

The Use of ^{13}C - $\{^1\text{H}$ Selective $\}$ Nuclear Overhauser Enhancement Experiments in the Determination of the Structure of a Highly Crowded Quinone-Diazoalkane Epoxide Adduct

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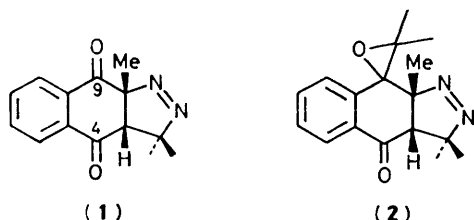
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Using heteronuclear nuclear Overhauser enhancement techniques the structure and conformation have been established for a highly crowded quinone-diazoalkane epoxide adduct, (3a*S**,9*S**,9a*R**)-3,9a-dihydro-3,3,3',3',9a-pentamethylspiro-[9*H*-benz[*f*]indazole-9,2'-oxiran]-4(3a*H*)-one, formed from 2-methylnaphthoquinone and 2-diazopropane.

The rapid reaction of 2-methylnaphthoquinone with 1 equiv. of 2-diazopropane in ether at 0 °C provided the expected adduct (1) in 60% yield as pale yellow rods, m.p. 105–110 °C (rapid heating; decomp.).[†] At –78 °C, but with a five-fold excess of 2-diazopropane, a second product (2) (12%) was also formed as white rhombs, m.p. 168–170 °C, having a ^1H n.m.r. spectrum including five methyl singlets. This suggested that 2 equiv. of 2-diazopropane had reacted with 1 equiv. of the quinone, implying a surprisingly easy reaction of the already bulky adduct (1) with 2-diazopropane; in agreement, the adduct (1) reacted with an excess of 2-diazopropane at –50 °C to give (2).

The presence of signals at δ 68.8 and 69.4 p.p.m. in the ^{13}C n.m.r. spectrum of (2), attributable to quaternary sp^3 carbons attached to oxygen, along with other spectroscopic evidence, strongly suggested that (2) was an oxiran derived from (1) by formation of an epoxide at one of the carbonyl groups. The stereochemistry of the adducts formed from quinones and diazoalkanes is known¹ to be *cis* as indicated in (1). Reaction of (1) with 2-diazopropane at C-9 has both steric and inductive factors in its favour, but the relative conformation of the derived oxiran clearly depends upon the direction of attack, the sterically favoured (but nevertheless hindered) direction being from the pyrazoline side. On the other hand, C-4 has a sterically favourable direction of attack *cis* to the methine hydrogen, the other side of this carbonyl group being effectively blocked by the *gem*-dimethyl group of the pyrazoline ring. Secondary orbital interactions between the pyrazoline ring nitrogens and the incoming diazoalkane could be important in determining the course of the reaction.²

The product (2) is obviously a highly crowded molecule formed under remarkably mild conditions and apparently with specificity, so a detailed n.m.r. study was undertaken to identify the structure, configuration, and conformation. Since standard n.m.r. practice gave ambiguous results, we turned to ^{13}C - $\{^1\text{H}$ -selective $\}$ nuclear Overhauser enhancement (n.O.e.) measurements. The possibilities here have been long recognised³ but used only once⁴ until a second example appeared⁵ during preparation of this paper.



[†] Satisfactory u.v., i.r., ^1H n.m.r., ^{13}C n.m.r., mass spectral, and analytical data were obtained for (1) and (2).

In the ^1H n.m.r. spectrum $\text{C}^{3a}\text{-H}$ can be unambiguously assigned as the singlet at δ 2.37 on the basis of shift and intensity. Single-frequency ^1H pre-irradiation at δ 2.37 produces an n.O.e. in the ^{13}C n.m.r. spectrum at δ 90.0, 90.5, and 195.0 p.p.m., these carbon atoms being non-proton bearing[‡] (see Figure 1). The signal at δ 195.0 p.p.m. must be due to the remaining $\text{C}=\text{O}$ and as $\text{C}^{3a}\text{-H}$ must be close to give this n.O.e., it must be the C^4 carbonyl group. Thus, it is the C^9 carbonyl group of the naphthoquinone adduct (1) that has formed the oxiran ring. The signals at δ 90.0 and 90.5 p.p.m. must be due to the two carbon atoms next to nitrogen in the pyrazoline ring, and these atoms must be approximately the same distance as $\text{C}^4(\text{O})$ from $\text{C}^{3a}\text{-H}$.[§] This proves that nitrogen is attached to $\text{C}^{9a}\text{-Me}$ in the pyrazoline ring and establishes the structure (2).

N.O.e. measurements showed the following sequence[¶] of spatial connectivity: δ 1.66($\text{C}^{9a}\text{-CH}_3$)— δ 2.37($\text{C}^{3a}\text{-H}$)— δ 1.84($\text{C}^3\text{-CH}_3$)— δ 1.22($\text{C}^3\text{-CH}_3$)— δ 1.54($\text{C}^{3'}\text{-CH}_3$)— δ 0.96($\text{C}^{3'}\text{-CH}_3$)— δ 7.55($\text{C}^8\text{-H}$)— δ 7.64($\text{C}^7\text{-H}$)— δ 7.46($\text{C}^6\text{-H}$)— δ 7.88($\text{C}^5\text{-H}$). The *cis*-ring fusion of the pyrazoline is clearly proven by the

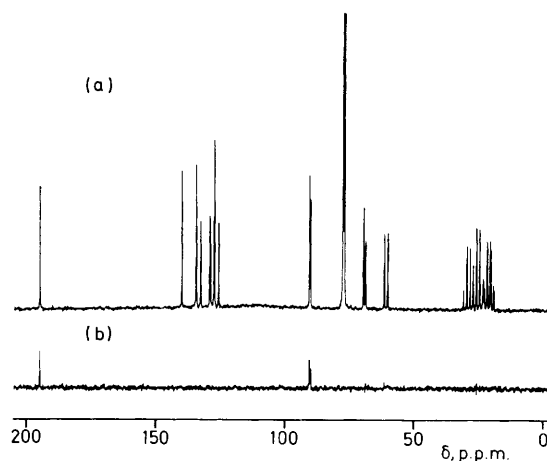


Figure 1. 100.6 MHz ^{13}C N.m.r. spectra of (2) in CDCl_3 : (a) spectrum with no ^1H irradiation; (b) difference spectrum obtained by pre-irradiating the proton at δ 2.37 due to H^{3a} at low power to develop an n.O.e. in the ^{13}C n.m.r. spectrum, and subtracting spectrum (a).

[‡] No n.O.e. is observed at $^{13}\text{C}^{3a}\text{-H}$ as only the $^{12}\text{C}^{3a}\text{-H}$ signal is irradiated with low-power ^1H irradiation.

[§] These assignments are also supported by ^{13}C and ^{13}C - $\{^1\text{H}$ -selective $\}$ decoupling measurements including $^2J(^{13}\text{C}, ^1\text{H})$ and $^3J(^{13}\text{C}, ^1\text{H})$.

[¶] The connectivity between the two methyl groups on $\text{C}^{3'}$ was also confirmed by the observation of $^4J(^1\text{H}, ^1\text{H}) = 0.5$ Hz.

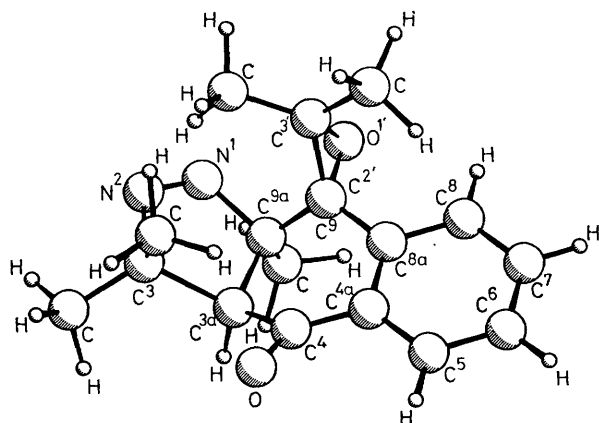


Figure 2. Proposed conformation of (2), drawn using the program PLUTO 78 (W. D. S. Motherwell, Cambridge Crystallographic Data Centre).

observation of n.O.e. between δ 2.37($C^{3a}\text{-H}$) and δ 1.66($C^{9a}\text{-CH}_3$).

The n.O.e. between δ 1.22($C^3\text{-CH}_3$) and δ 1.54($C^{3'}\text{-CH}_3$) not only establishes the relative stereochemistry of the pyrazoline

and oxiran rings, but also shows that the conformation must be such as to bring these two methyl groups together. These features are shown in Figure 2; this representation, based upon a Dreiding model, illustrates the essential nearness of the $C^3\text{-CH}_3$ to the $C^{3'}\text{-CH}_3$ ($H \cdots H$ ca. 0.24 nm).

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