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CYCLOADDITION REACTION OF BENZOCYCLOPROPENE WITH AROMATIC NITRILE OXIDES: A SYNTHETIC ENTRY INTO A BRIDGED OXAZONINE

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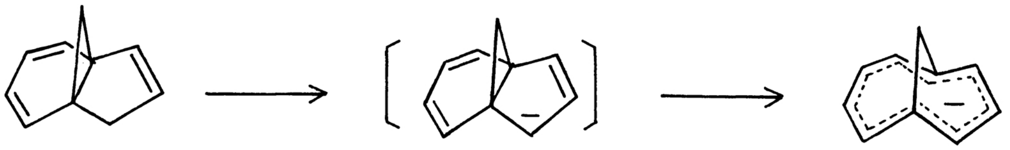
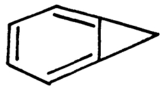
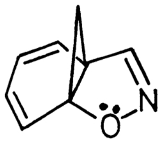
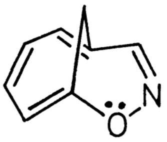
9-Aryl-7-oxa-8-azatricyclo[4.3.1.0]deca-2,4,8-trienes (Ia and Ib) were synthesized by the cycloaddition reaction of benzocyclopropene with benzonitrile oxide and mesitonitrile oxide, respectively. The closed norcaradiene structures were preferable to the opened bridged oxazonine isomers in the range of 25-120°C.

It is known that tricyclo[4.3.1.0]deca-2,4,7-triene (A) reacts with sodium methylsulfinyl anion in dimethyl sulfoxide to afford bicyclo[4.3.1]decatetraenyl anion (B).[1,2] This finding clearly indicates that the incorporation of negative charge into (A) makes more favorably the opened 10-pi-electron delocalized structure (B) rather than the closed anion (B'). The similar relation may be expected between (C) and (D). The heterocyclic analogue (C) having a lone pair electron on oxygen atom might also be the bridged oxazonine (D)[3] rather than norcaradiene type isomer (C). In this study we investigated the cycloaddition reaction of benzocyclopropene with aromatic nitrile oxides. Since benzocyclopropene is known to undergo cycloaddition reaction with various dienes,[4,5] it might be a promising precursor for synthesizing the skeleton of (C) and then (D).



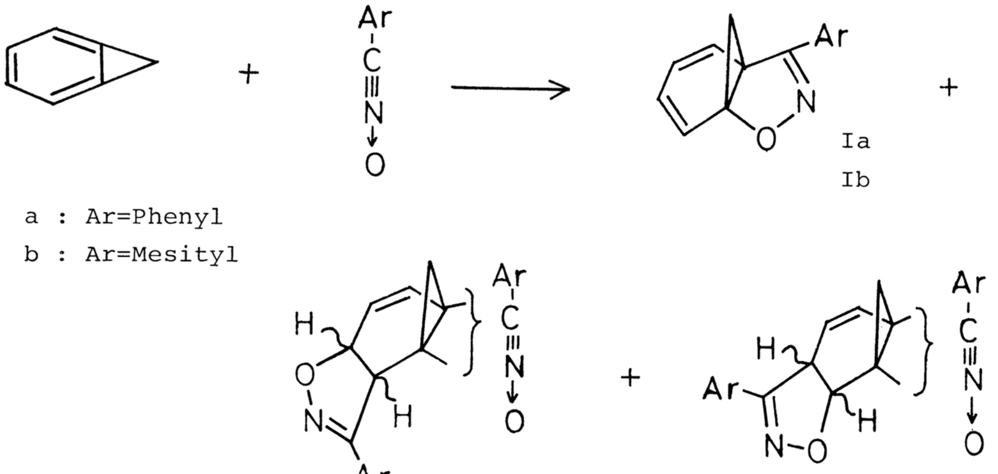



C


D

The solution of benzocyclopropene (8 mmol) and benzonitrile oxide[6] (4 mmol) in 20 ml of diethyl ether was stood for 1 week at 0°C. The subsequent TLC afforded monoadduct Ia,[7] mp 64-65°C, in 10 % yield and a mixture of bis-adducts. This mixture was also separated by independent TLC and afforded IIa, mp 162-163°C, IIIa, mp 143-

144°C, and IVa, mp 203-204°C in 47 %, 4 % and 2 % yields, respectively.[8] When the mixture of benzocyclopropene (8 mmol) and mesitonitrile oxide[9] (4 mmol) in 10 ml of methylene chloride was refluxed for 5 days, mono-adduct Ib, mp 95-96°C, bis-adducts IIb, mp 189-190°C, IIIb, mp 193-194°C, IVb, mp 122-124°C and Vb, mp 160-161°C were obtained in 27 %, 10 %, 22 %, 9 % and 7 % yields, respectively. The mono-adducts Ia and Ib exhibited the following nmr spectra: Ia, δ (CCl_4), 0.20 (1H, d, J=4.5 Hz), 1.29 (1H, d, J=4.5 Hz), 5.78 (2H, m), 6.38 (2H, m), 7.26 (3H, m), 7.46 (2H, m); Ib, δ (CCl_4), 0.33 (1H, d, J=4.5 Hz), 1.46 (1H, d, J=4.5 Hz), 2.05 (3H, s), 2.27 (3H, s), 2.38 (3H, s), 5.29 (3H, s), 6.55 (1H, m), 6.84 (1H, m), 6.88 (1H, br. s). The small geminal coupling constants (J=4.5 Hz) for hydrogens at C-10 and the chemical shifts of olefinic hydrogens of Ia and Ib support the closed norcaradiene structures for Ia and Ib as shown below. The partial structures of bis-adducts were also



Ia
Ib

a : Ar=Phenyl
b : Ar=Mesityl

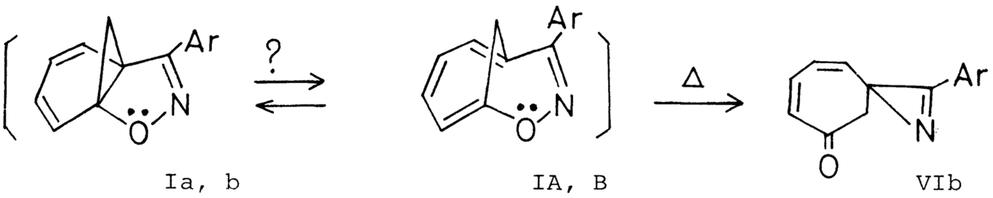
IIa, IIIa
IIb, IIIb

IVa
IVb, Vb

deduced from the nmr spectra which were shown in Table I. The stereochemistry of isoxazoline moieties as well as the regiochemistry of nitrile oxides at the cyclopropane moieties are not clear at the present stage. In order to clarify the reaction pathways of benzocyclopropene and the formation pathways of bis-adducts, the reactions of Ia with excess benzonitrile oxide and Ib with excess mesitonitrile oxide were carried out. As the results, bis-adducts IIa-IVa and IIb-Vb were obtained in the similar ratio described above. Consequently, it was suggested that cycloaddition reactions of aromatic nitrile oxides underwent across the 1-2 bond of benzocyclopropene to lead I and subsequent additions of aromatic nitrile oxides to I gave bis-adducts. The cycloaddition reaction across the 1-2 bond can be rationalized either as a symmetry allowed $[{}_{\pi}6_s + {}_{\pi}4_s]$ process or a $[{}_{\pi}2_s + {}_{\pi}4_s]$ process.[10] Furthermore the low yields of mono-adducts Ia and Ib suggest that the butadiene moieties of Ia and Ib are more reactive than benzocyclopropene in this 1,3-dipolar cycloaddition.

In order to elucidate the thermal behavior of Ia, b and the possible existence of opened oxazonine isomers IA, B, the nmr spectra of Ia, b were measured in the range of 25°C to 120°C in tetrachloroethylene. None of the spectral changes was observed except the coalescence of methyl signals at δ 2.05 and δ 2.27 of Ib above

82°C. This coalescence could be originated from the rotation of mesityl group. However, heating of Ib at 130-135°C in dimethyl sulfoxide solution caused formation of VIb in fairly good yield. The structure of VIb were deduced from the following spectral properties: ν (KBr), 1720, 1650 cm^{-1}, δ ($CDCl_3$), 2.31 (3H, s), 2.43 (6H, s), 2.26-2.48 (1H, d, J=14.0 Hz, overlapped with methyl signals), 3.42 (1H, d, J=14.0 Hz), 5.66 (1H, d, J=11.5 Hz), 6.00 (1H, dd, J=11.5, 8.0 Hz), 6.56 (1H, dd, J=12.0, 8.0 Hz), 6.12 (1H, d, J=12.0 Hz). The infrared spectra shows the existence of azirine ring[11] and α,β-unsaturated ketone, and the decoupling technique of nmr clarified the presented structure. This type of azirine formation are well known in the thermal[12] and photochemical[13] isomerization of isoxazoles and the photochemical reactions of isoxazoline derivatives.[14] In the present case the formation of VIb can be explained by two possible pathways through Ib or IB, however the evidence of the existence of IB could not be obtained.



Ia, b IA, B VIb

Ar=Mesityl

Even though a C=N-O group was introduced in the nine-membered perimeter of I, the evidence of the equilibrium between Ia, b and IA, B was not obtained. Since Ia, b have an aryl group which can conjugate with C=N-O group, this effect might be possible to stabilize Ia, b as well as IA, B. In order to elucidate the possibility and also the problems concerning the equilibrium between closed norcaradiene type isomer (C) and opened oxazonine type isomer (D), the syntheses and thermal behaviors of the derivatives having alkyl substituents on C=N-O group of I are now under investigation.

Table I The NMR Spectra of Bis-adducts (in $CDCl_3$ Solution).

IIa : 1.12 (1H, d, J=5.5 Hz), 1.18 (1H, d, J=5.5 Hz), 4.07 (1H, d, J=10.0 Hz), 4.99 (1H, dd, J=10.0, 5.0 Hz), 5.95 (1H, dd, J=10.5, 5.0 Hz), 6.72 (1H, d, J=10.5 Hz), 7.46 (7H, m), 7.74 (2H, m), 8.04 (2H, m).

IIIa : 1.22 (1H, d, J=5.5 Hz), 1.25 (1H, d, J=5.5 Hz), 3.72 (1H, d, J=9.0 Hz), 4.98 (1H, dd, J=9.0, 5.5 Hz), 6.00 (1H, dd, J=10.5, 5.5 Hz), 6.85 (1H, d, J=10.5 Hz), 6.84-7.48 (10H, m).

IVa : 1.32 (1H, d, J=5.0 Hz), 1.36 (1H, d, J=5.0 Hz), 4.45 (1H, m), 5.55 (1H, d, J=11.5 Hz), 5.72 (1H, dd, J=10.5, 4.0 Hz), 6.48 (1H, dd, J=10.5, 2.5 Hz), 7.17-7.86 (10H, m).

IIb : 1.34 (1H, d, J=5.5 Hz), 1.38 (1H, d, J=5.5 Hz), 3.85 (1H, d, J=9.5 Hz), 5.04 (1H, dd, J=9.5, 5.5 Hz), 5.93 (1H, dd, J=10.5, 5.5 Hz), 6.24 (1H, d, J=10.5 Hz), 2.12 (3H, s), 2.30 (9H, s), 2.40 (6H, s), 6.84-7.01 (4H, m).

IIIb : 1.28 (1H, d, J=5.5 Hz), 1.32 (1H, d, J=5.5 Hz), 3.48 (1H, d, J=9.5 Hz), 4.96 (1H, dd, J=9.5, 5.5 Hz), 6.02 (1H, dd, J=10.5, 5.5 Hz), 6.90 (1H, d, J=10.5 Hz), 6.28-6.79 (4H, m), 1.65 (3H, s), 1.72 (3H, s), 2.10 (3H, s), 2.22

(3H, s), 2.26 (3H, s), 2.38 (3H, s).

IVb : 1.33 (1H, d, J=5.5 Hz), 1.63 (1H, d, J=5.5 Hz), 4.23 (1H, m, J=11.5, 4.5, 2.5 Hz), 4.85 (1H, d, J=11.5 Hz), 5.34 (1H, dd, J=11.0, 4.5 Hz), 6.63 (1H, dd, J=11.0, 2.5 Hz), 6.91 (4H, m), 2.13 (6H, s), 2.26 (6H, s), 2.32 (3H, s), 2.48 (3H, s).

Vb : 1.32 (1H, d, J=5.5 Hz), 1.45 (1H, d, J=5.5 Hz), 4.29 (1H, m, J=12.0, 4.0, 2.0 Hz), 5.08 (1H, dd, J=10.0, 4.0 Hz), 5.45 (1H, d, J=12.0 Hz), 5.76 (1H, dd, J=10.0, 2.0 Hz), 6.72 (4H, m), 2.04-2.28 (18H, associated 6 Me).

References and Notes

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7) Elemental analyses and mass spectral properties are satisfactory for all new compounds described in this paper.

8) The yields for all products in this paper are isolated yields based on aromatic nitrile oxides.

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