Inter- and Intra-molecular 'Ene' Reactions of Aliphatic Nitroso Compounds

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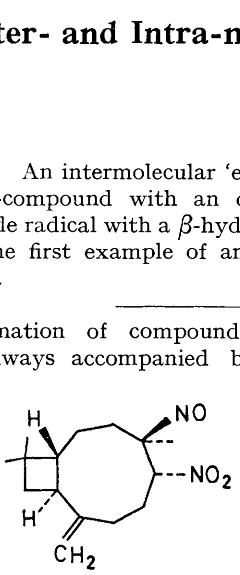
Summary An intermolecular 'ene' reaction of an aliphatic nitroso-compound with an olefin leading to a stable nitroxide radical with a β-hydrogen is described, together with the first example of an analogous intramolecular process.

The formation of compound (**1**) from caryophyllene (**2**) is always accompanied by a small amount of a stable yellow crystalline compound, m.p. 167°. On the basis of preliminary results we tentatively assigned structure (**3**) to this compound.[1] As a result of a more detailed investigation we have now shown that this structure is wrong and should be replaced by (**4**, R = $\dot{O}$) for the following reasons. The spectral characteristics of this unusual nitroxide radical are as follows: ν_{max} (CCl_4) 3080, 1644, 1560, and 901 cm^{-1}; λ_{max} (C_6H_{12}) 216 nm (ϵ = 4,830); $M^+ + 1$ 484, M^+ 483; e.s.r. ($CHCl_3$) triplet of doublets a_N = 14·2 and a_H = 2·3 Oe, g = 2·0061. Hydrogenation of (**4**, R = $\dot{O}$) over Lindlar catalyst yields the corresponding hydroxylamine (**4**, R = OH), m.p. 136°, [M^+ 484; τ($CDCl_3$) 9·02 (12H, s, 2 gem-dimethyls), 8·77 (3H, s, *Me*-C-NOH), 6·78 (1H, m, C*H*-NOH) and 5·02—5·26 (7H, m, C*H*-NO_2 and 3 = CH_2)]. Aerial oxidation of (**4**, R = OH) regenerates (**4**, R = $\dot{O}$). Clearly these data are consistent with the proposed structures.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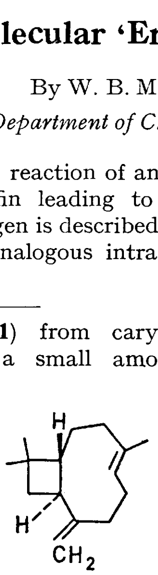
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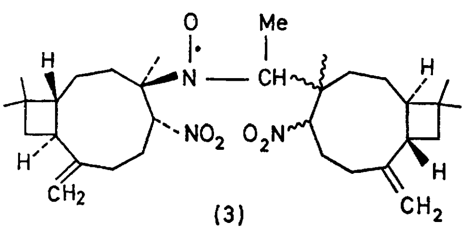
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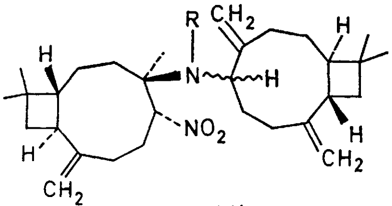
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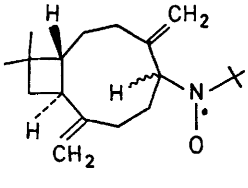
The mechanism of formation of (**4**, R = $\dot{O}$) can be considered in terms of an 'ene' reaction[2] between caryophyllene (**2**) and caryophyllene nitrosite (**1**) followed by oxidation of the initially formed hydroxylamine (**4**, R = OH). The compelling evidence in favour of this mechanism derives from the fact that (**4**, R = $\dot{O}$) can be obtained in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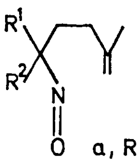
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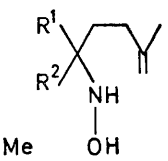
a, $R^1 = R^2 = Me$

b, $R^1,R^2 = -(CH_2)_5-$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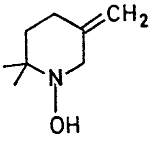
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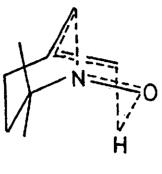
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high yield from the reaction of caryophyllene with caryophyllene nitrosite in chloroform solution in the dark. At the time this work was completed only one report[3] had been recorded concerning the 'ene' reaction of an olefin with a nitroso-compound but more recently there have been a number of additional examples[4]. The strained *trans*-trisubstituted double bond of caryophyllene also participates in an 'ene' reaction with maleic anhydride.[5]

Very few examples are known, however, of stable nitroxide radicals with a β-hydrogen atom.[6] The stability of these compounds has been attributed to the severe steric inhibition to hydrogen atom abstraction in the proposed bimolecular disproportionation to the corresponding nitrone and hydroxylamine. In agreement with this hypothesis the nitroxide radical (**5**) [$M^+ + 1$ 291, M^+ 290; e.s.r. ($CHCl_3$) triplet of doublets $a_N = 14{\cdot}9$ and $a_H = 2{\cdot}3$ Oe, $g = 2{\cdot}0067$] derived from the reaction of caryophyllene (**2**) with t-nitrosobutane proved to be considerably less stable.

In connection with our recent work[7] on the utilisation of the nitroso-olefins (**6a** and **b**) in the synthesis of stable nitroxides, we were surprised to find that these two compounds proved to be quite labile. For example, oxidation of the hydroxylamino-olefin (**7a**) with diethyl azodicarboxylate[8] yields the expected nitroso-olefin (**6a**) which rearranges rapidly at room temperature to a new hydroxylamine (positive test with alkaline 2,3,5-triphenyltetrazolium chloride). Although this new isomer also proved to be relatively unstable it was isolated by careful preparative t.l.c. The n.m.r. and i.r. spectra are entirely consistent with the cyclic hydroxylamine (**8**). The ready formation of this compound can be achieved by an intramolecular 'ene' reaction *via* the bicyclo[3,3,1] transition state (**9**).[9]

We wish to thank Dr. A. L. Porte for recording the e.s.r. data and one of us (W.B.M.) gratefully acknowledges receipt of a Carnegie Trust Grant.

(Received, 15th December 1971; Com. 2134.)

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