Intramolecular Photochemical Cycloaddition of a Vinylogous Imide. Crystal and Molecular Structure of a Tetracyclic $C_{17}H_{25}O_2N$ Product

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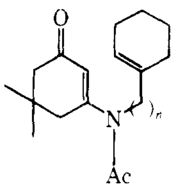
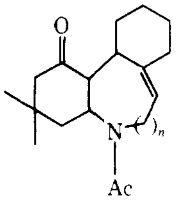
Received November 7, 1978

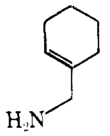
Pyrex-filtered irradiation of *N*-acetyl-3-(*N*-cyclohexenylmethyl)amino-5,5-dimethyl-2-cyclohexen-1-one (1) provides an acyl migration product and an intramolecular cycloaddition product. The cycloaddition reaction was shown to be thermally reversible. The structure of the tetracyclic product was inferred from chemical and spectroscopic data, and the stereochemistry was fully defined via X-ray crystal-structure analysis. Crystal data (from single-crystal diffractometry, Mo $K\alpha_1$, $\lambda = 0.70926$ Å, at $T = 20 \pm 1$ °C): $a = 20.815$ (8), $b = 10.875$ (2), $c = 6.625$ (1) Å; $P2_12_12_1$, $Z = 4$; $d_c = 1.218$ and $d_o = 1.19$ g cm^{-3} by flotation in NaBr solutions; $F(000) = 600$.

Recently we reported that irradiation of **2** and **3** produced the ene-type products **4** and **5**, respectively.[2] In contrast, other vinylogous imides have been reported to undergo intermolecular[3,4] and intramolecular[5,6] cycloadditions or acyl migration[7] when exposed to Pyrex-filtered radiation. Thus, it was of interest to investigate the photochemistry of **1** since a closely related case has been described in which cycloaddition occurs.[6]


1, $n = 1$
2, $n = 2$
3, $n = 3$


4, $n = 1$
5, $n = 2$

The required unsaturated amine **6** was prepared from cyclohexanone cyanohydrin by dehydration and lithium aluminum hydride reduction. Condensation of dimedone and amine **6** produced the vinylogous amide **7**, which in turn provided **1** by acetylation.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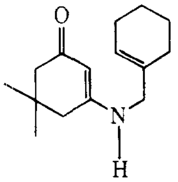
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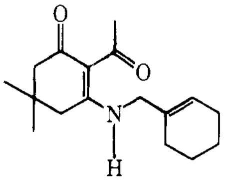
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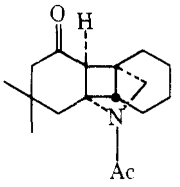
A dilute cyclohexane solution of **1** was irradiated through Pyrex for 2 h to afford a mixture of two products. The minor compound was assigned structure **8** on the basis of its NMR spectra and in analogy with the reactions of other vinylogous imides.[7] Thus, the proton spectrum displayed a single olefinic resonance at δ 5.61 and a very broad absorption at δ 12.70 due to the hydrogen-bonded NH, while the carbon spectrum had five downfield nonprotonated carbon resonances at δ 200.2, 194.0, 171.8, 132.2, and 107.3 and an olefinic methine resonance at δ 123.9.

The gross structure of the major compound, **9**, was determined by chemical and spectroscopic techniques, and the stereochemistry was fully defined by X-ray crystal-structure analysis. The production of the azabicyclo[2.1.1]hexane ring system was anticipated on the basis of previous results,[6,8] and this was confirmed prior to X-ray analysis by base hydrolysis of **9** and deuterium exchange of active hydrogens in the resulting diketone **10**. The ^{13}C NMR spectrun of the deuterated material lacked four carbon absorptions; thus, the alternative orientation for the cycloaddition step was eliminated. Enone **11**, the presumed intermediate in the formation of **10**, was produced by treatment of **9** with potassium *tert*-butoxide in *tert*-butyl alcohol.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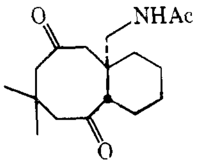
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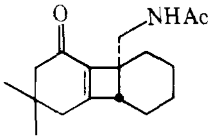
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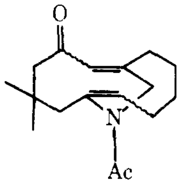
Although four chiral centers were produced in the formation of **9**, only two nonadjacent hydrogens were present on the four-membered ring. Thus, little stereochemical information was available from the ^{1}H NMR spectrun. Nevertheless, the relative stereochemistry of three of the four centers could be reasonably assigned. The azamethylene bridge must be attached in a cis manner. Based on Tamura's[6] results with closely related compounds, it was expected that **9** would undergo base-induced epimerization only if the A–B fusion was trans. Since no change occurred on base treatment of **9**, a cis fusion of the ketone-containing ring and the cyclobutane was assumed. Hence, only the nature of the cyclohexane and cyclobutane ring fusion was uncertain. This final point was resolved by X-ray analysis (vide infra).

The heavy substitution of the cyclobutane ring in **9** suggested that it might be thermally labile at reasonable temperatures. It was of interest to test this hypothesis since thermal reversal of the cycloaddition reaction could conceivably produce the bridged large ring system **12** and provide a route to macrocyclic rings. When **9** was heated to 400 °C, **1** was produced in 86% yield along with several minor products. No evidence for systems such as **12** was found, and the minor products were not investigated further.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The bond lengths and angles among the nonhydrogen atoms of the atoms not involved in the bridged cyclobutane ring are unexceptional. The average bond distances and angles in the cyclobutane ring (1.560 Å and 84.2° respectively) agree well with those reported for a number of similar compounds.[9] The conformation of the cyclobutane ring is puckered, with a di-

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hedral angle of 51.5°, which reflects the high degree of strain introduced by the linkage of the $-CH_2-N(Ac)-$ group to C-1 and C-7. The conformations of the two resulting five-membered rings are also highly puckered, as required by fusion to the cyclobutane fragment. The two cyclohexane rings are able to assume the minimally strained chair conformations despite the fact that one of them is trans-fused to the cyclobutane ring as shown in Figure 1.

Experimental Section

Melting points were measured on a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer and UV spectra on a Cary-17 spectrophotometer. Unless otherwise noted, ^1H and ^{13}C NMR spectra were obtained in deuteriochloroform solution. Proton spectra were recorded on Varian T60A and HA-100 spectrometers, and chemical shifts are reported in parts per million downfield from internal Me_4Si. Carbon spectra were recorded on a Nicolet TT-14 spectrometer, and chemical shifts, reported in parts per million downfield from Me_4Si, were determined using the solvent signal as an internal standard.

Photochemical reactions were carried out using a Pyrex immersion well and a Hanovia 450-W medium-pressure lamp. All experiments requiring anhydrous conditions were conducted under a positive pressure of dry nitrogen in glassware that had been flamed in a dry nitrogen stream. Tetrahydrofuran was distilled from lithium aluminum hydride immediately prior to use. Combustion analyses were carried out by Galbraith Laboratories, Knoxville, Tenn.

Cyclohexenylmethylamine (6). A solution containing 70 g of 1-cyanocyclohexene[10] in 400 mL of ether was slowly added over a period of 3 h to 24 g of lithium aluminum hydride in 200 mL of ether at −20 °C. After the resulting mixture was stirred overnight, the excess hydride was decomposed by cautious addition of 25% potassium hydroxide solution. The solution was filtered and the gritty precipitate washed well with ether. The organic solutions were combined and distilled to provide 29 g of unsaturated amine **6**: bp 58–60 °C (25 torr); IR (neat) 3.01, 3.07, 5.98 μm; ^1H NMR δ 1.21 (2 H, s), 1.38–2.37 (8 H, m), 3.14 (2 H, s), 5.34 (1 H, br s).

3-(*N*-Cyclohexenylmethyl)amino-5,5-dimethyl-2-cyclohexen-1-one (7). A solution of 2.8 g of dimedone and 1.9 g of amine **6** in 75 mL of benzene was refluxed overnight with continuous removal of water. The benzene was evaporated to provide a solid residue which was chromatographed on alumina with benzene. The yellow solid (3.4 g) obtained in this fashion was sufficiently pure for acetylation. An analytical sample was prepared by rechromatographing this material on alumina followed by recrystallization from ether–methylene chloride to give colorless crystals: mp 118–119 °C; IR ($CHCl_3$) 2.91, 3.08, 6.30, 6.62 μm; ^1H NMR δ 1.07 (6 H, s), 1.39–2.10 (8 H, m), 2.14 (2 H, s), 2.22 (2 H, s), 3.55 (2 H, br d, *J* = 6.0 Hz), 5.02 (1 H, s), 5.33 (1 H, br s), 5.57 (1 H, br s). ^{13}C NMR: CH_3 carbons at δ 28.0 (2 C); CH_2 carbons at δ 22.0, 22.3, 24.7, 26.4, 43.2, 49.0, and 50.2; CH carbons at δ 95.3 and 123.8; C carbons at δ 32.5, 132.7, 163.3, and 196.3. Anal Calcd for $C_{15}H_{23}NO$: C, 77.21; H, 9.93; N, 6.00. Found: C, 77.31; H, 9.81; N, 5.96.

***N*-Acetyl-3-(*N*-cyclohexenylmethyl)amino-5,5-dimethyl-2-cyclohexen-1-one (1).** A solution of 17.5 g of vinylogous amide **7** and 20 mL of pyridine in 200 mL of dry tetrahydrofuran was stirred under nitrogen at 0 °C while 7.85 g of acetyl chloride in 25 mL of tetrahydrofuran was slowly added. The mixture was stirred at room temperature for 1 h and then filtered to remove precipitated pyridine hydrochloride. The precipitate was washed with methylene chloride, and the organic solutions were combined and extracted with 10% hydrochloric acid. Evaporation of the organic solvents provided an oil containing the desired vinylogous imide **1** and diacylated (O,N) material. Without separation of the crude mixture, the diacylated material was hydrolyzed by stirring the crude product in 50 mL of methanol containing 10 mL of 10% hydrochloric acid. After 24 h, methylene chloride was added and the layers were separated. The aqueous layer was extracted with methylene chloride, the organic layers were combined and dried over potassium carbonate, and the solvent was removed at reduced pressure to provide 17.5 g of **1**. Recrystallization from ligroine gave colorless plates: mp 68–69 °C; IR ($CHCl_3$) 6.01, 6.20 μm; ^1H NMR δ 1.12 (6 H, s), 1.33–2.02 (8 H, m), 2.13 (3 H, s), 2.17 (2 H, s), 2.47 (2 H, s), 4.10 (2 H, br s), 5.53 (1 H, br s), 5.67 (1 H, s). ^{13}C NMR: CH_3 carbons at δ 23.0 and 28.0 (2 C); CH_2 carbons at δ 22.1, 22.2, 24.8, 26.2, 43.3, 50.8, and 53.4; CH carbons at δ 121.6 and 124.4; C carbons at δ 33.5, 132.7, 160.5, 170.0, and 199.2. Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.25; H, 8.85; N, 4.93.

Irradiation of 1. A degassed solution of 6.0 g of vinylogous imide 1 in 800 mL of cyclohexane was irradiated through Pyrex for 2 h. The solvent was evaporated and the residue recrystallized several times from ether–ligroine (1:1) to afford 2 g of crystalline **9**: mp 154–155 °C; IR ($CHCl_3$) 5.88 (s), 6.12 (s) μm; ^1H NMR δ 1.05 (3 H, s), 1.13 (3 H, s), 1.14–2.60 (17 H, complex m), 2.02 (3 H, s), 3.30 (2 H, AB q, *J* = 8.0 Hz). ^{13}C NMR: CH_3 carbons at δ 22.6, 27.7, and 33.7; CH_2 carbons at δ 21.0, 21.2, 23.8, 24.2, 39.4, 50.9, and 54.3; CH carbons at δ 50.9 and 62.4; C, carbons at δ 36.1, 47.4, 79.8, 170.2, and 209.1. Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.50; H, 9.36, N, 5.10.

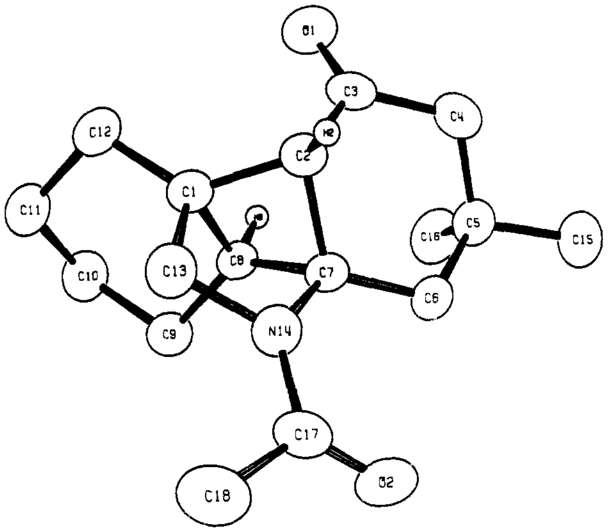

Figure 1. X-ray analysis structure of photoproduct **9**. Boundary thermal ellipsoids are drawn at the 50% probability level.

The combined mother liquors from the recrystallization of **9** were chromatographed on alumina with benzene to provide an additional 480 mg of **9** and 1.8 g of **8**. The latter material was further purified by preparative-layer alumina chromatography to give a white crystalline product: mp 172–173 °C; IR ($CHCl_3$) 3.18, 6.10 (s), 6.26–6.42 (vs) μm; ^1H NMR δ 1.01 (6 H, s), 1.40–2.10 (8 H, m), 2.21 (2 H, s), 2.41 (2 H, s), 2.49 (3 H, s), 3.81 (2 H, d, *J* = 6.0 Hz), 5.60 (1 H, br s), 12.70 (1 H, br s). ^{13}C NMR: CH_3 carbons at δ 27.8 (2 C) and 32.2; CH_2 carbons at δ 21.7, 21.9, 24.5, 26.1, 39.5, 48.9, and 51.6; CH carbon at δ 123.9; C carbons at δ 30.1, 107.5, 132.1, 171.6, 193.8, and 200.0. Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.97; H, 9.00; N, 4.93.

Diketone 10. A solution of 200 mg of **9** in 10 mL of 10% potassium hydroxide solution and 10 mL of methanol was refluxed for 5 h, cooled, and diluted with 25 mL of water. The mixture was extracted twice with methylene chloride, and the organic fractions were combined and dried over anhydrous potassium carbonate. Evaporation of the solvent provided a solid residue which was chromatographed on alumina with moist ether to give 158 mg of crystalline material: mp 178–179 °C; IR ($CHCl_3$) 2.95, 5.95 μm; ^1H NMR δ 1.10 (6 H, s), 1.30–3.15 (17 H, complex m), 2.00 (3 H, s), 4.18 (2 H, dd, *J* = 9.0 and 14.0 Hz), 6.38 (1 H, br s). ^{13}C NMR: CH_3 carbons at δ 22.9, 24.4, and 33.7; CH_2 carbons at δ 20.3, 24.2 (2 C), 35.3, 36.0, 53.6, 55.6, and 57.4; CH carbon at δ 60.9; C carbons at δ 36.9, 42.8, 169.6, 212.6, and 213.3. Anal. Calcd for $C_{17}H_{27}NO_3$: C, 69.59; H, 9.28; N, 4.77. Found: C, 69.74; H, 9.44; N, 4.65.

Deuteration of 10. A solution containing 200 mg of **10** and 10% sodium methoxide in methanol-*d* was stirred at room temperature for 2 weeks. After addition of 5 mL of deuterium oxide, the reaction mixture was extracted three times with 10-mL portions of benzene. The organic solutions were combined and dried over anhydrous potassium carbonate. Evaporation of the solvent at reduced pressure provided 184 mg of a crystalline solid whose ^{13}C NMR spectrum lacked decoupled absorptions at δ 60.9, 57.4, 55.6, and 53.6, but otherwise the same as that of **10**.

Cyclobutene 11. A solution of 210 mg of **10** and 15 mg of potassium *tert*-butoxide in 10 mL of *tert*-butyl alcohol was refluxed for 0.5 h. The solvent was removed at reduced pressure, and the residue was washed well with benzene. Evaporation of the benzene provided an oil which was passed through a short alumina column in ether to give 110 mg of oily enone **11**: IR ($CHCl_3$) 2.95, 5.95 (s) μm; ^1H NMR δ 1.02 (6 H, s), 1.33–2.47 (14 H, complex m), 2.00 (3 H, s), 2.50–3.47 (4 H, m), 6.38 (1 H, br s).

Pyrolysis of 10. An evacuated sealed glass tube containing 250 mg of **10** was placed in a 400 °C oven for 2 min. After being cooled, the tube was opened and the contents were submitted to preparative-layer alumina chromatography. The major product (214 mg) was shown to be vinylogous imide **1** by comparison of ^{1}H and ^{13}C NMR spectra.

Intensity Data, Structure Determination, and Refinement. Integrated intensities were measured with an Oak Ridge computer-controlled diffractometer by the θ–2θ scan technique, to a limit of $(\sin \theta)/\lambda \leq 0.60$ Å^{-1}, using Nb-filtered Mo Kα radiation. Of the 1540 unique reflections measured, 1423 had intensities greater than 3 times their esd's and were used in the subsequent analysis. Each intensity was assigned an estimated variance, $\sigma^2(I)$, based on counting statistics plus an empirical correction of $(0.02I)^2$, determined during the final cycles of refinement from plots of $|\Delta F|^2$ vs. $|F_o|^2$.

The structure was solved using the MULTAN program[11] after calculating E's assuming an anisotropic thermal model with the ORESTES program.[12] The structure was refined by least-squares in two blocks (nonhydrogen atoms anisotropic, hydrogens isotropic), the refinement converging on a final conventional $R(F)$ value of 3.3% (4.4% weighted) and a goodness-of-fit of 1.49. No significant features were found in a final difference map. The programs used subsequent to structure solution were from the XRAY system.[13]

Acknowledgment. Research was sponsored by the Division of Materials Sciences, U.S. Department of Energy, under contract W-7405-eng-26 with the Union Carbide Corp. and by the National Science Foundation (CHE 75-21386). We would like to thank Mr. J. P. Fillers for assistance with the data collection. The carbon NMR spectrometer used in this investigation was purchased in part with funds provided by the National Science Foundation (CHE 76-05478).

Registry No.—**1**, 69089-06-1; **6**, 32917-19-4; **7**, 69089-07-2; **8**, 69089-08-3; **9**, 69120-34-9; **10**, 69089-09-4; **11**, 69089-10-7; 1-cyanocyclohexene, 1855-63-6; dimedone, 126-81-8.

Supplementary Material Available: Tables Ia and Ib, final parameters of the anisotropically and isotropically refined atoms, respectively, and Figures 2 and 3, bond angles and bond lengths, respectively, for compound **9** (4 pages). Ordering information is given on any current masthead page.

References and Notes

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Steroid Photochemistry. Photocycloaddition of Cyclopropylenones to Dienes. An Example of a [$_\pi 2 + _\pi 2 + _\pi 2 + _\sigma 2$] Addition

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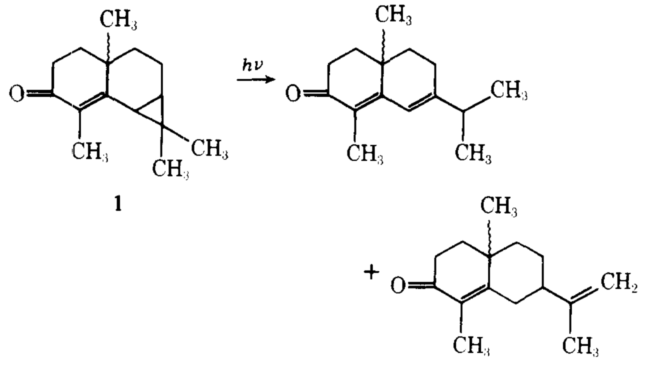
Received October 18, 1978

The photocycloaddition of a 3-keto-4,6-diene steroid **6** to 2,3-dimethylbutadiene formed the [4:4:4] ring adduct **7**, as well as the alternative [5:4:5] ring adduct **8**, which were differentiated mainly by their NMR spectra. The major product was the trans-4α,5β-[4 + 2] adduct **9**. Two other products were the 6α,7α- and 6β,7β-cis-[4 + 2] adducts. In agreement with past results, the direct irradiation of the 6α,7α- and 6β,7β-cyclopropylenones **4** and **5** demonstrated their remarkable photostability. They were also stereochemically stable when irradiated in the presence of dienes. However, the irradiation of both **4** and **5** in the presence of 2,3-dimethylbutadiene led to the same photoproduct **13** where both the double bond and the 6,7-cyclopropane bond of the steroids had added to both double bonds of the diene to form a [5:4:6] ring adduct. An equivalent head-to-head adduct is formed with 1-acetoxybutadiene. The photocycloaddition is not quenched with 3,3,4,4-tetramethyldiazetidine-1,2-dione indicating the singlet state, or a very short lived triplet, as the reactive state.

The investigation of the photochemistry of conjugated cyclopropylenones has been primarily concerned with either bond reorganizations of the cyclopropyl group or the influence of the cyclopropyl group upon the di-π-methane rearrangement. Direct irradiation of the epimeric *gem*-dimethylcyclopropylenones **1** caused opening of the external cyclopropyl bond and formation of two dienones.[1,2] Incidental to these results was the observation that these cyclopropylenones do not interconvert under the irradiation conditions, i.e., they maintain their stereochemical integrity.[1]



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In direct contrast to this facile ring opening was the total lack of reactivity found by Schaffner when the 6,7-cyclopropyl-3-keto-4-ene steroids were irradiated.[3] Again these isomeric cyclopropyl steroids **2** and **3** were not interconverted upon prolonged irradiation.[4] When the cyclopropylenone chromophore was part of a seven-membered ring, a bicyclic system was formed by a formal [$_\pi 2 + _\sigma 2$] cycloaddition between the internal cyclopropane bond and the double bond.[5] Our interest in this area stems from our investigations of the

0022-3263/79/1944-1382$01.00/0