Δ^2-Isoxazoline Derivatives. Part X.[1] 1,3-Dipolar Cycloadditions of Nitrones and Nitrile Oxides with Indene, 1,2-Dihydronaphthalene, and *trans*-1-Phenylpropene

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Reactions of cyclic and acyclic nitrones and nitrile oxides with 1,2-dihydronaphthalene, indene, and *trans*-1-phenylpropene give rise to mixtures of regioisomers. The results are analysed on the basis of frontier orbital interactions and the steric requirements of reagents.

ONE of the most valuable assets of the frontier orbital perturbation approach to regioselectivity in 1,3-dipolar cycloadditions is its capacity to predict the major product of the two possible regioisomers.[2,3] Several cases of 1,3-dipolar cycloadditions have been reported to give both possible regioisomers (these arise from reaction paths with transition states of very similar potential energy). Such reactions have been studied principally with the aim of verifying the validity of perturbation theory.

The present paper is concerned with regioselectivity. The data obtained from cycloadditions of nitrones and nitrile oxides with 1,2-dihydronaphthalene, indene, and 1-phenylpropene (only with the nitrile oxides) are reported. All the reactions studied yielded mixtures of regioisomers and several results contrast with data reported in the literature.

TABLE 1

Overall yields of cycloadditions of nitrile oxides (1) and regioisomer ratios

R	Total yield (%)	Ratio (2) : (3)	Total yield (%)	Ratio (4) : (5)	Total yield (%)	Ratio (6) : (7)
a; Me			34	51 : 49	50	95 : 5 [a]
b; Ph	43.5	66 : 34	90	83 : 17	91	98 : 2 [b]
c; *p*-MeC_6H_4	78	72 : 28	72.5	77 : 23		
d; *p*-$MeO{\cdot}C_6H_4$	55	58 : 42	65	73 : 27		
e; *p*-$NO_2{\cdot}C_6H_4$	72	72 : 25	77.5	70 : 30		
f; *m*-$NO_2{\cdot}C_6H_4$			70	69.5 : 30.5		
g; *p*-BrC_6H_4			65	80 : 20		
h; 2,4,6-$Me_3C_6H_2$	72.5	20 : 80	84	26 : 74	76	74 : 26
i; 2,4,6-Me_3-3,5-Cl_2C_6	80	19 : 81				
j; 2,4,6-$(MeO)_3C_6H_2$	82	61.5 : 38.5	59	53 : 47	80	84 : 16

[a] From ref. 6 for reaction in benzene. [b] From ref. 5 for reaction in ether.

RESULTS

Data from the reactions of nitrile oxides (1) with 1,2-dihydronaphthalene and *trans*-1-phenylpropene in anhydrous benzene at room temperature are shown in Table 1.†

† Compound (2b) was isolated as the sole product from the reaction of benzonitrile oxide with *trans*-1-phenylpropene.[4]

[1] Part IX, A. Cerri, C. De Micheli, and R. Gandolfi, *Synthesis*, 1974, 710.

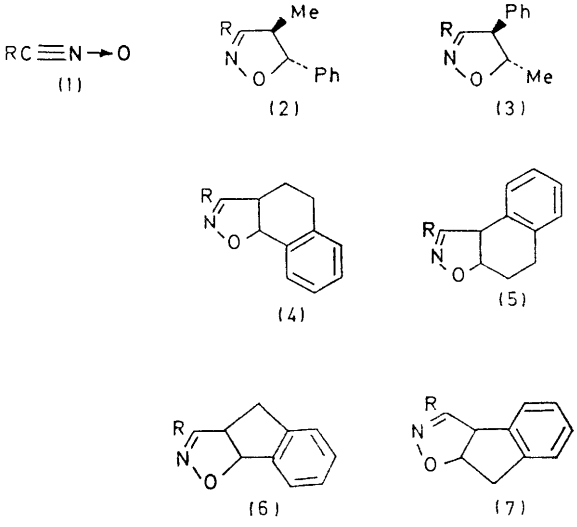
[2] K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Amer. Chem. Soc.*, 1973, **95**, 7301.

[3] J. Bastide, N. El Ghandour, and O. Henri-Rousseau, *Bull. Soc. chim. France*, 1973, 2290.

[4] K. Kotero, Y. Takano, A. Matsuura, and K. Kitahonoki, *Tetrahedron*, 1970, **26**, 539.

In order to evaluate solvent effects on the ratio of regioisomers formed, a few experiments were carried out with 2,4,6-trimethoxybenzonitrile oxide and β-methylstyrene. The results showed an increasing regioselectivity in the series: benzene [(2) : (3) 61.5 : 38.5], ethyl acetate [(2) : (3) 70 : 30], ethylene chloride [(2) : (3) 77 : 23]. The reactions of indene with benzonitrile oxide [5] and with acetonitrile oxide [6] have already been reported.

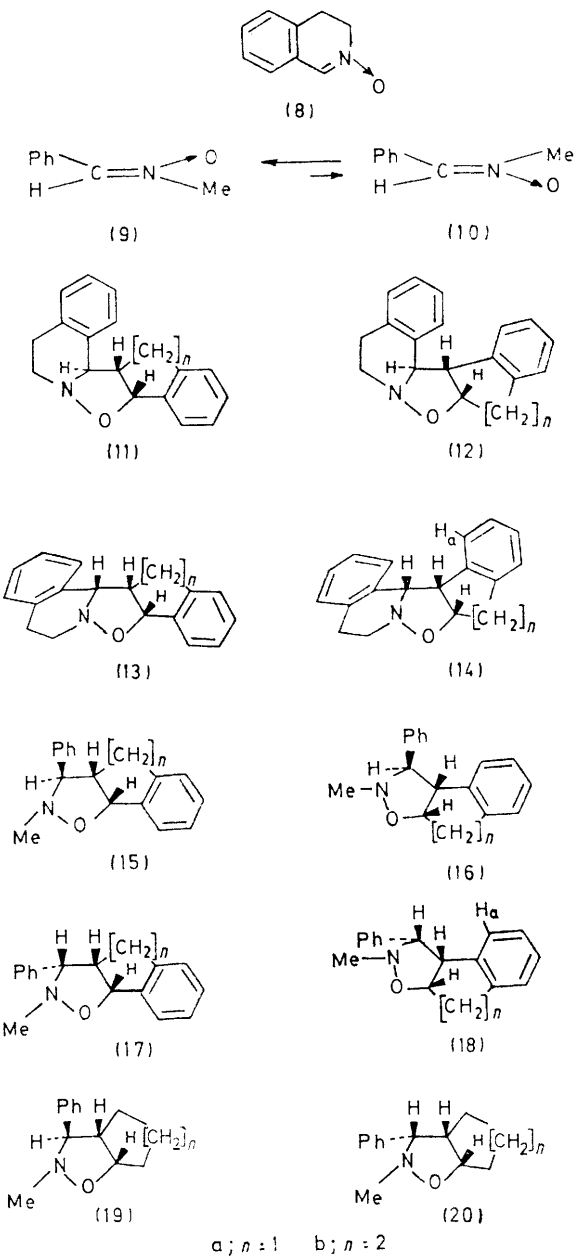
Structural assignments of the products were based on their proton n.m.r. spectra. In Δ^2-isoxazolines, the 5-proton is well known to absorb at lower field than the 4-proton, owing to the deshielding effect of the oxygen atom.[7] Moreover in the adducts (2), (4), and (6) the H-5 signal is a doublet, whereas it is a multiplet in compounds



(3), (5), and (7). Further support for the orientation of the cycloadducts can be obtained from the difference in chemical shifts of H-5 and H-4 ($\delta_5 - \delta_4$), which is larger for the adducts (2), (4), and (6) than for the regioisomers (3), (5), and (7). This is possibly due to the additive deshielding effect of the oxygen atom and the phenyl group on H-5.

3,4-Dihydroisoquinoline *N*-oxide (8) and *N*-benzylidenemethylamine *N*-oxide (9) have been treated with dipolarophiles in the absence of solvent at 70—100 °C to give stable adducts (11)—(18) (see Table 2) (no retrocycloaddition processes were detected). All the four possible isomers (15)—(18) were obtained in the reactions of the nitrone (9). In the case of dihydroisoquinoline *N*-oxide, with indene the four possible adducts (11a)—(14a) were obtained, whereas with dihydronaphthalene only the regioisomers (11b) and (12b) were formed.*

The assignment of regiochemistry to the pairs of epimers (11) and (13), and (15) and (17), and the related regioisomers (12) and (14), and (16) and (18) was made on the basis of n.m.r. data as previously for the Δ^2-isoxazolines. Of the two structures (11a) and (13a), the



a; $n = 1$ b; $n = 2$

former was assigned to the product formed in the larger amount (see Table 2) in view of its more stable transition state. The formation of the adduct (11a) goes through the *exo*-transition state, whereas (13a) is formed through the more hindered *endo*-transition state.

* The reactions of 3,4-dihydroisoquinoline *N*-oxide with indene and of *N*-benzylidenemethylamine *N*-oxide with indene and with 1,2-dihydronaphthalene have been reported to give the isoxazolidines with the methylene group directly attached to position 4 of the heterocycle as the sole isolated products. However the products were not fully characterized.[8]

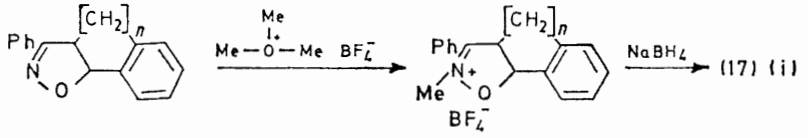
[5] G. Bailo, P. Caramella, G. Cellerino, A. Gamba Invernizzi, and P. Grünanger, *Gazzetta*, 1973, **103**, 47.

[6] G. Bianchi, R. Gandolfi, P. Grünanger, and A. Perotti, *J. Chem. Soc.* (*C*), 1967, 1598.

[7] G. Bianchi, C. De Micheli, R. Gandolfi, P. Grünanger, P. Vita Finzi, and O. Vaina de Pava, *J.C.S. Perkin I*, 1973, 1148, and references cited therein.

[8] R. Huisgen, R. Grashey, H. Seidl, and H. Hauck, *Chem. Ber.*, 1968, **101**, 2559.

In addition, definitive structural assignments were possible for compounds (12a), (14a), and (15)—(18) because the isoxazolidines (17a), (17b), and (18b) could be synthesized by an alternative route. Suitable Δ^2-isoxazolines are easily transformed into the above isoxazolidines with H-3 *cis* to H-4 [reaction (i)].[1]



Structure (18b) is further substantiated by the shielding effect experienced by H_a because of the phenyl ring at position 3 of the isoxazolidine ring.[1] A similar n.m.r. feature was found for the adducts (14a) and (18a).

TABLE 2

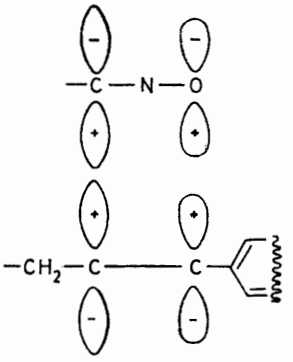
Overall yields of cycloadditions of nitrones (8) and (9) and isomer ratios

	Total	Ratio	Total	Ratio	Total	Ratio
n	yield (%)	(11) : (12) : (13) : (14)	yield (%)	(15) : (16) : (17) : (18)	yield (%)	(19) : (20)
a; 1	90	56 : 36 : 4 : 4	92	74 : 12 : 11 : 3	89	81 : 19
b; 2	91	8 : 92	97	26 : 59 : 4 : 11	78	87 : 13

DISCUSSION

As a general trend, the most favoured direction of addition of indene to the 1,3-dipoles is that which leads to adducts with the methylene group of the indene β to the carbon atom of the 1,3-dipole, as in (6), (11a), (15a), and (17a). However, as shown in Tables 1 and 2, more substantial amounts of the other regioisomer, *e.g.* (7), (12a), (14a), (16a), and (18a), are formed with more sterically hindered 1,3-dipoles, *e.g.* 2,4,6-trimethylbenzonitrile oxide (MNO) and nitrones. A lesser regioselectivity was observed in cycloadditions of 1,2-dihydronaphthalene and *trans*-1-phenylpropene, although the more favoured direction of addition was still that observed for indene. Exceptions to this rule were observed for cycloadditions of MNO, its 3,5-dichloro-derivative, and nitrones, which showed a reversed direction of addition with dominant adducts such as (3), (5), (12b), (16b), and (18b) being formed. The first conclusion to be drawn from the latter observed trends is that regioisomers with a methyl or methylene group attached to position 4 of the heterocyclic ring are favoured, and that the cases in which such an orientation is reversed concern 1,3-dipolar cycloadditions where steric considerations are dominant. That steric factors can play a determining role in controlling the direction of reaction for 1,3-dipolar cycloadditions has long been recognized.[9] However, recently it has been proposed that regiochemistry is mostly dependent on electronic factors.[2,3]

Our results throw some light on this point. Isoxazolidines and Δ^2-isoxazolines with a methylene or methyl group directly attached to C-4 of the heterocycle were obtained generally in larger amounts than the corresponding regioisomers. Although such a result conflicts with the expected unfavourable steric interaction in the reaction sequence of the major adduct, it can be explained in terms of perturbation theory. In terms of frontier orbital interactions it follows that electron-rich and conjugated alkenes react with nitrones and nitrile oxides by perturbing each other through the most effective interaction, *i.e.* LUMO(1,3-dipole)–HOMO(dipolarophile). The carbon coefficient of the LUMO of nitrile oxides and nitrones is larger than the oxygen coefficient.[10] As far as coefficients of the HOMO of the carbon–carbon double bond of alkenes studied in this work are concerned, although quantitative values have not appeared in the literature, it is reasonable to assume a larger coefficient at the carbon atom β rather than α to the phenyl group as consequence of a strong mesomeric effect.[10] In the case of 1,2-dihydronaphthalene, however, the two carbon atoms involved in the double bond should possess similar coefficients as a result of the less effective conjugative interaction with the aromatic system, which is not coplanar with the double bond.[11]



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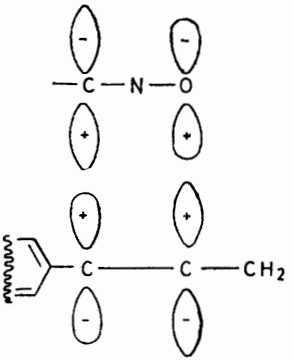

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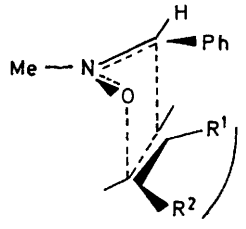
On the basis of this description of the ground states of reagents it is easy to explain the ratios and the formation of both regioisomers in the cycloadditions studied. The sizes of the lobes of the four interacting centres allow a strong overlapping as shown in a qualitative way in (21) and (22). The strongest overlap is in (21), where the atoms with largest coefficients interact with each other.[2] The dominant formation of one regioisomer over the other is hence easily explained.

[9] R. Huisgen, *Angew. Chem. Internat. Edn.*, 1963, **2**, 633.
[10] K. N. Houk, J. Sims, R. E. Duke, jun., R. W. Strozier, and J. K. George, *J. Amer. Chem. Soc.*, 1973, **95**, 7287.
[11] M. J. Cook, A. R. Katritzky, F. C. Pennington, and B. M. Semple, *J. Chem. Soc.* (*B*), 1969, 523.

These 1,3-dipolar cycloadditions of nitrones with indene and 1,2-dihydronaphthalene (dipolarophiles without strongly electron-withdrawing groups) represent the first examples to be reported in which such 1,3-dipoles react in a regioselective manner. The few cases in which mixtures of regioisomers were obtained concerned intramolecular cycloadditions in which steric constraints counterbalanced electronic factors.[12] The intermolecular cycloadditions of *N*-benzylidene-methylamine and -t-butylamine *N*-oxides with phenyl vinyl sulphone also exhibit this behaviour.[13]

The reactions of *N*-benzylidenemethylamine *N*-oxide to give mixtures of epimers (see configuration of C-3 of the isoxazolidine ring) deserve further comment. Epimers with H-3 and H-4 *trans* are always the major components of the mixtures. This has been already reported for cycloadditions of this nitrone with cyclobutenes,[14,15] norbornene,[14] and acenaphthylene.[1] Similarly, a clear predominance of the *trans*-epimers (19) (Table 2) has been observed for the reactions of the same 1,3-dipole with cyclopentene and cyclohexene. The latter reactions allowed us to check previous incomplete data.[16]

The observed favoured formation of adducts with H-3 and H-4 *trans* from the cycloadditions of the nitrone with planar and conjugated alkenes (acenaphthylene or indene) may be explained as due to a better stabilization of the transition state (24) than of (23), in which secondary orbital interactions [LUMO(1,3-dipole)–HOMO(dipolarophile)] involving the nitrogen atom of the 1,3-dipole and the double bonds of the dipolarophile are at



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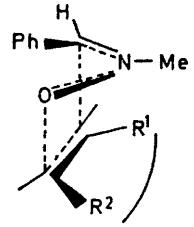

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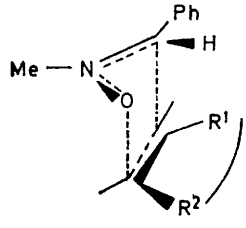

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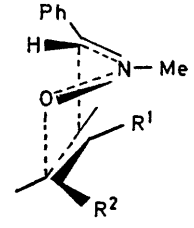

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work.[2] As far as steric effects are concerned, molecular models indicate a similar stereochemical encumbrance for the two transition states (23) and (24).

Although only electronic effects appear to be governing the above reactions, steric effects have to be invoked for the reactions of nitrones with non-conjugated alkenes such as cyclohexene and norbornene because secondary orbital interactions are not possible. The appropriate molecular models show that transition states of type (24) are more encumbered than the related transition states (23). Why, therefore, are epimers with H-3 and H-4 *trans* still favoured?

A typical property of open-chain nitrones should be taken into consideration at this stage. *N*-Benzylidene-methylamine *N*-oxide has been demonstrated to exist in the *trans*-form (9) at room temperature and as an equilibrium mixture with the *cis*-form (10) at higher temperatures, even though the *cis*-isomer has never been detected.[14] The latter highly reactive form of the nitrone, although present in low concentration, will overcome (9) in adding to the double bond of the dipolarophile. It follows, therefore, that the *trans*-epimers obtained from the reactions of the non-conjugated alkenes are formed mainly through transition states of type (25).

To conclude, the transition states of types (24) and (25), for non-conjugated and conjugated alkenes respectively, are also contributing to the cycloadditions, even though to a smaller extent. Transition state (26), however, should not contribute in the cycloadditions of nitrones considered here.

EXPERIMENTAL

N.m.r. spectra were recorded at 36 °C for solutions in $CDCl_3$ with a Perkin-Elmer R12A (60 MHz) spectrometer (Me_4Si as internal standard). Numbering of protons refers to the heterocyclic ring. Reaction mixtures were analysed by t.l.c. on silica gel GF 254 (Merck) and the spots were detected under u.v. light (254 nm). Column chromatographic separations were carried out with Kieselgel H (Merck). Isoxazolidines and Δ^2-isoxazolines from acetonitrile oxide could be detected on t.l.c. plates only after spraying with a 3% solution of chromic oxide in sulphuric acid (50%) followed by heating at 120 °C. Elemental analyses (performed by Dr. L. Maggi Dacrema) are reported in Table 3.

Reactions of Nitrile Oxides with 1,2-*Dihydronaphthalene, Indene, and* trans-1-*Phenylpropene.*—A mixture of the appropriate nitrile oxide and 1,2-dihydronaphthalene (three-fold excess), indene (two-fold excess), or *trans*-1-phenylpropene (two-fold excess) in anhydrous benzene was left at 20—25 °C until complete disappearance of the dipole was shown by t.l.c. The unstable nitrile oxides were generated *in situ* from the corresponding hydroximic acid chloride and triethylamine. After work-up the n.m.r. spectrum of the crude product was recorded (*ca.* 10% solution in $CDCl_3$). The signals due to H-5 of the two regioisomers were distinct. Planimetric integration of the peak areas gave the isomer proportions. Analyses of synthetic mixtures of the regioisomeric Δ^2-isoxazolines afforded an accuracy of $\pm 5\%$ by this method. Regioisomers were separated either by column chromatography or (less frequently) by preparative

[12] N. A. LeBel and E. G. Banucci, *J. Org. Chem.*, 1971, **36**, 2440.
[13] J. Sims and K. N. Houk, *J. Amer. Chem. Soc.*, 1973, **95**, 5798.
[14] L. W. Boyle, M. J. Peagram, and G. H. Whitham, *J. Chem. Soc.* (*B*), 1971, 1728.
[15] G. Bianchi, A. Gamba, and R. Gandolfi, *Tetrahedron*, 1972, **28**, 1601.
[16] R. Huisgen, R. Grashey, H. Hauck, and H. Seidl, *Chem. Ber.*, 1968, **101**, 2043.

t.l.c. As eluants mixtures of cyclohexane and ethyl acetate were used.

As examples we report here salient n.m.r. data for three pairs of regioisomeric Δ^2-isoxazolines: (2h), δ 5.04 (1 H, d, H-5, $J_{4,5}$ 8.0 Hz), 3.26 (1 H, m, H-4), and 1.36 (3 H, d, Me, $J_{Me,H-4}$ 7.0 Hz); (3h), δ 4.96 (1 H, m, H-4, $J_{4,5}$ 6.0 Hz), 4.14 (1 H, d, H-4), and 1.50 (3 H, d, Me, $J_{Me,H-5}$ 6.0 Hz); (4h), δ 5.61 (1 H, d, H-5, $J_{4,5}$ 9.3 Hz), and 3.69 (1 H, m, H-4); respectively, to give the adducts (18a), (17a), (16a), and (15a) in that order. N.m.r. data: (15a), δ 5.66 (1 H, d, H-5, $J_{4,5}$ 7.3 Hz), 2.80—3.65 (4 H, m, H-3, H-4, and CH_2), and 2.49 (3 H, s, Me); (16a), δ 5.10 (1 H, m, H-5), 4.10 (1 H, t, H-4, $J_{3,4} = J_{4,5} = 6.7$ Hz), 3.32 (1 H, d, H-3), and 2.51 (3 H, s, Me); (17a), δ 5.65 (1 H, d, H-5, $J_{4,5}$ 7.3 Hz), 3.30—4.20 (3 H, m, H-4 and CH_2), 2.65 (1 H, d, H-3, $J_{3,4}$ 6.0 Hz), and 2.60 (3 H, s, Me); (18a), δ 5.95 (1 H, dd, H_a), 5.21 (1 H, d, H-5, $J_{4,5}$ 10.6 Hz) and 4.73 (1 H, d, H-4); (6h), δ 6.10 (1 H, d, H-5, $J_{4,5}$ 8.58 Hz), 4.30 (1 H, m, H-4), and 3.00 (2 H, m, CH_2); (7h), δ 5.50 (1 H, m, H-5), 4.90 (1 H, d, H-4, $J_{4,5}$ 8.70 Hz), and 3.30 (2 H, m, CH_2).

TABLE 3

Physical and analytical data for Δ^2-isoxazolines and isoxazolidines

Compound	Cryst. solvent	M.p. (*T*/°C)	Found (%) C	H	N	Formula	Required (%) C	H	N
(2b)	EtOH [b]	79—80 [a]	80.9	6.3	6.1	$C_{16}H_{15}NO$	81.0	6.4	5.9
(3b)	EtOH [c]	112	80.8	6.2	6.0				
(2d)	Cyclohexane [b]	102	76.1	6.4	5.3	$C_{17}H_{17}NO$	76.4	6.4	5.2
(3d)	Cyclohexane [e]	96	76.8	6.4	5.6				
(2e)	MeOH [d]	111—113	67.8	5.2	10.0	$C_{16}H_{14}N_2O_3$	68.0	5.0	9.9
(3e)	EtOH [e]	141—142	67.9	5.1	9.9				
(2h)	Pentane [f]	87	81.6	7.5	5.1	$C_{19}H_{21}NO$	81.7	7.6	5.0
(3h)	Pentane [b]	91—92	81.7	7.7	5.2				
(2i)	EtOH [c]	119—120	65.8	5.6	4.4	$C_{19}H_{19}Cl_2NO$	65.5	5.6	4.0
(3i)	EtOH [c]	149—150	65.5	5.6	4.4				
(2j)	EtOH [b]	129	69.8	6.5	4.3	$C_{19}H_{21}NO_4$	69.7	6.5	4.3
(3j)	EtOH [c]	109	69.5	6.4	4.4				
(4a)	*g*	(Oil)	76.3	6.9	7.0	$C_{12}H_{13}NO$	77.0	7.0	7.5
(5a)	Sublimed [c]	45	77.1	7.2	7.5				
(4c)	EtOH [h]	129—132	81.8	5.4	6.6	$C_{18}H_{17}NO$	82.1	5.3	6.5
(5c)	EtOH [h]	107—109	81.9	5.3	6.6				
(4d)	Benzene [h]	130—132	77.1	6.1	5.0	$C_{18}H_{17}NO_2$	77.4	6.1	5.0
(5d)	EtOH [c]	107—109	77.7	6.1	5.0				
(4e)	Benzene [d]	218	69.3	5.0	9.4	$C_{17}H_{14}N_2O_3$	69.4	4.7	9.5
(5e)	Benzene [d]	183—185	69.5	4.9	9.3				
(4f)	EtOH [c]	141	69.0	4.9	9.6	$C_{17}H_{14}N_2O_3$	69.4	4.7	9.5
(5f)	EtOH [c]	121	69.4	4.8	9.5				
(4g)	EtOH [b]	121—122	62.5	4.3	4.3	$C_{17}H_{14}NOBr$	62.2	4.3	4.3
(5g)	EtOH [h]	105—106	61.8	4.3	4.4				
(4h)	EtOH [b]	134—135	82.4	7.3	5.1	$C_{20}H_{21}NO$	82.4	7.3	4.8
(5h)	EtOH [f]	138—139	82.5	7.2	4.7				
(4j)	EtOH [c]	163	71.0	6.1	4.3	$C_{20}H_{21}NO_4$	70.8	6.2	4.1
(5j)	MeOH–H_2O [c]	116	70.4	6.2	4.3				
(6h)	EtOH [f]	154—155	82.4	7.0	5.1	$C_{19}H_{19}NO$	82.3	6.9	5.1
(7h)	Pentane [c]	100	82.3	7.1	5.1				
(6j)	EtOH [b]	184—185	69.9	5.9	4.2	$C_{19}H_{17}NO_4$	70.1	5.9	4.3
(7j)	EtOH [f]	157—158	69.9	5.6	4.3				
(11a)	EtOH [b]	133—134	82.3	6.3	5.4				
(12a)	EtOH [b]	106—107	81.8	6.6	5.5	$C_{18}H_{17}NO$	82.1	6.5	5.3
(13a)	MeOH [c]	197—199	82.0	6.6	5.3				
(14a)	MeOH [c]	149—150	81.7	6.3	5.5				
(11b)	MeOH [c]	130—132	82.0	6.5	5.4	$C_{19}H_{19}NO$	82.3	6.9	5.1
(12b)	EtOH [b]	122—123	81.9	6.7	5.0				
(15a)	EtOH [c]	89—90	81.4	6.6	5.4				
(16a)	*g*	(Oil)	81.5	6.5	5.5	$C_{17}H_{17}NO$	81.2	6.8	5.6
(17a)	Petroleum [b]	105—106	81.5	7.0	5.5				
(18a)	EtOH [b]	80—81	81.1	7.1	5.3				
(15b)	EtOH [c]	84—85	81.7	7.5	5.0				
(16b)	EtOH [c]	82—83	81.2	7.0	5.5	$C_{18}H_{19}NO$	81.5	7.2	5.5
(17b)	Ether [c]	93—95	81.4	7.4	5.1				
(18b)	Petroleum [c]	56—58	81.0	7.2	5.2				
(19a)	Petroleum [c]	56—58	76.7	8.5	6.8	$C_{13}H_{17}NO$	76.8	8.4	6.9
(19b)	*g*	(Oil)	77.3	8.6	6.4	$C_{14}H_{19}NO$	77.4	8.8	6.4

[a] Lit.,[4] m.p. 81.5—82. [b] As needles. [c] As prisms. [d] Yellowish prisms. [e] Yellow needles. [f] Plates. [g] B.p. not determined; compounds were purified by chromatography. [h] Leaflets.

Reactions of N-Benzylidenemethylamine N-Oxide with Indene and 1,2-Dihydronaphthalene.—(i) The nitrone (1.70 g) and indene (5 ml) were heated in a stainless steel bomb in an oil-bath at 90 °C for 65 h. Column chromatographic separation of the reaction mixture was accomplished with two eluant systems, cyclohexane–ethyl acetate (98 : 2) and (95 : 5), respectively, to give the adducts (18b), (17b), (15b), and (16b). N.m.r. data: (15b), δ 5.21 (1 H, d, H-5, $J_{4,5}$ 7.8 Hz), 3.30 (1 H, d, H-3, $J_{3,4}$ 7.5 Hz), and 2.59 (3 H, s, Me); (16b), δ 4.74 (1 H, m, H-5), 3.75 (H-4, t, $J_{3,4} = J_{4,5} = 9.0$ Hz), 2.93 (1 H, d, H-3), and 2.51 (3 H, s, Me); (17b), δ 5.22 (1 H, d, H-5, $J_{4,5}$ 7.4 Hz), 4.20 (1 H, t, H-4, $J_{3,4}$ 7.4 Hz), 3.81 (1 H, d, H-3), and 2.59 (3 H, s, Me).

(ii) The nitrone (1.0 g) was treated with 1,2-dihydronaphthalene (4.0 ml) at 100 °C for 139 h as described in (i). Chromatographic separation as in (i) gave, in order of elution, the adducts (18b), (17b), (15b), and (16b). N.m.r. data: (15b), δ 5.21 (1 H, d, H-5, $J_{4,5}$ 7.8 Hz), 3.30 (1 H, d, H-3, $J_{3,4}$ 7.5 Hz), and 2.59 (3 H, s, Me); (16b), δ 4.74 (1 H, m, H-5), 3.75 (H-4, t, $J_{3,4} = J_{4,5} = 9.0$ Hz), 2.93 (1 H, d, H-3), and 2.51 (3 H, s, Me); (17b), δ 5.22 (1 H, d, H-5, $J_{4,5}$

6.0 Hz), 4.12 (1 H, d, H-3, $J_{3,4}$ 6.0 Hz), and 2.76 (3 H, s, Me); (18b), δ 6.26 (1 H, dd, H_a), 4.84 (1 H, m, H-5), 4.06 (2 H, m, H-3 and H-4), and 2.58 (3 H, s, Me).

Reactions of 3,4-*Dihydroisoquinoline* N-*Oxide with Indene and* 1,2-*Dihydronaphthalene*.—3,4-Dihydroisoquinoline *N*-oxide (1.60 g) was treated separately with indene (3.6 ml) and with 1,2-dihydronaphthalene (6.5 ml) in a bomb at 70 °C for 20 h. Adducts (11)—(14) were separated by column chromatography (cyclohexane–ethyl acetate, 4 : 1). N.m.r. data: (11a), δ 5.86 (1 H, d, H-5, $J_{4,5}$ 7.4 Hz); (12a), δ 5.20 (1 H, m, H-5); (13a), δ 5.75 (1 H, d, H-5, $J_{4,5}$ 7.8 Hz); (14a), δ 6.13 (1 H, dd, H_a) and 5.15 (1 H, m, H-5); (11b), δ 5.21 (1 H, d, H-5, $J_{4,5}$ 8.1 Hz); (12b), δ 4.90 (1 H, m, H-5).

Reactions of N-*Benzylidenemethylamine* N-*Oxide with Cyclopentene and Cyclohexene*.—The nitrone (0.75 g) and cyclopentene (or cyclohexene) (3 ml) were heated in a bomb at 150 °C for 39 h. Column chromatographic separation [eluants cyclohexane and cyclohexane–ethyl acetate (98 : 2 and 95 : 5)] gave pure epimers (20a) (first eluted) and (19a) (second eluted) and (20b) and (19b), respectively. [Compounds (20a and b) have been reported.[1]] N.m.r. data: (19a), δ 4.68 (1 H, m, H-5), 2.90 (2 H, m, H-3 and H-4), and 2.48 (3 H, s, Me); (19b), δ 4.25 (1 H, m, H-5), 3.37 (1 H, d, H-3, $J_{3,4}$ 7.3 Hz), and 2.68 (3 H, s, Me).

Preparation of Isoxazolidines (17a), (17b), *and* (18b).—A solution of the appropriate Δ^2-isoxazoline [(4b), (5b), or (6b)] (1.0 mmol) and a two-fold excess of trimethyloxonium tetrafluoroborate (2.00 mmol) in anhydrous nitromethane (10 ml) was left at room temperature for 48 h [until complete disappearance of the Δ^2-isoxazoline (t.l.c.)]. The solvent was removed under reduced pressure and the oily residue was treated with anhydrous ethanol. To the resulting solution or suspension an excess of sodium borohydride was added in small portions at room temperature over 30 min. Stirring was continued for a further 30 min, the solvent was then removed under reduced pressure, and the residue was treated with water and extracted with ether. The ether solution was dried, filtered, and evaporated to dryness to give the isoxazolidine (17a) (95%), (17b) (94%), or (18b) (85%); the products were homogeneous (t.l.c. and n.m.r.)

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