

Unusual Chemo- and Stereo-selectivities in the Reactions of 1,2-Dichlorocyclopropenes with Nitrile Oxides

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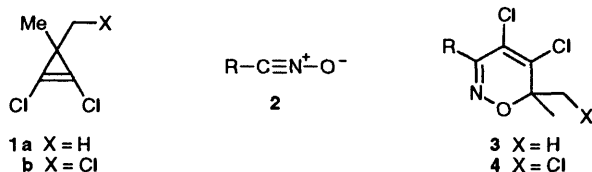
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1,2-Dichloro-3,3-dimethylcyclopropene reacts with a number of nitrile oxides to produce oxazines in moderate to good yield in a reaction which apparently involves an unusual formal 3-centre plus 3-centre cycloaddition of the dipole to an intermediate vinylcarbene. In contrast, 1,2-dichloro-3-chloromethyl-3-methylcyclopropene undergoes a dipolar cycloaddition to produce a 2-oxa-3-azabicyclo[3.1.0]-hex-3-ene in which the 6-chloromethyl substituent occupies the *endo*-position.

6H-1,2-Oxazines have been prepared by a number of routes, many of which involve the cyclisation of a four-atom unit with a two-atom unit, such as the cycloaddition of an alkenyl nitroso compound to an alkene to give a 4,5-dihydro compound,¹ or to an allene to give a 6-methylene-4,5-dihydro compound which may be isomerised, by treatment with base, to the 1,2-oxazine.² There are few examples of the formation of the heterocycle by combination of two three-atom components to form the ring, although addition of sulfoxonium allylides to nitrile oxides does lead to 1,2-oxazines as minor products together with furans.³ We now report that reaction of a 1,2-dichloro-3,3-dialkylcyclopropene with nitrile oxides leads to 1,2-oxazines in moderate to good yield.

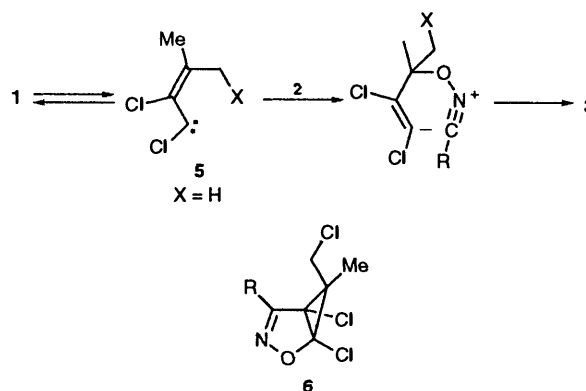
Treatment of **1a**⁴ with the nitrile oxide **2a**[†] for 18 h at 20 °C in diethyl ether gave the oxazine **3a** (65%), m.p. 125–127 °C.



a, R = 2,4,6-(MeO)₃C₆H₂; b, R = 3,4-(MeO)₂C₆H₃
 c, R = 2-O₂NC₆H₄; d, R = C₆H₅; e, R = (PrⁱO)₂PO

The structure of **3a**, the ¹³C NMR of which included a signal at δ 84 for C-6,[‡] was confirmed by an X-ray crystal structure determination and is given in Fig. 1.§ This reaction is quite different from the addition of nitrile oxides to simple alkyl- and aryl-cyclopropenes which has been reported to lead to 2-oxa-3-azabicyclo[3.1.0]hex-3-enes in a typical dipolar addition to the strained alkene.⁵ It is known that cyclopropenes such as **1a** ring-open at ambient temperature to produce vinylcarbenes which may be trapped in a range of intermolecular reactions such as addition to alkenes, insertion into carbon–hydrogen bonds adjacent to oxygen and addition to carbon–phosphorus triple bonds.^{4,6} The formation of oxazines **3** could formally occur by addition of the singlet vinylcarbene **5** (X = H), which may be regarded as an allyl cation orthogonal to an anion on C-1, to the

nitrile oxide, although it is not clear as yet whether this process occurs in a stepwise or concerted manner, *e.g.*:



The reaction is also successful with a range of other nitrile oxides **2b–e** as shown in Table 1; in each case the ¹³C spectrum included a signal at δ 80–84 for C-6. However, the related cyclopropene **1b**, which is also known to rearrange to a carbene **5** (X = Cl) at ambient temperature,⁷ reacts with the nitrile oxides by an apparent direct dipolar cycloaddition to give the oxabicycles **6** rather than **4**.¶ These showed a characteristic signal for C-5 at δ 90–95, but no signal at δ 80–84. The stereochemistry of **6a** was established by X-ray crystallography.§ The reason for the difference in behaviour of the two cyclopropenes may lie in the kinetics of their ring-opening to carbenes; thus, it is known that the trapping of the carbene **5** (X = H) derived from **1a** by alkenes occurs somewhat faster than the corresponding sequence from **1b**, probably reflecting a difference in the rates of ring-opening.⁷ However, the formation of the more hindered *endo*-isomer may reflect a more subtle effect of the remote C–Cl bond in controlling the stereochemistry of the reaction at the π-bond of **1b** and/or in increasing the rate of cycloaddition relative to that for **1a**. Further work is in progress to analyse the effect, which may be related to the high degree of stereocontrol of ring-opening of **1b** to the carbene **5** (X = Cl),⁷ which has been explained in terms of electronic interactions in the transition state involving the orbitals of the chloromethyl group,⁸ and to π-facial selectivity observed in the additions of 7-methylenebicyclo[2.2.1]heptane derivatives induced by an *endo*-2-substituent.^{9,10} It should be noted, however, that addition of *e.g.*, nitrile oxides to the π-bond to 3-methyl-3-phenyl- and 3-cyano-3-methyl-cyclopropene also occurs in a highly stereocontrolled manner.^{5,11}

† The nitrile oxide **2a** was used as a crystalline solid. In the other cases, the compounds were prepared *in situ* by reaction of the corresponding chloro oxime with triethylamine in diethyl ether.

‡ Compound **3b** showed δ_H 7.1 (1 H, d, *J* 7), 7.05 (1 H, s), 6.85 (1 H, d, *J* 7), 3.85 (3 H, s), 3.84 (3 H, s), 1.5 (6 H, s); δ_C 155.9, 150.6, 148.7, 140.3, 124.3, 111.4, 110.5, 80.2, 56.0, 55.95 and 23.7.

§ Thanks are due to the SERC Crystallography service in Swansea for carrying out this structure determination.

¶ See Experimental section for spectroscopic data for **6a**.

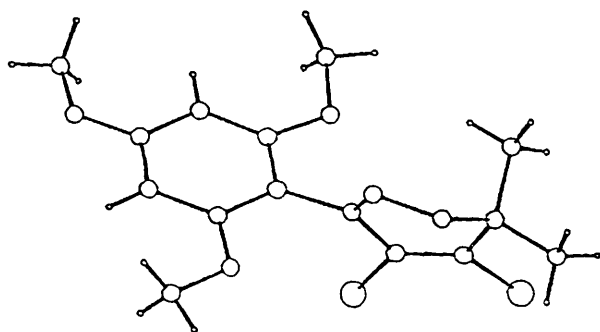


Fig. 1 X-Ray crystallographic structure of 3a

Table 1 Reactions of cyclopropenes (1a) and (1b) with nitrile oxides

Cyclopropene	Nitrile oxide	Product	Yield (%)
1a	2a	3a	65
1a	2b	3b	55
1a	2c	3c	35
1a	2d	3d	35
1a	2e	3e	80
1b	2a	6a	65
1b	2b	6b	60
1b	2d	6d	30
1b	2e	6e	45

Experimental

Reaction of 1,2-Dichloro-3-chloromethyl-3-methylcyclopropene 1b with 2,4,6-Trimethoxybenzoxonitrile Oxide 2a.—A solution of 1,1,2,2-tetrachloro-3-chloromethyl-3-methylcyclopropene (1.0 g, 4.12 mmol) in dry diethyl ether (10 cm³) was stirred under argon and cooled in an ice-salt bath. Methyllithium (1.5 mol dm⁻³; 3.29 cm³, 1.2 mol equiv.) was then added dropwise to it over 1 min. After 10 min the mixture was quenched with water (10 cm³) whilst being cooled in an ice-bath. The aqueous phase was extracted with diethyl ether (3 × 5 cm³) and the combined extracts, containing 3-chloromethyl-3-methyl-1,2-dichlorocyclopropene, were dried (MgSO₄). A solution of 2,4,6-trimethoxybenzoxonitrile oxide (0.86 g, 1.0 mol equiv.) in dry diethyl ether (20 cm³) was added to the above ethereal solution and the reaction mixture was then stored at 20 °C for 24 h. Evaporation of the reaction mixture to dryness gave the crude product which was purified by column chromatography (10:3, light petroleum–diethyl ether as eluent) on silica gel, to give white crystals of compound 6a (1.0 g, 65%), m.p. 118–120 °C (Found: C, 47.7; H, 4.3; N, 3.6. Calc. for C₁₅H₁₆Cl₃NO₄: C, 47.30; H, 4.20; N, 3.68%); δ_H 6.10 (2 H, s), 3.80 (3 H, s), 3.75 (6 H, s), 3.46 (1 H, d, *J* 11.8), 3.23 (1 H, d, *J* 11.8) and 1.6 (3 H, s); δ_C 163.9s, 160.3s, 156.4, 153.5s, 97.4, 92.3, 90.9d, 65.4, 56.1q, 55.6q, 47.2s, 43.2t, 32.9 and 15.7; on running the ¹³C spectrum at –20 °C, the signal at δ 90.9 was split into two signals at δ 90.5 and 89.9. The presence of additional ¹³C signals is presumed to be caused by restricted rotation of the aryl-group.

Reaction of 1,2-Dichloro-3,3-dimethylcyclopropene 1a with Benzoxonitrile Oxide 2d.—A solution of 3-bromo-1,1,3-trichloro-

2,2-dimethylcyclopropene (1.0 g, 3.95 mmol) in dry diethyl ether (10 cm³) was stirred under argon and cooled to –78 °C. Methyllithium (1.5 mol dm⁻³; 2.9 cm³, 1.1 mol equiv.) was added to the solution which was then kept < –40 °C for 10 min. After being quenched with water (10 cm³) at –40 °C the mixture was extracted with diethyl ether (3 × 5 cm³) and the combined extracts, containing 3,3-dimethyl-1,2-dichlorocyclopropene, were dried (MgSO₄) at –40 °C. A solution of benzohydroxamoyl chloride (0.62 g, 3.95 mmol) in dry diethyl ether (20 cm³) was stirred at 0 °C and treated with freshly distilled triethylamine (0.45 g, 1.0 mol equiv.), added in one portion. The mixture was then shaken continuously for 5 min while being cooled in an ice-bath. The two ethereal solutions were combined and kept at room temperature for 24 h. The mixture was washed with hydrochloric acid (10%; 10 cm³) and water (3 × 10 cm³), dried (MgSO₄) and evaporated to dryness; the crude product was purified by column chromatography (10:2, light petroleum–diethyl ether) on silica gel, to give white crystals of compound 3d (0.55 g, 55%), m.p. 102–104 °C (Found: C, 56.7; H, 4.3; N, 5.9. Calc. for C₁₂H₁₁Cl₂NO: C, 56.25; H, 4.30; N, 5.47%); δ_H 8.02–7.95 (2 H, m), 7.48–7.45 (3 H, m) and 1.08 (6 H, s); δ_C 139.0, 134.1, 132.9, 130.3, 129.0, 128.6, 128.2, 125.6, 121.8, 79.6 and 23.1.

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