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2-ISOXAZOLINE DERIVATIVES—III[1]

SYNTHESIS AND REACTIONS OF THE 2,3-OXAZABICYCLO[3.2.0]HEPTA-3,6-DIENE SYSTEM

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Abstract—The structure and the stereochemistry of the mono-adducts, obtained by 1,3-dipolar cycloaddition of nitrile oxides to cyclooctatetraene, have been elucidated on chemical evidence. Thermolysis of their Diels-Alder adducts with acetylenedicarboxylate yielded 4-aryl (or alkyl)-2,3-oxazabicyclo[3.2.0]hepta-3,6-dienes. Some reactions of this new heterocyclic condensed system are described.

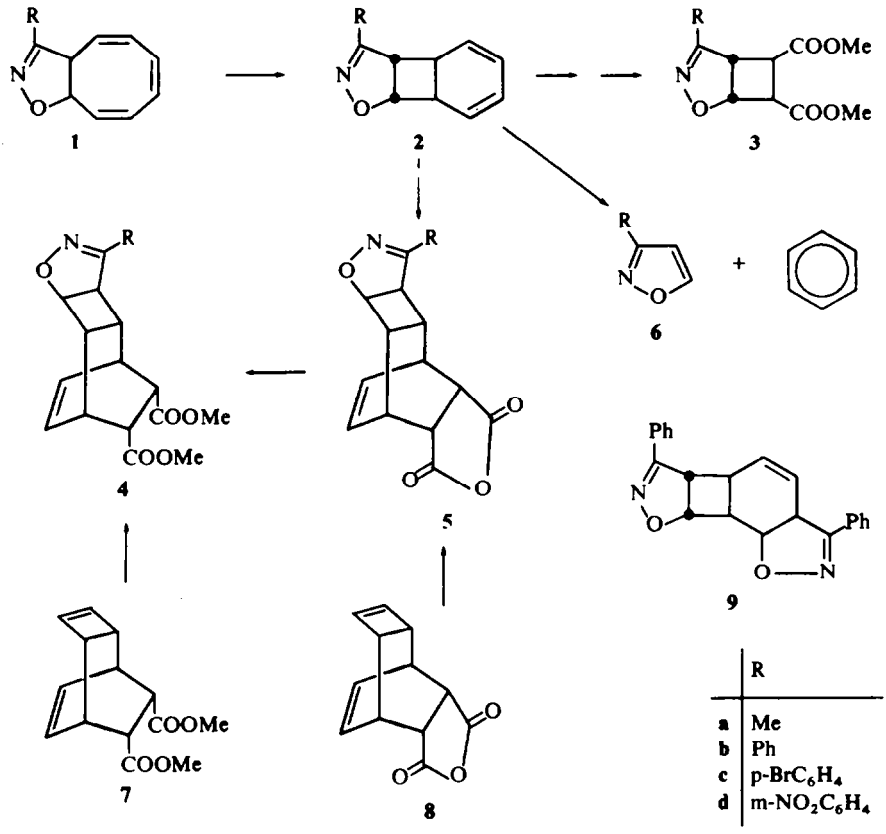
THE 1,3-dipolar cycloaddition of fulminic acid[2] and other aromatic nitrile oxides[3,4] to cyclooctatetraene is known to yield a 1:1 adduct. PMR evidence showed[3] that the primary product, not isolated, is the bicyclic adduct **1**, which readily gives **2** through valence tautomerization.

As partly anticipated in our preliminary account,[4] the tricyclic structure **2** was confirmed by chemical evidence (Scheme 1): (i) Oxidation and methylation yielded the bicyclic 2-isoxasolines **3**; (ii) Diels–Alder reaction of **2b** led to the *endo*-anhydride **5b** and subsequently to the related dimethyl ester **4b**, both compounds being also synthesized from the anhydride **8**[5–7] and ester **7**[7] of well-established stereochemistry; (iii) Thermolytic breakdown gave high yields of 3-monosubstituted isoxazoles (**6**) and benzene. Acetonitrile oxide was shown to react, although with lower yield, with cyclooctatetraene in an analogous manner as the aromatic homologs to yield **2a**. The diene system of **2b** is still reactive toward benzonitrile oxide and from the reaction mixture two monoadducts were isolated and characterized. Structure **9** is proposed for the most abundant isomer.

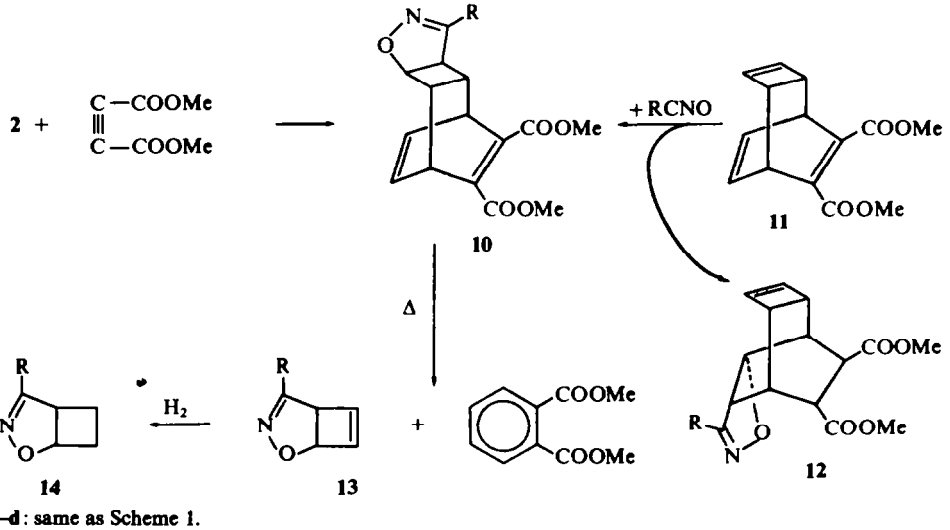
Since vicinal *cis* and *trans* coupling constants in the PMR spectra of cyclobutane rings are not sufficiently characteristic to allow assignment of the *syn* or *anti* configuration with reasonable assurance,[8] the stereochemistry of the tricyclic compounds (**2**) is based on following considerations.

Cycloaddition of **2a–d** to dimethyl acetylenedicarboxylate led to Diels–Alder monoadducts with good yields: their structures **10a–d** were deduced from the identity with products obtained by another route, as shown in Scheme 2. 1,3-Dipolar cycloadditions of the adduct cyclooctatetraene-dimethyl acetylenedicarboxylate, whose configuration (**11**) is known,[6,7] to benzonitrile oxide and its *p*-bromoderivative gave two types of monoadducts. The principal products, obtained in 50–60% yields, were assigned structures **12b** and **12c** resp. An attack on the double bond conjugated with the carbomethoxy groups to yield the isomeric product **15** is far less probable owing to the lower reactivity of tetrasubstituted double bonds towards nitrile oxides and to the thermal stability of the adducts. Indeed the condensed pyrazolines (**16**)

SCHEME 1

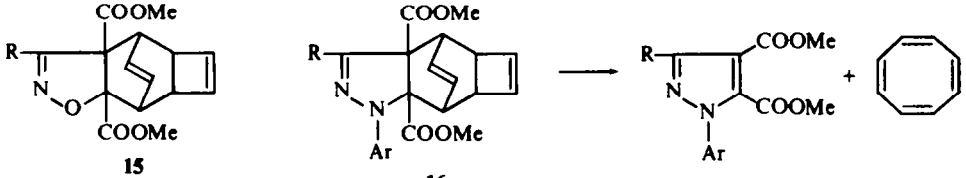


SCHEME 2



a–d: same as Scheme 1.

whose structure is analogous to **15**, decomposed easily by heating to cyclooctatetraene and to 1,3-disubstituted pyrazole dicarboxylates.[9] The by-products of the cycloaddition of **11** to nitrile oxides, obtained in 17–19% yields, were shown to be identical with the adducts obtained from **2b–c** and dimethyl acetylene dicarboxylate. It is worth noting the different behaviour of **7** and **11** towards nitrile oxides: in the former case the 1,3-dipole attacks only the more strained and less hindered cyclobutene double bond, whilst in the latter cycloaddition both unsubstituted double bonds are dipolarophilic, the cyclohexadiene bond being here more reactive.



15 **16**

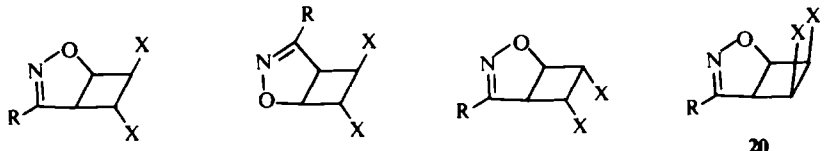
From the above facts the *anti*-configuration of **2** can be safely deduced. The 1,3-dipolar cycloaddition of tetracyanoethylene oxide to cyclooctatetraene and to its tetracyanoethylene adduct[10] are known to lead to products of similar stereochemistry.

The thermal decomposition of **10a–d** resulted in good yields of the new heterocyclic-condensed cyclobutene system (**13**) i.e. 4-aryl(or alkyl)-2,3-oxazabicyclo[3.2.0]-hepta-3,6-diene. This interesting bicyclic structure is supported by spectroscopic data and chemical properties.

Selective hydrogenation of the cyclobutene double bond without affecting the 2-isoxazoline ring was achieved using experimental conditions already employed for isoxazole derivatives.[11] The 4-aryl-2,3-oxazabicyclo[3.2.0]hepta–3–enes (**14b** and **14c** resp.) were thus obtained in good yield from **13b** and **13c**. The structure of **14c** was confirmed by direct comparison with a synthetic sample prepared by 1,3-dipolar cycloaddition of *p*-bromobenzonitrile oxide to cyclobutene.

The general applicability of the selective hydrogenation to condensed 2-isoxazoline systems was demonstrated by extension to the adducts **2b** and **2c**, which yielded the corresponding tricyclic 2-isoxazoline tetrahydro derivatives.

The strained double bond of the 2,3-oxazabicyclo[3.2.0]hepta-3,6-diene is reactive toward electrophilic reagents and several 2-isoxazoline derivatives condensed with a cyclobutane ring through a 4–5 junction could thus be prepared. Halogenation led to a mixture of three isomeric dihalogeno derivatives (**17**, **18** and **19**) whose configurations were ascertained by PMR analysis.[12] Two isomers, i.e. **17** and **18**, arise from the *trans*-addition to the double bond, whereas to the third isomer obtained in lower yields, the *anti-cis* configuration **19** was allotted, thus involving a *cis*-addition of chlorine or bromine from the less hindered side of the cyclobutene double bond. It is worth pointing out that the isomers ratio shows some solvent dependence: a polar solvent such as acetic acid decreases the yield of the *cis*-product **19b** from 11·6 (in CCl_4) to 5·4%.



17 18 19 20

a: R = Ph; X = Cl
b: R = Ph; X = Br
c: R = *p*-BrC_6H_4; X × Br

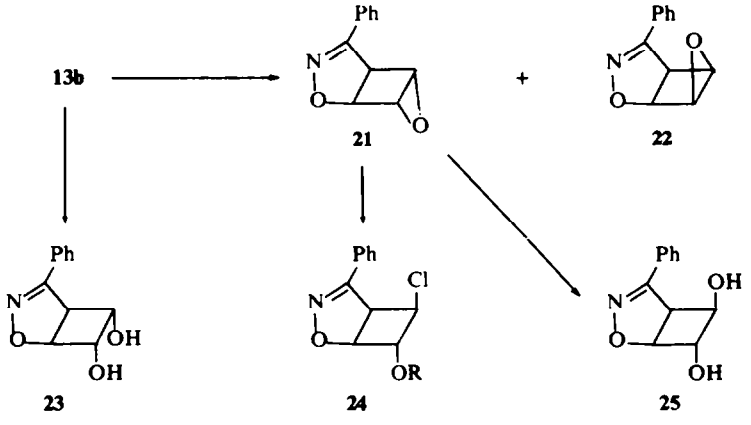
Concerning dipolarophilic activity of *cis*-3,4-dichlorocyclobutene, only recently has the cycloaddition with diazoalkanes been studied. Whilst 2-diazopropane reacts to yield a mixture of the two possible isomers, possessing the *anti-syn*-configurations resp. in a 2·5:1 ratio,[13] a single isomer, *viz* the more heavily crowded *syn*-pyrazoline, was obtained with diazomethane or diazoethane.[14]

The cycloaddition of benzonitrile oxide to *cis*-3,4-dichlorocyclobutene does not show any remarkable stereoselectivity. Though the conversion yield was not quantitative, we obtained nearly equimolecular amounts of the two possible isomers, *viz* the *syn*-4-phenyl-6,7-*cis*-dichloro-2,3-oxazabicyclo[3.2.0]hept-3-ene (**20a**) and the *anti*-isomer **19a**. This latter compound is identical with the product obtained in the chlorination of **13b**.

As expected, all four dihalides **17–20** dehalogenated to **13** when treated with zinc and ethanol, the dibromides reacting faster.

Treatment of **13b** with performic acid gave a 79% yield as major product *viz* the *anti*-epoxide **21**, which could be produced by an electrophilic attack on the cyclobutene double bond from the least hindered side. The *anti*-configuration could be deducted from hydrolytic cleavage to the chlorohydrin **24** (R=H), whose stereochemistry was confirmed by PMR analysis.[12] Consistent with these facts, the treatment of **13b** with osmium tetroxide yielded a single glycol, which was assigned the *anti-cis* configuration **23**. In the epoxidation reaction a minor amount (4%) of the *syn*-epoxide **22** was isolated, and during the chloridrin formation the *trans*-glycol **25** was formed as a by-product. Consistent with these facts, the *trans*-glycol shows only one OH-band in the IR spectrum whilst the *cis*-glycol shows two bands, owing to intramolecular H-bonding.

SCHEME 3:



23 24 25

We are now exploring the dienophilic and dipolarophilic reactivity of the 2,3-oxazabicyclo[3.2.0]hepta-3,6-diene system, which should lead to heterocyclic polycondensed cyclobutanes.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were measured from Nujol mulls on a Perkin–Elmer 257 spectrophotometer. UV spectra were obtained from solns in 95% EtOH, using a Perkin–Elmer 135 recording spectrophotometer. Mycroanalyses were performed by Dr. Lucia Maggi Dacrema. Unless otherwise specified, analytical and preparative chromatographies were run on Silicagel H (Merck) plates resp. columns, eluant cyclohexane-ethyl acetate = 70:30. The identity of different samples of the same products was established by determination of the mixed m.p. and comparison of the IR spectra.

Cycloaddition of nitrile oxides to cyclooctatetraene

Acetonitrile oxide was prepared *in situ* from nitroethane and phenyl isocyanate by the general procedure[16] and condensed with a slight excess of cyclooctatetraene in benzene soln. Diphenylurea separated out in 100% yield. Benzonitrile oxide was prepared *in situ* from the appropriate hydroximic acid chloride by the general procedure[17] and condensed with an excess of the dipolarophile in anhyd ether. The reaction with isolated *p*-bromo[18] and *m*-nitrobenzonitrile oxides[19] lead to slightly minor yields. After evaporation of the solvent the residues were eluted on silica with benzene. Recrystallization solvents, m.ps, yields and combustion analysis data are collected in Table 1.

Oxidation of the adducts **2**. The monoadducts **2b–d** were dissolved in pure acetone and added with a slight excess of $KMnO_4$ in acetone. After 12 hr the solvent was removed under reduced press, and the residue was dissolved in water. The filtered soln was acidified and extracted continuously with ether. Treatment with ethereal diazomethane yielded **3**, whose characterization data are reported in Table 1.

Thermal decomposition of **2**. The monoadduct **2b** was heated for a few min in an oil bath at 100°. The residue was chromatographed to give an 80% of 3-phenylisoxazole, identical with an authentic sample.[20] Benzene was identified by preparative GLC.

The decomposition of **2c** and **2d** was accomplished under reduced press in a sublimator heated in an oil bath at 140°, and afforded 3-*p*-bromophenylisoxazole[21] (70%) and 3-*m*-nitrophenylisoxazole[22] (68% yield). The products were identified by comparison with authentic samples prepared by known procedures. In the former reaction a 28% yield of a higher melting by-product, m.p. 237°, was obtained, which was not analysed, being probably a dimer of **2c** analogous to the dimer of **2b**.[3]

Reaction of **2b** *with maleic anhydride*. The adduct **2b** (0·1 g) and maleic anhydride (0·1 g) were heated together in a few ml of anhyd ether. The separated products **5b** (0·13 g, 93%) was filtered off and recrystallized.

Reaction of benzonitrile oxide with **8**. Benzonitrile oxide was prepared in $CHCl_3$ soln from benzohydroximic acid chloride (3·5 g) and 14% NaOH aq and added to a hot $CHCl_3$ soln (70 ml) of the cyclooctatetraene/maleic anhydride adduct (3·0 g).[23] After refluxing for 3 hr, the ppt was collected (3·8 g, 80%) and found identical with **5b** from the previous reaction. Preparation of the nitrile oxide by the *in situ* technique increased the yield to 85%.

Methanolysis of **5b**. The anhydride **5b** (2·0 g) in MeOH (15 ml) was refluxed for 1·5 hr in the presence of conc H_2SO_4 (1·5 ml). After cooling the reaction mixture practically pure **4b** separated out.

Reaction of benzonitrile oxide with **7**. Working as above, from benzonitrile oxide in $CHCl_3$ soln and the cyclooctatetraene/dimethyl maleate adduct[23] a 90% yield of a product identical in all respects with **4b** (from the previous reaction) was obtained.

Reaction of benzonitrile oxide with **2b**. To an ethereal soln of **2b** (1·0 g) and benzohydroximic acid chloride (0·35 g) an ethereal soln of triethylamine (0·25 g) was added dropwise, and the mixture was left overnight. The white ppt was filtered off and thoroughly washed with water. Chromatography on silica afforded a product (0·25 g), whose analytical and spectral data are consistent with structure **9**. Chromatography of the residue from the mother liquor yielded starting material (0·6 g) and crude material, m.p. 150–175° (0·20 g), from which an isomer of **9**, m.p. 164–165° could be isolated. (Found: C, 77·10; H, 5·30; N, 8·18. Calc. for $C_{22}H_{18}N_2O_2$: C, 77·17; H, 5·53; N, 8·31).

Reaction of **2** *with dimethyl acetylenedicarboxylate*

General procedure. An ethereal soln of the adducts **2a–d** and a large excess of dimethyl acetylenedicarboxylate was kept at r.t. for some days. The separated crystals were filtered off and recrystallized from the appropriate solvent to give the Diels–Alder adducts **10a–d**. Characterization data are collected in Table 1.

TABLE 1. CHARACTERIZATION OF PRODUCTS

Compound	M.p. (b.p./mm)	Recrystal. solvent	% Yield (purified product)	Analyses Calc. C	H	N	Found C	H	N	UV Spectrum λ_{max} (mμ)	log ε
2a	52–53°	Petrol ether	38	74·51	6·88	8·69	74·70	6·82	8·69	229, 281	3·55; 3·27
2b	90°	n-C_6H_{14}	50	80·69	5·87	6·27	81·11	6·09	6·31	261·5	4·14
2c[a]	128°	EtOH	70	59·70	3·98	4·64	59·98	4·28	4·75	265	4·28
2d	144–145°	EtOH	75	67·15	4·51	10·44	67·52	4·73	10·47	257	4·27
3b	116–117°	MeOH	50	62·28	5·23	4·84	62·13	5·25	4·90	267	4·11
3c[b]	93°	Pr_2O	49	48·93	3·83	3·80	49·35	3·65	3·90	274	4·25
3d	116·5–117·5°	MeOH	30	53·89	4·22	8·38	54·31	4·37	8·32	262	4·23
5b	276° dec	Xilene	93	71·02	4·71	4·36	71·34	4·60	4·38		
4b	207–209° dec	AcOEt	100	68·65	5·76	3·81	68·53	5·72	3·90	269	4·06
9	198–199°	EtOH	32	77·17	5·30	8·18	77·00	5·32	8·14		
10a	110·5–111·5°	C_6H_6/n-C_6H_{14}	88	63·36	5·65	4·62	63·5	5·62	4·55		
10b	161–162°	MeOH	80	69·03	5·24	3·83	69·38	5·20	3·88	268	4·11
10c[c]	201–202°	AcOMe	68	56·77	4·08	3·15	57·12	4·09	3·10		
10d	154–155°	AcOMe	85	61·46	4·42	6·83	61·52	4·54	6·84		
12b	204–205°	MeOH	57	69·03	5·24	3·83	68·97	5·35	3·93	258, 5	4·05
12c[d]	201–202°	AcOMe	70	56·77	4·08	3·15	57·09	4·01	3·31		
13a	(80–82°/2·5)	AcOMe	65	66·03	6·47	12·84	66·10	6·75	12·92	234	2·99
13b	45–46°	Petrol ether	85	77·17	5·30	8·18	76·91	5·23	8·30	268·5	3·98
13c	106–106·5°	MeOH	88	52·82	3·22	5·60	53·16	3·25	5·69	274	4·17
13d	143°	Toluene	57	61·11	3·73	12·96	61·76	3·94	12·83	262	4·22
14b	33–34°	n-C_5H_{12}	67	76·27	6·40	8·09	76·22	6·69	8·22	269	4·00
14c[f]	130–131°	EtOH	(i) 64	52·40	3·99	5·55	52·58	4·33	5·44	276·5	4·22

[a] Br: calc. 26·50; found 26·94.
[b] Br: calc. 21·70; found 21·55.
[c] Br: calc. 17·98; found 18·04.
[d] Br: calc. 17·98; found 17·94.
[e] Br: calc. 31·95; found 32·27.
[f] Br: calc. 31·70; found 31·66.

TABLE 2. 4-ARYL-6,7-DIHALO-2,3-OXAZABICYCLO[3.2.0]HEPT-3-ENES

Compound	M.p.	Recrystallization	% Yield[a]		Analyses Calc.				Analyses Found			
			A	B	C	H	N	X[b]	C	H	N	X[b]
17a	80°	EtOH	19·2	—	54·57	3·74	5·78	29·29	54·55	4·15	6·01	28·94
18a	119–121°	EtOH	21·2	—	54·57	3·74	5·78	29·29	54·74	3·91	5·68	29·10
19a	112–113°	MeOH	20·2	42·5	54·57	3·74	5·78	29·29	54·30	3·81	5·78	29·36
20a	163°	MeOH	—	43·5	54·57	3·74	5·78	29·29	55·02	3·80	6·00	29·42
17b	110–111°	n-hexane	42	—	39·91	2·74	4·23	48·29	40·13	2·74	4·30	48·41
18b	111–112°	n-hexane	28	—	39·91	2·74	4·23	48·29	40·23	2·72	4·31	48·29
19b	120–121°	n-hexane	11·6	—	39·91	2·74	4·23	48·29	40·06	2·82	4·22	48·73
17c	139·5–140·5°	EtOH	29·5	—	32·23	1·96	3·41	58·48	31·94	2·18	3·54	58·52
18c	139°	MeOH	28·5	—	32·23	1·96	3·41	58·48	32·32	2·09	3·65	58·12
19c	166–168°	EtOH	24	—	32·23	1·96	3·41	58·48	32·44	2·04	3·54	58·17

[a] Method A: Halogenation of **13** in CCl_4.
Method B: Cycloaddition benzonitrile oxide + *cis*-3,4-dichlorocyclobutene.

[b] X: Cl for **a**: Br for **b** and **c**.

Reaction of nitrile oxides with **11**. To an ethereal soln of benzo- and *p*-bromobenzo-hydroximic acid chlorides and an 80% excess of cyclooctatetraene/dimethyl acetylenedicarboxylate adduct[6] the theoretical amount of Et_3N was added dropwise. After standing at r.t. for 2 hr the ppt was filtered off, washed with water and crystallized from MeOH to yield pure **12b** and **12c** resp. The residue from the methanolic and ethereal mother liquors was chromatographed on silica and yielded further amounts of **12b** or **12c** from amounts of **10b** (17%) and **10c** (18·5%), identical with the products obtained from the previously described reaction.

Thermal decomposition of **10**. The adducts **10a**, **10b**, **10c** or **10d** were heated under reduced press at 200° (oil bath). After completion the distillate or sublimate was chromatographed on silica in the usual manner, resulting in separation of the 4-aryl (or methyl) **13a–d** and dimethyl phthalate. Characterization data of the former compounds are collected in Table 1, yields of the latter product are: 98% from **10a**, 85% from **10b**, 88% from **10c**.

4-p-*Bromophenyl*-2,3-*oxazabicyclo*[3.2.0]*hept*-6-*ene* (**14c**)

(i) Compound **13c** (1·0 g) in a mixture of EtOAc/AcOH (4:1: 90 ml) was hydrogenated at room temp and press in the presence of 10% Pd/C (20 mg). After filtration and removal of the solvent the residue was chromatographed (eluant cyclohexane/$(CH_2Cl)_2$ = 3:2) and recrystallized (Table 1).

(ii) An excess of cyclobutene[24] was added at 7–10° to an ethereal soln of *p*-bromobenzohydroximic acid chloride (5·0 g). During stirring the theoretical amount of Et_3N was added dropwise. The ppt was filtered off and washed with water. The insoluble solid (0·3 g) was shown to be 3,3-di-*p*-bromophenyl-5,5'-diisoxazoline by comparison with an authentic sample (see below). After removal of the solvent from the mother liquor, the residue was chromatographed. Besides small amounts of impure 3,4-di-*p*-bromophenylfuroxan a 74% yield of **14c**, was obtained, identical with the product prepared by route (i).

Reaction of p-*bromobenzonitriloxide with butadiene*. To a well cooled soln of *p*-bromobenzohydroximic acid chloride (5·0 g) and butadiene in ether (100 ml) the theoretical amount of Et_3N was added dropwise. After standing 2–3 hr the ppt was filtered off and thoroughly washed with water. The insoluble solid was recrystallized from dioxan to give colourless leaflets (0·45 g, 4%) of 3,3'-di-*p*-bromophenyl-5,5'-diisoxazol-2-ine, m.p. 235° dec. (Found: C, 48·08; H, 3·41; N, 6·27; Br, 35·40. Calc. for $C_{18}H_{14}Br_2N_2O_2$: C, 48·03; H, 3·13; N, 6·22; Br, 35·51).

Evaporation of the filtrate gave a 53% yield of the 1:1 cycloadduct, i.e. 3-*p*-bromophenyl-5-vinyl-2-isoxazoline, as colourless needles from EtOH, m.p. 98°.

Selective hydrogenation of condensed 2-*isoxazolines*

(i) Hydrogenation of **13b** (1·0 g) dissolved in AcOEt/AcOH (4:1) at room temp and press in the presence of 10% Pd/C afforded **14b**, purified by column chromatography, sublimation and recrystallization (Table 1).

(ii) A soln of **2b** in AcOEt/AcOH (4:1) was hydrogenated in the presence of 10% Pd/C during 2 hr. After usual working up, a 79% yield of 5-phenyl-3,4-oxazatricyclo[5.4.0.$0^{2,6}$]undec-4-ene was obtained as colourless plates from n-hexane, m.p. 63°. (Found: C, 79·68; H, 7·53; N, 6·24. Calc. for $C_{15}H_{17}NO$: C, 79·26; H, 7·54; N, 6·16%).

(iii) An analogous hydrogenation of **2c** afforded, after column chromatography on silica (eluant cyclohexane/$(CH_2Cl)_2$ = 1:1), two products: a 14% yield of 5-phenyl-3,4-oxazatricyclo[5.4.0.$0^{2,6}$]undec-4-ene, identical with the compound obtained in route (ii), and a 52·4% yield of the *p*-bromophenyl derivative, m.p. 131–132°, colourless plates from EtOH. (Found: C, 48·79; H, 5·47; N, 4·60; Br, 25·95. Calc. for $C_{15}H_{16}BrNO$: C, 58·83; H, 5·26; N, 4·57; Br, 26·10%).

Halogenation of 4-*aryl*-2,3-*oxazabicyclo*[3.2.0]*hepta*-3,6-*dienes* (**13**).

(i) A saturated soln of Cl_2 in CCl_4 was slowly added to an ice-cooled soln of **13b** (1·4 g) in CCl_4 (40 ml). After disappearance of the starting material (TLC), the solvent was removed under reduced press. The oily residue (three spots in TLC) was chromatographed on silica column, using benzene as eluent. Two fractions were separated: the former (0·85 g) was a mixture of two products, the latter contained pure **17a** (0·38), total yield 62%. The former mixture was rechromatographed with cyclohexane/AcOEt = 9:1 as eluent, which separated the two other components. The isomers ratio and characterization data are collected in Table 2.

(ii) A soln of Br_2 (slight excess) in CCl_4 was added dropwise to a soln of **13b** (1·55 g) in CCl_4 (30 ml). After disappearance of the starting material (4 hr) the solvent was removed and the residue was chromatographed on a silica column (eluent EtOAc/cyclohexane = 20:80). Three isomers (**17b**, **18b** and **19b**) were thus separated and identified by PMR analysis (Table 2).

When the bromination was carried out in AcOH soln, after the usual work-up, the following yields of the three isomers were obtained: **17b**, m.p. 110–111°, 54%; **18b**, m.p. 111–112°, 29%; **19b**, m.p. 120–121°, 5·4%.

(iii) By analogous bromination of **13c**, after solvent removal and chromatography on silica column (eluent cyclohexane/benzene = 50:50), three isomers were separated (**17c**, **18c** and **19c**) and identified by PMR analysis (Table 2).

Cycloaddition of benzonitrile oxide to cis-3,4-*dichlorocyclobutene.* To a soln of *cis*-3,4-dichlorocyclobutene (1·4 g) and benzohydroximic acid chloride (0·7 g) in ether (15 ml) an ethereal soln of Et_3N (0·65 ml) was added dropwise during 2 hr. After standing for an hr, the ppt was filtered off and washed with water. The mother liquor was evaporated to a small volume and filtered again. The combined insoluble solids were recrystallized from MeOH as colourless plates of **20a** (0·46 g). The residue was chromatographed, using cyclohexane/ether = 80:20 as eluent, and **19a** (0·47 g) was thus separated from small amounts of diphenylfuroxan.

Dehalogenation of dihalo derivatives **17–20**. The dihalo derivative was heated with a large excess of Zn in MeOH. The dehalogenation was followed by TLC. After completion of the reaction the mixture was filtered and the solvent removed from the filtrate. The residue was chromatographed or directly crystallized to yield **13b**, m.p. 45°, identical in all respect with the product prepared previously. Starting material, reaction time and yield were as follows: (i) **19a**, 166 hr, 82%; (ii) **20a**, 480 hr, 78%; (iii) **17b**, **18b** or **19b**, 2 hr, 83–85%.

Reaction of **13b** *with performic acid.* To a stirred mixture of 30% H_2O_2 (10 ml) and 95% formic acid (35 ml) **13b** (2·5 g) was added in portions during 0·5 hr at r.t. After standing for 48 hr at 50° and for the same time at r.t. the solvent was removed under reduced press. The oily residue soon solidified and was recrystallized from n-hexane to give the epoxide **21** (1·15 g) as colourless needles, m.p. 78–79°. (Found: C, 70·54; H, 5·08; N, 7·60. Calc. for $C_{11}H_9NO_2$: C, 70·58; H, 4·85; N, 7·48%); UV: λ_{max} 267 mμ (log ε 4·11).

From the mother liquor evaporation of the solvent and column chromatography afforded a further amount of the *anti*-epoxide (1·0 g; total yield 79%) and a minor isomer (0·11 g; 4%), m.p. 169–171° (from EtOH). (Found: C, 70·55; H, 4·85; N, 6·83. Calc. for $C_{11}H_9NO_2$: C, 70·58; H, 4·85; N, 7·48%); UV: λ_{max} 266 mμ (log ε 4·10).

Reaction of **21** *with conc HCl.* The epoxide **21** was dissolved in hot conc HCl and the mixture was left. The ppt was filtered off and crystallized from MeOH/H_2O to give the chloridin **24** (R=) (75%) as colourless needles from H_2O–EtOH, m.p. 175–176°. (Found: C, 59·34; H, 4·56; N, 6·32; Cl, 15·97. Calc. for $C_{11}H_{10}ClNO_2$: C, 59·06; H, 4·50; N, 6·26; Cl, 15·85).

A more polar by-product was isolated from the mother liquor by column chromatography. The analytical and spectral data are consistent with a structure of *trans*-diol—colourless needles from water, m.p. 187–188°. (Found: C, 64·53; H, 5·76; N, 6·58. Calc. for $C_{11}H_{11}NO_3$: C, 64·38; H, 5·40; N, 6·83%); IR: ν_{OH} = 3420 cm^{-1} (*only* one band).

The chloridrin **24** (R=H; 0·5 g) was dissolved in Ac_2O in the presence of a drop of conc H_2SO_4 and left for 1 hr. After pouring in water the ppt was filtered off and crystallized from iso-Pr_2O to afford **24** (R=$COCH_3$; 0·5 g, 84%) as colourless prisms, m.p. 126–127°. (Found: C, 58·84; H, 4·45; N, 5·27; Cl, 13·95. Calc. for $C_{13}H_{12}ClNO_2$: C, 58·75; H, 4·55; N, 5·27, Cl, 13·34%).

Reaction of **13b** *with osmium tetroxide.* To a soln of **13b** (0·4 g) in anhyd pyridine (20 ml) OsO_4 (0·5 g) was added at once. The mixture was left at r.t. in the dark for 10 days. The solvent was then removed under reduced press and the pasty residue was treated with Na_2SO_3 (2·2 g) in H_2O (15 ml) and EtOH (15 ml). After boiling for 4 hr the solvent was removed under reduced press, the residue was redissolved in water, acidified and extracted continuously with ether for 30 hr. A crystalline product was obtained, which after chromatography on silica column (eluent AcOEt) yielded the *cis*-diol **23** (0·24 g, 60%) as colourless needles from benzene, m.p. 124–127°. (Found: C, 64·69; H, 5·41; N, 7·14. Calc. for $C_{11}H_{11}NO_3$: C, 64·38; H, 5·40; N, 6·83%); IR: ν_{OH} = 3420, 3370 cm^{-1}.

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