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SENSITIZED PHOTOOXIDATION OF GURJUNENE: CLEAVAGES OF THE CYCLOPROPANE RING

Shô Itô, Hitoshi Takeshita, Masahiro Hirama and Yoshimasa Fukazawa
Department of Chemistry, Tohoku University
Sendai 980, Japan

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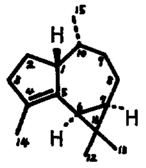
The sensitized photooxidation of monoterpenic (1) and sesquiterpenic vinylcyclopropanes (2) uncovered a contrast between two series on the cleavage of C=C bond therein, although both series uniquely afforded products with the cyclopropane ring retained. In order for the deeper understanding of the detailed features of the reaction, we have extended the reaction to gurjunene, a sesquiterpene having heteroannular transoid vinylcyclopropane, as all the vinylcyclopropanes so far investigated have the homoannular cisoid orientation.

Gurjunene (I) (3) was subjected to oxidation (350w tungsten lamp, methylene blue) in methanol-benzene (2 : 1) for 3 hrs. Four major products, II, III, IV and V were isolated in 7, 17, 40 and 12% yields, respectively, by silica gel column and preparative thin layer chromatography (4).

The first product (II), colorless liquid, was identical (IR and NMR) with the authentic cyclopropylketone prepared from I by the known procedure (5).

The second product (III), colorless liquid, ν 1705 cm^{-1} (br.), δ 0.92 (d, J=6.7, 15-CH_3), 1.08 (s, 12- and 13-CH_3), 2.07 (s, 14-CH_3), 3.13 (s, OCH_3), $[\Phi]^{26}_{314}$ +480°, $[\Phi]^{26}_{275}$ -810°, bis-2,4-DNP, m.p. 189-191°, afforded by acid the known dienone VI (3) (UV, IR and NMR).

The cleavage of the double bond is again observed in II and III and furthermore the original cyclopropane ring was cleaved in III for the first time. This is another evidence for the dioxetane intermediate because the fragmentation of a dioxetane is well known to yield two carbonyl groups, one of which is in electronically excited state (6) and therefore capable to further chemical change. In fact, when II was irradiated in methanol with a high-pressure mercury lamp (7), a complex mixture was obtained from which isolated were VII, colorless liquid (8%), ν 1711 cm^{-1} (br.), δ^{CCl_4} 1.05, 1.09 (each s, 12- and 13-CH_3), 2.04 (s, 14-CH_3), 3.13 (s, OCH_3),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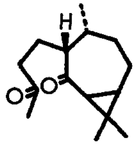
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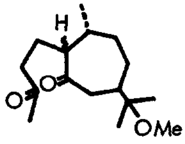
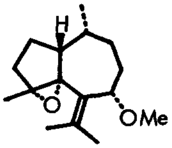

III, VII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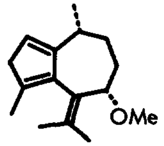
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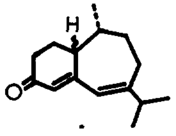
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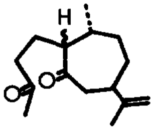
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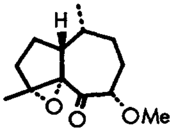
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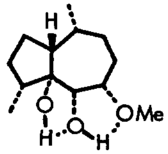
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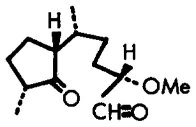
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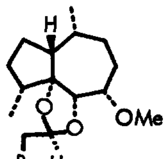
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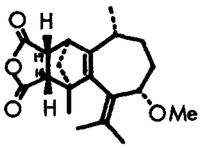
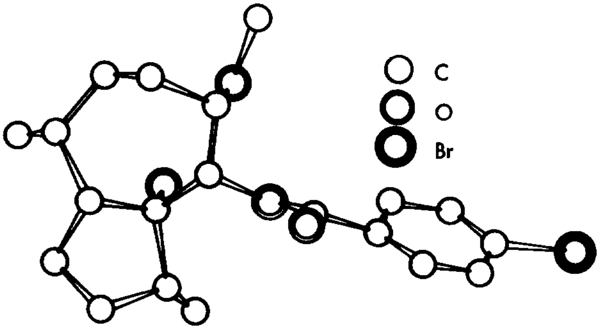

XIII

$[\phi]^{21}_{310}$ +1370°, $[\phi]^{21}_{270}$ -2170°, and VIII, colorless liquid (20%), ν 1712, 1700 cm^{-1}, δ 1.72 (t, J=1.1, 13-CH_3), 2.11 (s, 14-CH_3), 4.72 (m, 12-Hs), $[\phi]^{26}_{313}$ +1790°, $[\phi]^{26}_{276}$ -2820°. VII was converted to VI by acid.

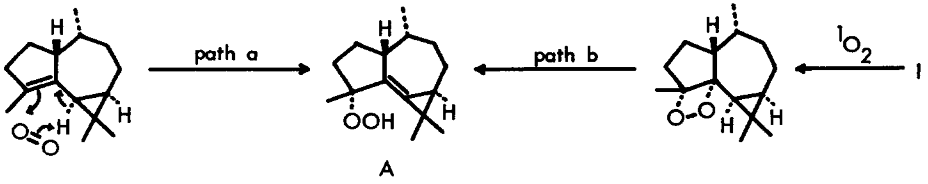
The third product is IV, colorless plates, m.p. 81-83°, ν 1647, 1101, 958, 887, 860 cm^{-1}, δ 1.00 (d, J=6.6, 15-CH_3), 1.29 (s, 14-CH_3), 1.68 and 1.82 (both s, 12- and 13-CH_3), 3.22 (s, OCH_3), 4.34 (dd, J=8.2, 6.7, 7-H). Ozonolysis of IV at -60° yielded, the trisnor-ketone IX, colorless needles, m.p. 135.0-135.5°, λmax 217 (ε 2750), 303 nm (34), ν 1706 cm^{-1}, δ 0.90 (d, J=7.0, 15-CH_3), 1.43 (s, 14-CH_3), 3.30 (s, OCH_3), 4.15 (m, 7-H), $[\theta]^{23}_{308}$ +4090, $[\theta]^{23}_{220}$ +18430. $LiAlH_4$ reduction of IX gave the glycol X, colorless needles, m.p. 103-104°, ν_{OH} 3577, 3534 cm^{-1} (no change on dilution), δ 1.01 (d, J=6.7, 15-CH_3), 1.06 (d, J=6.3, 14-CH_3), 2.70 (s, 5-OH), disappeared on adding D_2O), 2.96 (d, J=7.6, 6-OH, disappeared on adding D_2O), 3.34 (s, OCH_3), 3.41 (dd, J=7.6, 4.0, 6-H, changes to d, J=4.0, by D_2O), 3.54 (ddd, J=7.0, 4.0, 1.3, 7-H). Lead tetraacetate oxidation of X afforded the ketoaldehyde XI, colorless liquid, ν 1736 cm^{-1}, δ 0.95 (d, J=6.7, 14-CH_3), 1.03 (d, J=7.3, 15-CH_3), 3.40 (s, OCH_3), 3.50 (ddd, J=6.5, 5.5, 2.0, 7-H), 9.63 (d, J=2.0, 6-H). X yielded the bromoethylidene derivative XII, colorless liquid. Its NMR data, δ 0.99 (d, J=7.2, 15-CH_3), 1.04 (d, J=5.8, 14-CH_3), 3.13 (ddd, J=9.8, 1.8, 1.6, 7-H), 3.38 (s, OCH_3), 3.43 (d, J=4.9, CH_2Br), 4.35 (dd, J=1.8, 1.4, 6-H), 5.21 (t, J=4.9, $CH\overset{O}{\underset{O}{<}}$), especially the splitting pattern of 6-H and 7-H, confirmed cis-orientation of all the oxygen functions. Whole absolute stereochemistry of X was established as shown below by the X-ray analysis of its p-bromobenzoate, m.p. 96.5-97.5° (8).



The fourth product V, colorless liquid, $\lambda_{max}^{isooctane}$ 226 (7900 sh), 250 nm (4000 sh), δ 1.16 (d, J=6.6, 15-CH_3), 1.58, 1.80, 1.83 (all s, allylic CH_3), 2.79 (m, 3-H_2), 3.00 (s, OCH_3), 4.24 (br. d, J=5.6, 7-H), 5.62 (dt, J=1.9, 1.5, 2-H), was also obtained from IV upon being kept in methanol at room temperature for a few hours. On mixing with maleic anhydride V afforded XIII, amorphous solid, $\lambda_{max}^{diox.}$ 223 nm (ϵ 7400 end abs), ν 1857, 1775 cm^{-1}, δ 1.14 (d, J=7.2, 15-CH_3), 1.40 (s, 14-CH_3), 1.68, 1.81 (both s, 12- and 13-CH_3), 3.05 (ddd, J=7.7, 1.5, 1.0, 17-H), 3.23 (s, OCH_3), 3.35 (dd, J=7.7, 1.2, 16-H), 3.36 (q, J=1.0, 2-H), 4.21 (t, J= 4.6, 7-H).

The cleavage of a cyclopropane ring was observed again in IV and V, but in a different manner from in III. The formation of IV can be visualized as follows: Either direct allylic oxidation of I (path a) or the abstraction of the cyclopropyl hydrogen from the intervening dioxetane (or its equivalent) intermediate (path b) would yield the allylic hydroperoxide A, which would decompose directly to IV by the formation of epoxide ring, C-C bond migration and nucleophilic attack of solvent. Acidic nature of the cyclopropyl hydrogen due to the increased s-character of the hybridized orbital of the carbon in three-membered ring would be the reason for the prefered abstraction of the hydrogen to the other axially oriented hydrogens on sp^3 carbons (9). The formation of V from IV is the precedented acid-catalyzed dehydration reaction (10).

In any events, the cleavage of the cyclopropane during reaction of singlet oxygen has no precedence. Experiments along the line to determine the geometrical requirements for the cleavage are now in progress.



Structures of III and IV, and V are reminiscent of those of the seco-guaianolides (11) and zierone (12), respectively. This implied the above type of the process could be one of the candidates for the transformation occurring in nature (13). Experiments along this line are also in progress.

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References and Footnotes

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4) Although the crude product mixture showed a few more minor spots on tlc, none of them were obtained pure because of their instability.

5) All compounds described in this paper gave satisfactory elemental analyses. UV spectra were measured in MeOH unless otherwise stated, and IR spectra in KBr for crystalline compounds and in film for liquid. NMR spectra were recorded in $CDCl_3$ and expressed in ppm from internal TMS. ORD and CDs were measured in MeOH and E.P.A. solvent, respectively.

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7) Irradiation of this solution by a tungsten lamp with or without the sensitizer caused no reaction.

8) The crystal was orthorhombic (a=16.276 Å, b=21.417 Å, c=5.738 Å, $P2_12_12_1$). Three-dimensional data were collected from Rigaku-Denki diffractometer, with θ-2θ scan technique. 603 independent structure factors were evaluated. The heavy atom method and refinement by least squares method were used to establish the structure. At the final stage of refinement the R factor was 12.1%. The absolute configuration was determined by the anomalous dispersion effect of bromine atoms for copper K_α radiation.

9) Abstraction of olefinic hydrogen by oxygen has precedences. Y. Isoe, S.B. Hyeon, H. Ichikawa, S. Katsumura and T. Sakan, *Tetrahedron Letters*, 5561 (1968).

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13) Barton and Gupta postulated (12) a biogenesis which involves either a 1,2-shift of the isopropyl group in the guaiane system or another type of cleavage of a peroxy cyclopropane ring in the gurjunene system.