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Photocycloaddition of 5,5-dimethyl-6-oxocyclohex-1-ene-1-carbonitrile to alkenes

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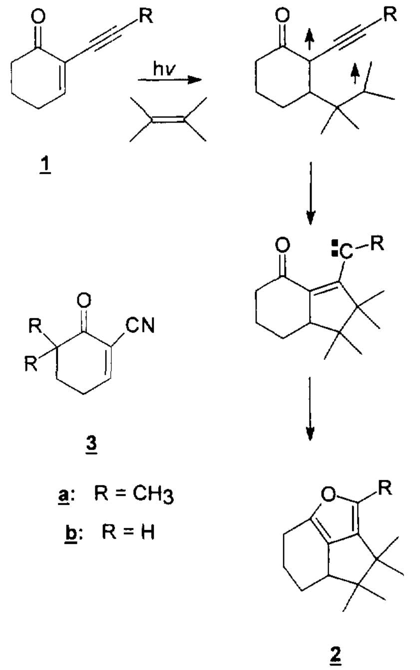
Abstract

While irradiation (350 nm) of the title cyanocyclohexenone **3a** in the presence of 2,3-dimethylbut-2-ene affords hexahydroindeno-1,2-oxazole **6** selectively, photolysis of **3a** in the presence of 2-methylbut-2-ene or isobutene gives mixtures of tricyclic 1,2-oxazoles and 2-oxobicyclooctane-1-carbonitriles, the product ratio oxazole/bicyclooctane decreasing with increasing I_p of the alkene. The constitution of the photoproducts indicate that oxazoles and bicyclooctanes result from two isomeric triplet 1,4-biradicals, formed by addition of the less substituted C-atom of the alkene to either of the olefinic C-atoms of triplet **3a**, respectively.

Keywords: Photocycloaddition; Irradiation; Cyanocyclohexenone

1. Introduction

Irradiation of 2-(alk-1-ynyl)-cyclohex-2-enones **1** in the presence of alkenes, e.g., 2,3-dimethylbut-2-ene, affords tricyclic furans **2** via addition of the alkene to C(3) of the triplet enone, 1,5-cyclization of the alkyl propargyl 1,4-biradical [1], and electrocyclic ring closure of the β-acylvinyl carbene [2]. Six-membered cyclic α-acylacrylonitriles, e.g., 2-cyano-cyclohex-2-enones **3a** [3] or **3b** [4], have only been prepared recently. Both **1** and **3** (Scheme 1) represent 2-carbinylcyclohex-2-enones, i.e., cyclohexenones bearing a digonal C-atom as substituent on C(2). Here, we report on photochemical reactions of **3a** with alkenes [5].



Scheme 1.

2. Results

Due to the very low yield of **3a** obtained in the bromination/dehydrobromination sequence from **4**, we improved the synthesis by converting **4** into ist trimethylsilyl enol ether **5** which was then dehydrosilylated with one equivalent of $Pd(OAc)_2$ [6] to give **3a** in 70% yield (Scheme 2).

Irradiation (350 nm) of **3a** in benzene in the presence of excess 2,3-dimethylbut-2-ene affords a single product **6** in 92% yield (after chromatography), whose ^{13}C NMR spectrum allows the unambiguous assignment of a tricyclic 1,2-oxazole structure. Irradiation of **3a** in the presence of an excess of 2-methylbut-2-ene affords a 1:3 mixture of two products **7** and **8**, isolated by chromatography in 4% and 15%, respectively. The major product **8** exhibits the same characteristic [7] ^{13}C NMR signals as **6**, its constitution being

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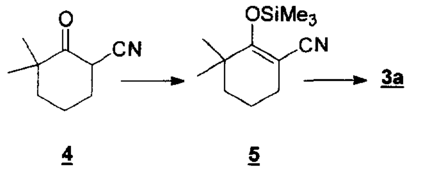
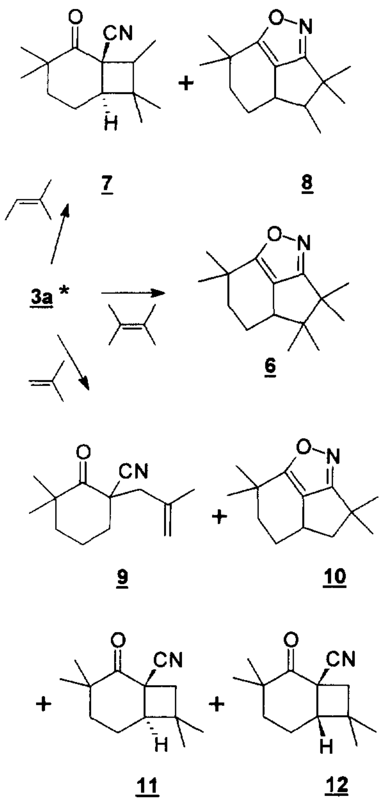


Scheme 2.

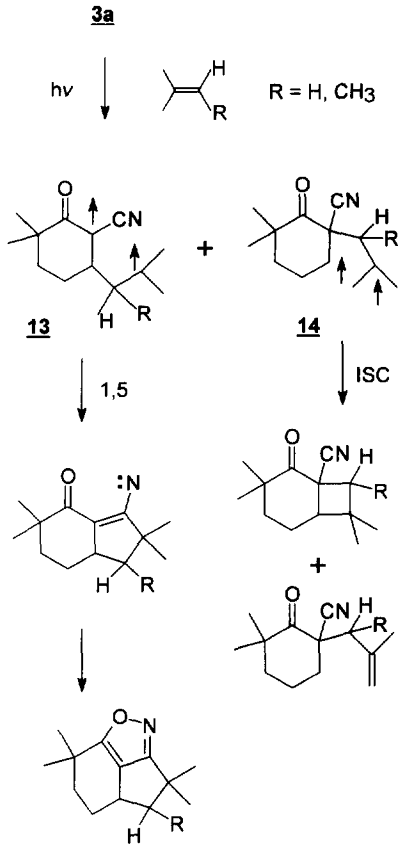


Scheme 3.

assigned by ist ^{1}H NMR spectrum, wherein the bridgehead methine proton appears as a *ddd* system. The assignment of the bicyclooctanone structure to **7** stems from ist ^{13}C NMR spectrum which shows typical C=O and C ≡ N signals, while its constitution becomes evident again from the ^{1}H NMR spectrum wherein the $CH(CH_3)$ methine proton appears as a simple quartet. Finally, irradiation of **3a** in benzene saturated with isobutene affords four products **9–12** in roughly equal amounts, chromatography allowing to isolate cyclohexanone **9** (5%), a 1:1 mixture of isoxazole **10** and bicyclooctanone **11** (7% and 6%), and bicyclooctanone **12** (5%). The assignment of the *trans* ring fusion to **7** and **11** and of the *cis* ring fusion to **12**, stemming from ^{13}C and ^{1}H NMR spectral data as well as similarities in R_f values of **7** and **11**, is tentative (Scheme 3).

3. Discussion

From studies on both 3-(alk-1-ynyl)-cyclohex-2-enones [8] and 3-cyanocyclohex-2-enones [9], it was known that triplet alkyl-propargyl- and alkyl-cyanoalkyl 1,4-biradicals undergo 1,5-cyclization to vinyl carbenes and nitrenes, respectively [10]. Compounds like **1** or **3** seem to be synthetically even more promising as on irradiation in the presence of alkenes they undergo two consecutive cyclization steps. In this context, the formation of **6**, **8** and **10** is noteworthy because these compounds represent the first examples of tricyclic[*c*,*d*]fused isoxazoles. One related dihydroisoxazole, obtained by intramolecular nitriloxide to alkene cycloaddition has been reported [11] as intermediate in the synthesis of a model insect antifeedant.



Scheme 4.

The constitution of the photocycloadducts of **3a** affords evidence for the occurrence of two isomeric triplet 1,4-biradicals **13** and **14**, formed by addition of the less hindered C-atom of the alkene to C(3) or C(2) of triplet **3a**, respectively. While **13** apparently undergoes selective 1,5-cyclization to a *β*-acylvinyl nitrene which then closes to the 1,2-oxazole, biradical **14** undergoes spin inversion to the singlet biradical followed by 1,4-cyclization to afford bicyclo[4.2.0]octan-2-ones (Scheme 4). From the three alkenes investigated, it becomes apparent that the relative amount of products derived from **14** increases in going from 2,3-dimethylbut-2-ene via 2-methylbut-2-ene to isobutene, i.e., reflecting either the increasing ionisation potential of the alkene or simply the decrease in steric hindrance in the approach of the less substituted C-atom of the alkene to the triplet enone. Further experiments to clarify this important mechanistic aspect are now in progress.

4. Experimental

^{1}H NMR (500 MHz), ^{13}C NMR (125.77 MHz) and mass (MS, 70 eV) spectra were obtained using Bruker DRX 500 and Varian MAT 311A spectrometers. Photolyses were performed in a Rayonet RPR-100 photoreactor equipped with 350 nm lamps. Chromatographic purification and separation of the photoproducts was achieved on silica gel (0.040–0.063 mm).

4.1. Synthesis of 3,3-dimethyl-2-(trimethylsilyloxy)-cyclohex-1-ene-1-carbonitrile (5)

To an argon degassed solution of **4** (2.26 g, 15 mmol) in CH_3CN (15 ml) are added triethylamine (1.89 g, 19 mmol) and chlorotrimethylsilane (2.04 g, 19 mmol). After stirring for 5 min at r.t. the solvent is evaporated, pentane (30 ml) is added to the residue, and the precipitated triethylamonium hydrochloride is filtered off and washed with pentane (10 ml). The solvent is then evaporated to afford crude **5** (3.27 g, 97%) as colourless oil. ^{1}H NMR (C_6D_6) δ: 0.21 (s, 9H), 0.75 (s, 6H), 1.02–1.06 (m, 4H), 1.77–1.80 (m, 2H). ^{13}C NMR (C_6D_6) δ: 1.1 (q), 18.6 (t), 26.7 (q), 27.2 (q), 36.4 (s), 37.9 (t), 90.1 (s), 119.9 (s), 170.3 (s). MS (*m/z*): 223 (M$^+$, 12%), 73 (100%).

4.2. Synthesis of 5,5-dimethyl-6-oxocyclohex-1-ene-1-carbonitrile (3a)

To an argon degassed solution of $Pd(OAc)_2$ (3.30 g, 14.7 mmol) in CH_3CN (80 ml) is added **5** (3.27 g, 14.5 mmol) in CH_3CN (10 ml). After stirring for 18 h at r.t. the mixture is filtered over Celite and the solvent evaporated. Diethyl ether (20 ml) is added and the filtration repeated. Evaporation of the solvent affords **3a** of > 95% purity (1.54 g, 70%). For spectral data cf. [3].

4.3. Irradiation of 3a in the presence of alkenes

An argon degassed solution of **3a** (100 mg, 0.68 mmol) in benzene (6 ml) containing either 2,3-dimethylbut-2-ene or 2-methylbut-2-ene (15 mmol), or saturated with isobutene, is irradiated for 12 h. After evaporation of the solvent, the residue is subject to chromatographic work-up on SiO_2 (12 g) using a 5:1 mixture of pentane/diethyl ether as eluent.

*4.3.1. **3a** and 2,3-dimethylbut-2-ene*

We obtained 3,3,4,4,7,7-hexamethyl-3,4,4a,5,6,7-hexahydroindeno[1,2-*c*,*d*]-1,2-oxazole (**6**), $R_f=0.3$, 145 mg (92%), m.p. 53–55°. ^{1}H NMR ($CDCl_3$) δ: 0.62 (s, 3H), 1.06 (s, 3H), 1.16 (s, 3H), 1.17 (s, 3H), 1.33 (s, 3H), 1.34 (s, 3H), 1.60–1.68 (m, 3H), 1.86 (ddd, $J=2$, 13, 13 Hz), 2.65 (dd, $J=6$, 10 Hz). ^{13}C NMR ($CDCl_3$) δ: 18.5 (q), 20.7 (q), 21.8 (q), 22.1 (t), 23.9 (q), 26.1 (q), 27.2 (q), 35.6 (s), 41.2 (d), 42.5 (t), 49.8 (s), 58.2 (s), 124.8 (s), 171.8 (s), 176.5 (s).

*4.3.2. **3a** and 2-methylbut-2-ene*

First, we obtained 1α,6β-2-oxo-3,3,7,7,8-pentamethylbicyclo[4.2.0]octane-1-carbonitrile (**7**), $R_f=0.4$, 5.2 mg (4%), colourless oil. ^{1}H NMR ($CDCl_3$) δ: 1.05 (s, 3H), 1.14 (d, $J=7$ Hz, 3H), 1.23 (s, 3H), 1.25 (s, 3H), 1.26 (s, 3H), 1.72–1.80 (m, 2H), 1.99–2.04 (m, 2H), 2.34 (q, $J=7$ Hz), 2.42 (dd, $J=6$, 11 Hz). ^{13}C NMR ($CDCl_3$) δ: 11.0 (q), 16.9 (q), 17.8 (t), 28.4 (q), 29.5 (q), 30.1 (q), 36.9 (t), 41.8 (s), 43.0 (d), 46.0 (s), 50.0 (s), 51.8 (d), 118.2 (s), 205.1 (s). MS (*m/z*): 219 (M$^+$,.5%), 69 (100%). Then, we gathered 3,3,4,7,7-pentamethyl-3,4,4a,5,6,7-hexahydroindeno[1,7-*c*,*d*]-1,2-oxazole (**8**), $R_f=0.3$, 21 mg (15%), colourless oil. ^{1}H NMR ($CDCl_3$) δ: 0.91 (m, 1H), 1.05 (d, $J=7$ Hz, 3H), 1.17 (s, 3H), 1.27 (s, 3H), 1.28 (s, 3H), 1.36 (s, 3H), 1.72 (m, 1H), 1.84 (m, 1H), 2.00 (m, 1H), 2.39 (ddd, $J=6$, 8, 9 Hz). ^{13}C NMR ($CDCl_3$) δ: 12.4 (q), 20.9 (q), 23.1 (q), 26.2 (q), 27.6 (q), 28.5 (t), 35.9 (s), 38.7 (d), 43.0 (t), 47.1 (s), 63.0 (d), 126.6 (s), 171.9 (s), 177.6 (s).

*4.3.3. **3a** and isobutene*

Here, we first obtained 3,3-dimethyl-1-(2-methylprop-2-enyl)-2-oxocyclohexane-1-carbonitrile (**9**), $R_f=0.4$, 5 mg (4%), colourless oil. ^{1}H NMR ($CDCl_3$) δ: 1.15 (s, 3H), 1.43 (s, 3H), 1.63 (m, 2H), 1.84 (s, 3H), 1.85 (m, 2H), 2.15 (m, 1H), 2.35 (m, 1H), 2.37 and 2.80 (AB, $J=14$ Hz, 2H), 4.82 (s, 1H), 4.98 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 18.5 (t), 23.8 (q), 27.3 (q), 27.6 (q), 36.5 (t), 40.1 (t), 42.7 (t), 46.5 (s), 47.1 (s), 116.9 (s), 117.0 (t), 139.7 (s), 205.3 (s). Then, we gathered a 7:6 mixture of 3,3,7,7-tetramethyl-3,4,4a,5,6,7-hexahydroindeno[1,2-c,d]-1,2-oxazole (**10**) and 1α,6β-2-oxo-3,3,8,8-tetramethyl-bicyclo[4.2.0]octane-1-carbonitrile (**11**), $R_f=0.3$, 18 mg (13%). **10**: ^{1}H NMR ($CDCl_3$) δ: 0.97 (m, 1H), 1.17 (s, 3H), 1.26 (s, 3H), 1.27 (s, 3H), 1.36 (s, 3H), 1.68–1.75 (m, 2H), 1.85 (dd, $J=8$, 12 Hz), 1.93–1.98 (m, 2H), 2.33 (dd, $J=6$, 12 Hz), 2.84 (m, 1H). ^{13}C NMR ($CDCl_3$) δ: isoxazole C-atoms 128.6 (s), 172.1 (s), 177.1 (s). **11**: ^{1}H NMR ($CDCl_3$) δ: 1.11 (s, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 1.47 (s, 3H), 1.76–1.82 (m, 2H), 2.05 (m, 1H), 2.13 and 2.27 (AB, $J=11$ Hz, 2H), 2.21 (m, 1H), 2.44 (dd, $J=6$, 12 Hz). ^{13}C NMR ($CDCl_3$) δ: 120.3 (s, **CN**), 204.5 (s, **CO**). Finally, we obtained 1α, 6α-2-oxo-3,3,8,8-tetramethylbicyclo[4.2.0]octane-1-carbonitrile (**12**), $R_f=0.1$, 5 mg (4%), colourless oil. ^{1}H NMR ($CDCl_3$) δ: 0,94 (s, 3H), 1.19 (s, 3H), 1.23 (s, 3H), 1.33 (s, 3H), 1.49–1.56 (m, 2H), 1.85–1.91 (m, 2H), 2.34 and 2.51 (AB, $J=12$ Hz, 2H), 3.07 (dd, $J=6$, 7 Hz). ^{13}C NMR ($CDCl_3$) δ: 18.5 (t), 23.9 (q), 25.3 (q), 27.2 (q), 31.3 (q), 36.0 (s), 36.1 (s), 36.8 (t), 42.4 (t), 45.2 (s), 53.4 (d), 120.8 (s), 209.9 (s).

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