

TETRACYCLIC DITERPENOIDS BY INTRAMOLECULAR C-ALKYLATION
OF $\gamma\delta$ -UNSATURATED DIAZO KETONES

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The acid catalyzed decomposition of $\gamma\delta$ -unsaturated diazo ketones has been indicated as a potentially useful synthetic method for the preparation of the [3.2.1]octane moiety present in several tetracyclic diterpenoids. In this connection a number of diazo ketones derivatives of hydroaromatic systems chosen as simplified models for preliminary studies has been prepared and their acid catalyzed decomposition shown to lead to the formation of cyclopentanones as the only annelation products.¹

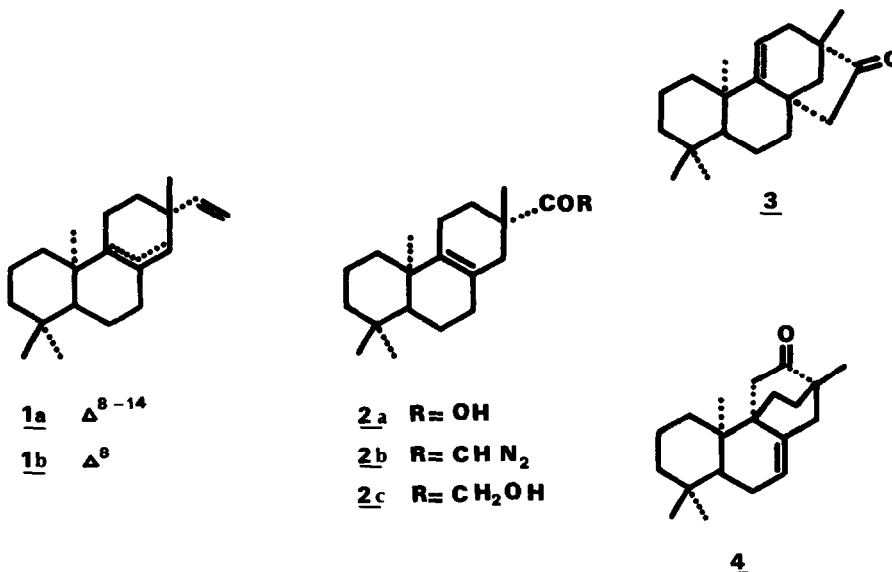
An important role in the selectivity of this annelation reaction can be attributed to the Ar₁-5 or benzylic π -bond participation in the displacement of nitrogen from the protonated diazo ketones. Aiming to find a direct synthetic route for the preparation of tetracyclic diterpenoids of the stachane skeletal type we have examined, as a continuation of previous work in this area,² the acid catalyzed decomposition of diazo ketones prepared from natural tricyclic diterpenes with pimarane skeleton chosen as precursors.

The starting diazo ketones 2b and 6b were easily prepared by the following procedure: the pimaric derivative 1a² readily undergoes an acid-catalyzed isomerization³ to afford the compound 1b. [δ : 0.85, 0.90, 0.95, 0.97 (each s, Me₄)]⁴ which was converted into the carboxylic acid derivative 2a [δ : 0.85, 0.90, 0.95, 1.15 (each s, Me₄), 11,3 (m, COOH); ν_{\max} : 1690] by permanganate-periodate oxidation of the vinyl side chain.²

The sodium salt of 2a was then sequentially treated with oxalyl chloride (1.5 molar equiv.) and diazomethane (3 molar equiv.) to give the diazo ketone 2b in 90% yield [δ : 5.35 (s, CHN_2); ν_{max} : 1630, 2110, 3120].

When 2b was treated in ether with sulphuric acid (5%) at r.t. for 15' an unseparable mixture (60:40) (70% yield) of the two isomeric ketones 3 [δ : 0.92, 0.97, 0.98, 1.12 (each s, Me_4), 5.28 (m, 11-H); ν_{max} : 1730] and 4 [δ : 0.87, 0.90, 1.02, 1.10 (each s, Me_4), 5.50 (m, 7-H); ν_{max} : 1700], respectively, was obtained.

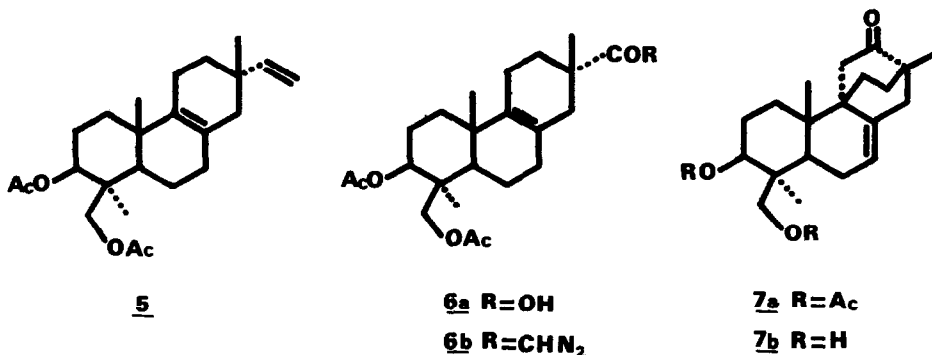
The hydroxy-methyl ketone 2c [δ : 0.88, 0.90, 1.05, 1.15 (each s, Me_4), 4.35 (s, $-\text{CH}_2\text{-OH}$); ν_{max} : 1710, 3500] was quantitatively obtained as the only product when $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (1.1 molar equiv.) was used in the decomposition of 2b. This product was formed by solvent participation, followed by hydrolysis during the work-up



As a further attempt to find a selective method for the synthesis of the [3.2.1] octanone system, the method was extended to the isopimaric diazo ketone 6b [δ : 5.38 (s, CHN_2); ν_{max} : 1630, 2110, 3120] prepared in 90% yield from the acid 6a [δ : 1.0, 1.05, 1.25 (each s, Me_3), 2.0 (s, 2 x OCOCH_3), 10.2 (m, COOH)] starting from isovirescenol B(5).³

Treatment of 6b with sulphuric acid or $\text{BF}_3 \cdot \text{Et}_2\text{O}$, under the above conditions led to the formation of 7a [δ : 0.98, 0.99, 1.01 (each s, Me_3), 2.0 (s, OCOCH_3),

5.30 (m, 7-H)] as the only product in 80% yield. 7a was hydrolyzed with NaOH (5% in MeOH) at r.t. for 2 hrs to the ketoalcohol 7b [δ : 0.90, 1.0, 1.26 (each s, Me₃); ν_{\max} : 1720].



Our results indicate that when the annelation reaction is carried out starting from diazo-ketonic intermediates deprived of stereoelectronic driving forces, the outcome of the reaction is subject to subtle steric factors and, therefore, the annelation products are not predictable; thus, in our case, while the acid decomposition of the pimanic diazo ketone 2b led to a mixture of the annelation products 3 and 4, the decomposition of isopimanic diazo ketone 6b led to the selective formation of the six membered ring derivative 7b. This last result, which has never been reported previously, suggests that in an appropriate steric environment the acid catalyzed decomposition of unsaturated diazo-ketones can be utilized for the preparation of the elusive 2.2.2 octane ring system.

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FOOTNOTES AND REFERENCES

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- 2) P. Ceccherelli, M. Tingoli, M. Curini, R. Pellicciari, Tetrahedron Lett., in press.
- 3) J. Polonsky, Z. Baskevitch, N. Cagnoli Bellavita and P. Ceccherelli, J. C. S. Chem. Comm., 1404 (1968).
- 4) New compounds gave satisfactory analytical values. NMR (δ) spectra were measured at 60 MHz in CDCl_3 vs. Me_4Si as internal reference. IR (ν_{max}) spectra were run in CCl_4 .

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