The First Example of Epoxide Formation by the Action of a Diazoalkane upon an Ester Carbonyl Group

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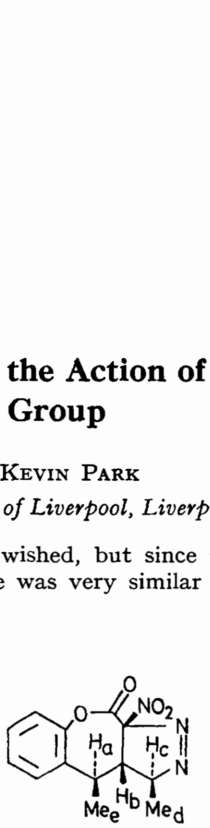
Summary Diazoethane converts the carbonyl group of the electronegatively substituted ester (I) into an oxiran ring to form compound (II).

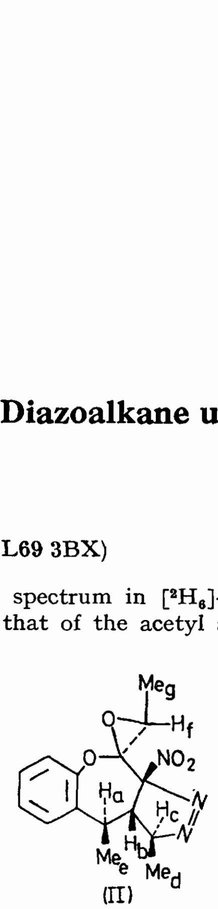
Apart from one reference to unpublished work,[1] the ester carbonyl group is considered to be inert towards diazoalkanes except for ester interchange with alcohols, when diazoalkanes merely act as catalytic bases.[2] Nevertheless, Billett, Fleming, and Hanson have recently described reactions which they interpret in terms of nucleophilic attack by diazoalkanes upon ester carbonyl groups.[3] The incidence of this attack was very difficult to detect and establish because, having been attacked, the ester group was then reconstituted in a subsequent rearrangement. We now describe the first example of the production of an epoxide by the action of diazoethane upon an ester (lactone) carbonyl group.

Diazoethane reacts with 3-nitrocoumarin in tetrahydrofuran at 0° for 0·5 h forming the pyrazoline derivative (I) m.p. 112—116° (decomp.), which lost nitrogen readily but gave satisfactory elemental analyses and an i.r. spectrum (KBr) including strong bands at 1765 (aryl ester), 1570 and 1330 cm^{-1} (NO_2).

Because of a combination of solubility and instability problems we could not study the n.m.r. spectrum as fully as we wished, but since the spectrum in [$^2H_6$]-deuterioacetone was very similar to that of the acetyl analogue[4] (I; Ac instead of NO_2) we have confidence in the assignments [τ 2·6—3·0 (mm, Ar*H*), 5·17 (1H, dq, H_c), 6·75 (1H, dq, H_a), 7·21 (1H, dd, H_b), 8·27 (3H, d, Me_d or Me_e), and 8·48 (3H, d, Me_e or Me_d)]. That the stereochemistry and systems of the two lactones are the same is shown by the coupling constants (first order analysis only): J_{ab} 12, J_{bc} 9, J_{cd} 7, and J_{ae} 7 Hz.



(I)



(II)

When diazoethane and either 3-nitrocoumarin or the pyrazoline derivative (I) were allowed to interact for a longer time, (1·5 h), the chief product was the oxiran derivative (II), m.p. *ca.* 140° (decomp.), a relatively stable compound corresponding to the addition of an ethylidene residue to the pyrazoline derivative (I). The i.r. spectrum ruled out the presence of OH or NH functions, or of carbonyl groups and showed by strong bands at 1550 and 1342 $\mathrm{cm^{-1}}$ that the nitro group was intact. The n.m.r. spectrum confirmed that there are two independent spin systems, one as present in the original pyrazoline derivative, the other a new one corresponding to an ethylidene grouping; [τ 2·78—3·46 (Ar*H*), 5·50 (1H, dq, $\mathrm{H_c}$), 6·38 (1H, q, $\mathrm{H_f}$), 6·63 (1H, dq, $\mathrm{H_a}$), 7·36 (1H, dd, $\mathrm{H_b}$), 8·38 (3H, d, $\mathrm{Me_d}$), 8·40 (3H, d, $\mathrm{Me_e}$), 8·54 (3H, d, $\mathrm{Me_g}$). The coupling constants J_{ac} 7, J_{cd} 7, and J_{fg} 4·5 Hz were obtained directly, and two others J_{ab} 6·0 and J_{bc} 9·0, were obtained by double irradiation experiments which also confirmed the spin patterns. Important is the small value of J_{fg} which is indicative of a heterocyclopropane,[5] the chemical shift of $\mathrm{H_f}$ confirming an oxiran derivative. The value of J_{ab} is only half what it is in compound (I) thus signalling a change in the conformation of the oxepin ring which alters the $\mathrm{H_aH_b}$ torsion angle from about 180° to about 35°, a possibility which, with the aid of models, allows the oxiran ring to be tentatively assigned the configuration shown in (II), the methyl substituent being attached at the less restricted of the two sites available.

Since it is well known that electronegative substituents greatly increase the tendency of carbonyl compounds to yield epoxides when treated with diazomethane,[1] we suppose that the electronegative character of the two substituents ($\mathrm{NO_2}$ and N=N) in (I) is chiefly responsible for making the ester behave like a ketone. It is also possible that the highly polar character and the situation of the nitro group enable it to play a second role in 'solvating' a highly ionic intermediate or transition state.

It is commonly held that epoxide formation requires nucleophilic attack by the diazoalkane at carbonyl carbon.[1,6] The results of the present work justify the interpretation offered by Fleming *et al.* whose esters lacked any activating substituents but possessed exceptionally favourable stereochemistries.

(*Received*, 19*th November* 1973; *Com.* 1597.)

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