

Synthesis and photolysis behaviour of 2-(Δ^1 -pyrazoliny)- Δ^3 (1,3,4) oxadiazolines. Application to the synthesis of *gem*-dimethylcyclopropane ketone

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Received 26 September 1999; accepted 7 October 1999

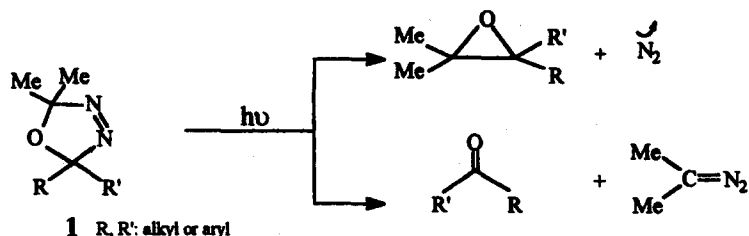
Abstract

The photolysis of 2-(Δ^1 -pyrazoliny)- Δ^3 (1,3,4) oxadiazoline **5** led to exclusive formation of *gem*-dimethylcyclopropane ketone **6**. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Keywords: cycloaddition; pyrazoline; oxadiazoline; irradiation.

The *gem*-dimethylcyclopropane unit is a key structural feature of many valuable natural products^{1,2} such as phorbol, aristolone and chrysanthemic acid.

So far, access to this element have relied primarily upon photolysis of Δ^1 -pyrazoline. Thus, Van Auken and Rinehart³ have shown that the stereochemistry of the small cycles thus obtained in this way is, in general, the same as that of starting enones. Thus, photolysis of 5,5-dimethyl- Δ^3 (1,3,4) oxadiazoline **1** can lead to the formation of an oxirane and/or to recovered starting enone along with the reacting 2-diazopropane^{4–6} (Scheme 1).



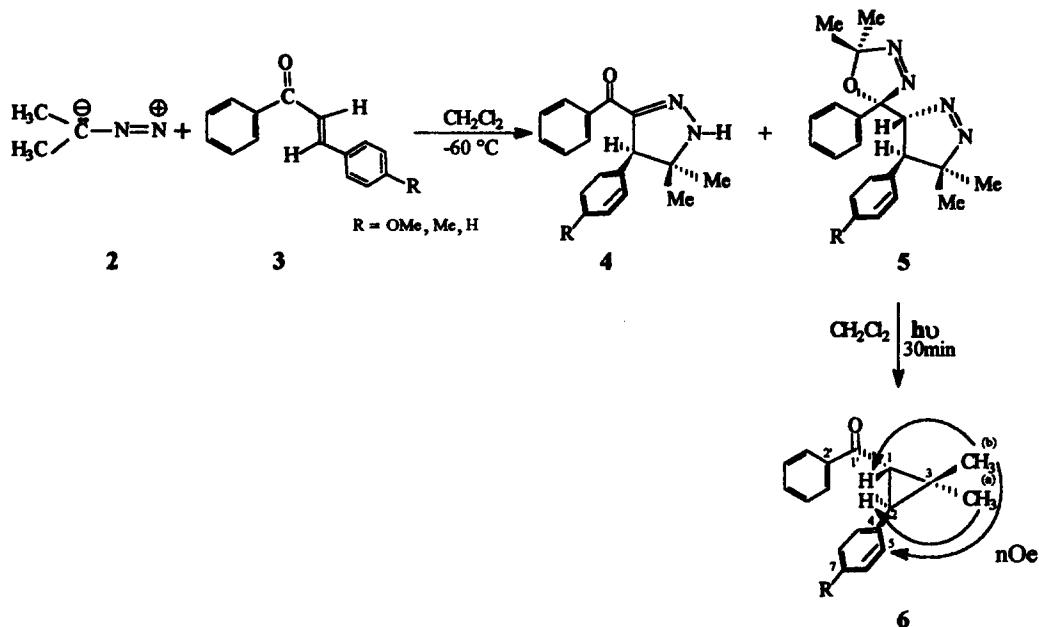
Scheme 1.

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Previously, the photolysis of Δ^3 -(1,3,4) oxadiazolines and Δ^1 -pyrazoline have been the subject of separate studies.^{3,5,6}

We wish to report herein on our own work on the photolysis of compound **5** whose structure comprise both the oxadiazoline and pyrazoline moieties.

In addition to the expected cycloaddition adduct **4**, compound **5** was also obtained in 20% yield upon reaction of a 2-diazopropane (DAP)⁴ **2** and an α,β -unsaturated ketone **3** at low temperature (-60°C)⁷⁻⁹ (Scheme 2).



Scheme 2.

Irradiation of **5** in dry dichloromethane at room temperature led to exclusive formation of *gem*-dimethylcyclopropane **6**¹⁰ (Scheme 2), whose structure was further secured through a detailed ¹³C NMR study of the photolysis products. Thus, a signal at 197.5 ppm¹⁰ was attributed to the aromatic carbonyl group C₁'. The *gem*-dimethylcyclopropane structure was deduced from an analysis of HMBC spectra which indicate that the methyl protons H_a and H_b correlate with carbon atoms C₁, C₂, C₃ via ²*J* and ³*J* coupling constants, whereas protons H₁ and H₂ exhibit correlations with carbons C₂, C₃ and C₁, C₃, C₄, respectively. The relative stereochemistry of compound **6** was established through an analysis of its NOESY spectrum.

The *trans* relationship between protons H₁ and H₂ was deduced from the observation of an NOE effect between H₁ and the methyl protons H_b, while H₂ correlates with the methyl protons H_a. In addition, the NOE effect between the aromatic proton H₅ and the methyl group H_b was further evidence of the spatial structure of compound **6** (Scheme 2).

In conclusion, this study demonstrates that the *gem*-dimethylcyclopropanes subunit which is often incorporated into biologically important natural products can be easily obtained in a two-step sequence from α,β -unsaturated ketones. Additionally, the present work provides further evidence that the key step in this transformation i.e, the photolysis of 2-(Δ^1 -pyrazolynyl)- Δ^3 (1,3,4) oxadiazolines intermediates, does proceed with retention of configuration.

Acknowledgements

We wish to thank Dr. Olivier Laprevote for help in mass spectroscopy analysis.

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9. Preparation of **5a**: small fractions of 2-diazopropane (10 ml, 2.8 M ethereal solution) were added gradually to a solution of enone **3a** (2 g, 1.5 mmol) in dry dichloromethane (100 ml) at -60° . After enone **3a** had totally disappeared, a new product **5a** was noticed beside Δ^2 -pyrazoline **4a**. Products **4a** and **5a** were separated by column chromatography (SiO₂: hexane/ethylacetate 8:2). Product **5a** crystallized from CH₂Cl₂–hexane (20%) mp 110°C. IR [ν cm⁻¹] (KBr): 950–1080; 1520; 2940. ¹H NMR (300 MHz, CDCl₃): δ 0.79 (s, 3H, CH_{3(a)}); 1.36 (s, 3H, CH_{3(c),(d)}); 1.51 (s, 3H, CH_{3(b)}); 1.58 (s, 3H, CH_{3(c),(d)}); 3.69 (s, 3H, OCH₃); 5.62 (d, 1H, H_{3'}); 2.68 (d, 1H, H_{4'}) J_{H3'-H4'}=9.8 Hz; 6.53 (d, 2H, H_{8',10'}); 6.61 (d, 2H, δ H_{7',11'}) AA'BB'; 7.05–7.46 (m, 5H, H_{phén}). ¹³C NMR (75.47 MHz, CDCl₃): δ 22 (CH_{3(a)}); 24.4 (CH_{3(c),(d)}); 25.1 (CH_{3(b)}); 26.6 (CH_{3(c),(d)}); 55.3 (OCH₃); 95.25 (C_{3'}); 49.8 (C_{4'}); 90.9 (C_{5'}); 122.7 (C₂); 122.8 (C₅). MS (FAB+) *m/z*=379 ([MH⁺], 61).
10. Preparation of **6a**: 600 mg (1.6 mmol) of 2-(Δ^1 -pyrazoliny)- Δ^3 (1,3,4) oxadiazoline **5a** was diluted in 100 mL of dry dichloromethane, and was irradiated at 300 nm in a Rayonet apparatus for 30 min. A yellow colour was observed during the reaction. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (SiO₂: hexane/CH₂Cl₂ 5:1) to provide **6a** (111 mg, 25%) as a yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 1.12 (s, 3H, CH_{3(a)}); 1.26 (s, 3H, CH_{3(b)}); 3.78 (s, 3H, OCH₃); 3.05 (d, 1H, H₁); 2.82 (d, 1H, H₂). Syst AB J_{H1-H2}=7 Hz. ¹³C NMR (75.47 MHz, CDCl₃): δ 19.7 (CH_{3(a)}); 21.7 (CH_{3(b)}); 54.7 (OCH₃); 36.1 (C₁); 37.32 (C₂); 32.5 (C₃); 138.5 (C₄); 157.7 (C₇); 197.5 (C_{1'}); 141.5 (C_{2'}).