0.70. ^{1}H NMR: δ 2.96−2.90 (m, 1H, H-4a), 2.67−2.60 (m, 1H, H-4b), 2.67−2.60 (m, 1H, H-3a), 2.22−2.17 (m, 1H, H-3b), 1.63 (s, 3H), 1.25 (s, 9H). ^{13}C NMR: δ 193.6 (C-3′), 118.1 (CN), 91.8 (C-1′), 91.4 (C-2′), 57.9 (C-1), 44.8 ($C(CH_3)_3$), 43.3 (C-2), 35.9 (C-4), 30.7 (C-3), 25.9 ($C(CH_3)_3$), 22.6 (CH_3). EI-MS [*m*/*z*] 181 ($M^+ - 56$, <1%), 57 (100%). **8b** (data from product mixture): R_f 0.70. ^{1}H NMR: δ 2.95−2.87 (m, 1H, H-4a), 2.71 (sept, 1H, H-4′, $^{3}J = 6.9$ Hz), 2.71−2.62 (m, 1H, H-4b), 2.62−2.57 (m, 1H, H-3a), 2.21−2.17 (m, 1H, H-3b), 1.71 (s, 3H), 1.23 (d, 6H, $^{3}J = 6.9$ Hz). ^{13}C NMR: δ 191.6 (C-3′), 116.9 (CN), 91.5 (C-1′), 83.8 (C-2′), 56.5 (C-1), 45.9 (C-2), 43.2 ($CH(CH_3)_2$), 35.2 (C-4), 31.4 (C-3), 24.1 (CH_3), 17.8 ($CH(CH_3)_2$). EI-MS [*m*/*z*] 223 (M^+, <1%), 93 (100%). **9b** (data from product mixture): R_f 0.70. ^{1}H NMR: δ 2.95−2.91 (m, 1H, H-4a), 2.71 (sept, 1H, H-4′, $^{3}J = 6.9$ Hz), 2.66−2.59 (m, 1H, H-4b), 2.59−2.51 (m, 1H, H-3a), 2.27−2.12 (m, 1H, H-3b), 1.62 (s, 3H), 1.22 (d, 6H, methyl, $^{3}J = 6.9$ Hz). ^{13}C NMR: δ 191.6 (C-3′), 117.9 (CN), 91.1 (C-1′), 84.3 (C-2′), 57.8 (C-1), 43.4 ($CH(CH_3)_2$), 43.0 (C-2), 34.9 (C-4), 31.1 (C-3), 22.6 (CH_3), 17.8 ($CH(CH_3)_2$). EI-MS [*m*/*z*] 223 (M^+, <1%), 93 (100%). **10**: R_f 0.40; 60% yield. ^{1}H NMR: δ 2.44 (dd, 1H, H-8a, $^{3}J = 6.3$ Hz, $^{2}J = 9.3$ Hz), 2.28 (dddd, 1H, H-1, $^{3}J = 3.2$ Hz, $^{3}J = 6.5$ Hz, $^{3}J = 11.7$ Hz, $^{3}J = 11.7$ Hz), 2.18 (dd, 1H, H-8b, $^{2}J = 9.3$ Hz, $^{3}J = 12.8$ Hz), 1.94−1.87 (m, 2H, H-5), 1.85−1.77 (m, 4H, H-3/H-4), 1.77−1.65 (m, 1H, H-2a), 1.58 (s, 3H), 1.46−1.40 (m, 1H, H-2b), 1.24 (s, 9H). ^{13}C NMR: δ 193.2 (C-3′), 123.0 (CN), 93.2 (C-1′), 86.3 (C-2′), 51.2 (C-7), 44.7 ($C(CH_3)_3$), 44.0 (C-1), 43.9 (C-6), 40.7 (C-8), 34.0 (C-5), 26.0 (C-2), 25.9 ($C(CH_3)_3$), 25.6 (C-4), 22.6 (C-3), 20.9 (CH_3). EI-MS [*m*/*z*] 257 (M^+, <1%), 133 (100%). **11**: R_f 0.30; 6% yield. ^{1}H NMR: δ 2.68 (dd, 1H, H-8a, $^{2}J = 10.1$ Hz, $^{3}J = 12.1$ Hz), 2.22−2.13 (m, 1H, H-1), 2.05 (dd, 1H, H-8b, $^{3}J = 7.1$ Hz, $^{2}J = 10.1$ Hz), 1.92−1.83 (m, 2H, H-5), 1.85−1.58 (m, 6H), 1.61 (s, 3H), 1.28 (s, 9H). ^{13}C NMR: δ 193.3 (C-3′), 121.7 (CN), 86.6 (C-1′), 74.8 (C-2′), 51.2 (C-7), 44.9 ($C(CH_3)_3$), 43.0 (C-6), 42.7 (C-1), 39.4 (C-8), 34.3 (C-5), 25.9 ($C(CH_3)_3$), 25.7 (C-2), 22.8 (C-4), 22.5 (C-3), 17.8 (CH_3). EI-MS [*m*/*z*] 257 (M^+, <1%), 133 (100%). **12**: R_f 0.51; 60% yield (>75% purity). ^{1}H NMR: δ 4.81 (t, 1H, H-2″a, $^{4}J = 1.5$ Hz), 4.63 (br s, 1H, H-2″b), 2.21−2.14 (m, 6H), 1.71−1.60 (m, 5H), 1.65 and 1.40 (s, 3H), 1.21 (9H). ^{13}C NMR: δ 194.2 (C-3′), 150.4 (C-1″), 109.0 (C-2″), 94.8 (C-1′), 48.8 (C-7), 44.1 ($C(CH_3)_3$), 39.4 (C-8), 26.9 ($C(CH_3)_3$), 23.7 and 21.9 (CH_3), 21.6 (C-3′/C-4′). EI-MS [*m*/*z*] 272 (M^+, 37%), 187 (100%). **13**: R_f 0.75; 42% yield. ^{1}H NMR: δ 2.88 (dd, 1H, H-8a, $^{3}J = 6.7$ Hz, $^{2}J = 10.5$ Hz), 2.72 (dd, 1H, H-8b, $^{2}J = 10.5$ Hz, $^{3}J = 13.2$ Hz), 2.16−2.08 (m, 1H, H-1), 2.04−1.94 (m, 2H, H-2), 1.89−1.78 (m, 6H), 1.25 (s, 9H). ^{13}C NMR: δ 193.2 (C-3′), 117.7 (CN), 90.1 (C-1′), 87.1 (C-2′), 56.9 (C-6), 55.7 (C-7), 45.8 (C-8), 44.9 ($C(CH_3)_3$), 42.2 (C-1), 33.8 (C-2), 26.0 ($C(CH_3)_3$), 26.5 (C-4), 25.5 (C-5), 22.6 (C-3). EI-MS [*m*/*z*] 277 (M^+, <1%), 57 (100%). **14**: R_f 0.65; 26% yield. ^{1}H NMR: δ 3.04 (dd, 1H, H-8a, $^{2}J = 11.6$ Hz, $^{3}J = 11.7$ Hz), 2.63−2.56 (m, 1H, H-1), 2.51 (dd, 1H, H-8b, $^{3}J = 6.9$ Hz, $^{2}J = 11.6$ Hz), 2.00−1.92 (m, 1H, H-2a), 1.85−1.70 (m, 7H), 1.27 (s, 9H). ^{13}C NMR: δ 193.2 (C-3′), 116.4 (CN), 90.9 (C-1′), 86.7 (C-2′), 58.6 (C-7), 54.5 (C-6), 45.8 ($C(CH_3)_3$), 45.3 (C-8), 42.2 (C-1), 32.5 (C-2), 26.9 ($C(CH_3)_3$), 25.8 (C-5), 22.6 (C-3), 20.2 (C-4). EI-MS [*m*/*z*] 277 (M^+, <1%), 57 (100%).

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