Syntheses and 1,3-Dipolar Cycloaddition Reactions of Benz[*de*]isoquinolinium-1-ides

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Benz[*de*]isoquinolinium-1-ides prepared *in situ* by treatment of 2-substituted 2,3-dihydro-1*H*-benz[*de*]isoquinoline *N*-oxides with acetic anhydride, reacted with dimethyl acetylenedicarboxylate and with maleimides to give 1 : 1 cycloadducts. The stereochemistry of the maleimide cycloadducts was determined by n.m.r. spectroscopy. Exclusive or predominant formation of the *endo*-adducts is in sharp contrast with the case of naphtho[1,8-*cd*]-thiopyran, which reacts with maleimides to give exclusively or predominantly *exo*-adducts. The adducts were converted into cyclohepta[*de*]naphthalene derivatives.

CYCLOADDITION reactions of cyclic 1,3-dipoles with alkynes and alkenes are now recognised to provide useful synthetic routes to a variety of two-ring heterocycles. For instance, 1-methyl-3-oxidopyridinium undergoes a 1,3-dipolar cycloaddition with acrylonitrile to give a 1 : 1 cycloadduct which can be converted into tropone derivatives.[1] We have now prepared benz[*de*]isoquinolinium-1-ides (I) by dehydration of 2-substituted 2,3-dihydro-1*H*-benz[*de*]isoquinoline *N*-oxides (III), and examined their 1,3-dipolar reactivity.

The *N*-oxides (IIIa and b) were synthesised by oxidation of 2,3-dihydro-1*H*-benz[*de*]isoquinolines (IIa and b) [2] with 30% hydrogen peroxide in 58 and 65% yields, respectively. When compound (IIIa) was treated with acetic anhydride and triethylamine [3] in the presence of dimethyl acetylenedicarboxylate at −10 °C, a crystalline 1 : 1 adduct (IV) was obtained in 83% yield. The i.r. spectrum showed a carbonyl band at 1 715 cm^{-1}, and the n.m.r. spectrum a methoxy-singlet at δ 3.86 (6 H), an *N*-methyl singlet at δ 2.55 (3 H), and a singlet due to bridgehead protons at δ 4.96 (2 H).

The similar reaction of (IIIa) with *N*-methyl- and *N*-phenyl-maleimides gave exclusively *endo*-adducts, (V) and (VI), in 80 and 59% yields, respectively. Compound (IIIb) also reacted with maleimides but more slowly than (IIIa); with *N*-phenylmaleimide only the *endo*-adduct (VII) was obtained, in 61% yield, and with *N*-methylmaleimide the *exo*-adduct (IX) was obtained in 9% yield along with the *endo*-adduct (VIII) (52% yield).

The stereochemistry of these cycloadducts was assigned by n.m.r. spectroscopy (Table). The imide *N*-methyl signal of the *endo*-adducts (V)—(VIII) appears *ca.* 0.8 p.p.m. to higher field than that of *N*-methylsuccinimide (δ 2.98) or that of the *exo*-adduct (IX) because the *N*-methyl group is situated almost directly over the naphthalene ring in the *endo*-adducts. The signal of H_b of the *exo*-adduct (IX) appears *ca.* 0.66—0.89 p.p.m. to higher field than that of *endo*-adducts (V)—(VIII) owing to the anisotropic effect of the naphthalene ring. Both H_a and H_b in the *exo*-adduct (IX) resonate as sharp singlets, whereas the *endo*-adducts (V)—(VIII) give as AA'XX' multiplets; molecular models indicate that the torsion angle between H_a and H_b in (IX) is about 90°, whereas that in (V)—(VIII) is about 30°.

These reactions are considered to involve ylide intermediates (I) which form 1 : 1 cycloadducts with the dipolarophiles. Involvement of the intermediates (I) was in fact suggested by the development of a green colour when the reaction was carried out at −10 °C in the absence of dipolarophile, although attempts to isolate them were unsuccessful owing to their sensitivity to heat.

The stereochemistry of the cycloadditions of the ylides (I) is in sharp contrast to the case of naphtho[1,8-*cd*]-

[1] N. Dennis, A. R. Katritzky, and Y. Takeuchi, *Angew. Chem. Internat. Edn.*, 1976, **15**, 1.

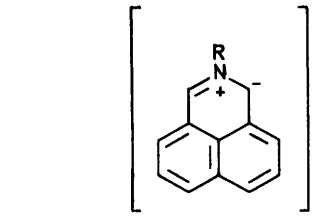
[2] A. I. Tochilkin, S. M. Feigina, V. Z. Gorkin, and G. V. Polyakova, *Khim.-Farm. Zhur.*, 1969, **3**, 30.

[3] R. Kreher and J. Seubert, *Angew. Chem.*, 1964, **76**, 682.

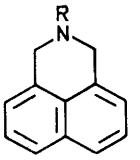
thiopyran analogue (XI), which has been reported to give solely the *exo*-adduct (XII) with *N*-phenylmaleimide.[4] We have not only confirmed this result but also obtained both *exo*- and *endo*-adducts in a reaction with *N*-methylmaleimide. Refluxing the naphthothiopyran *S*-oxide (X) in acetic anhydride in the presence of *N*-methylmaleimide gave *exo*- (XIII) and *endo*-adducts (XIV) in 52 and 13% yields, respectively. Both were stable under the reaction conditions and unchanged after refluxing in acetic anhydride for 1 h. Their stereochemistry was assigned by n.m.r. spectroscopy (Table), as in the cases of (VIII) and (IX).

We cannot explain the differences in stereochemical results from the systems (I) and (XI) at this time in terms of conventional electronic and steric considerations.

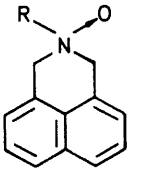
The cycloadducts (V) and (VI) were converted into



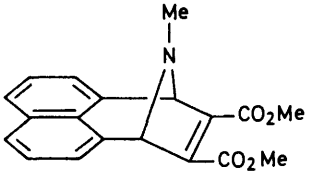
(I) a; R = Me
b; R = Ph



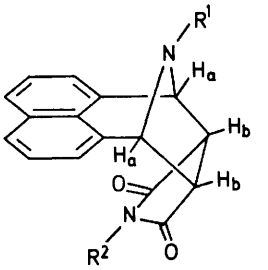
(II) a; R = Me
b; R = Ph



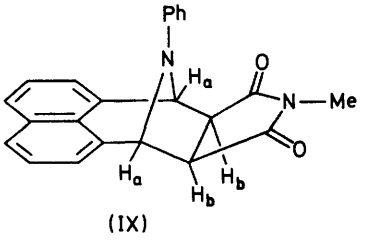
(III) a; R = Me
b; R = Ph



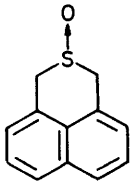
(IV)



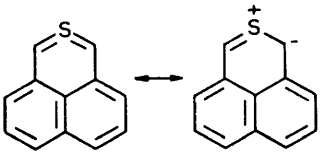
(V) $R^1 = R^2 = Me$
(VI) $R^1 = Me$, $R^2 = Ph$
(VII) $R^1 = R^2 = Ph$
(VIII) $R^1 = Ph$, $R^2 = Me$



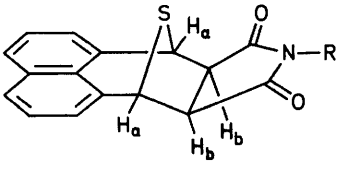
(IX)



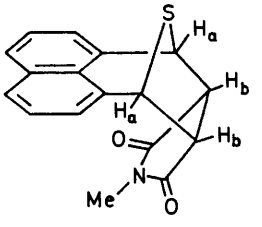
(X)



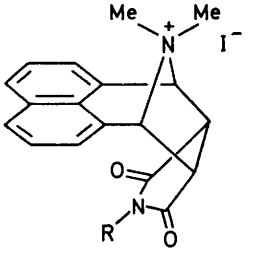
(XI)



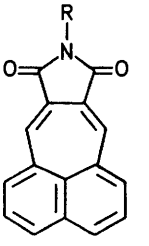
(XII) R = Ph
(XIII) R = Me



(XIV)



(XV) a; R = Me
b; R = Ph



(XVI) a; R = Me
b; R = Ph

[4] (*a*) M. P. Cava, N. M. Pollack, and D. A. Repella, *J. Amer. Chem. Soc.*, 1967, **89**, 3640; (*b*) R. H. Schlessinger and I. S. Ponticello, *ibid.*, p. 3641.

cyclohepta[*de*]naphthalene derivatives (XVI) by treatment with methyl iodide in ethyl acetate to give the quaternary salts (XVa and b), followed by methanolic potassium hydroxide. Structures were assigned on the basis of the elemental analyses and spectral data [5] (see Experimental section).

EXPERIMENTAL

N.m.r. spectra were determined with a Hitachi R-20A spectrometer (tetramethylsilane as internal standard). I.r. spectra were recorded with a Hitachi EPI-G2 spectrophotometer, and u.v. spectra with a Hitachi 124 spectrophotometer. Mass spectra were obtained with a Hitachi RMU-6D instrument with a direct inlet system operating at 70 eV. Preparative layer chromatography (p.l.c.) was carried out on Merck alumina PF_{254}.

N.m.r. spectra of cycloadducts (δ values)

	H_a	H_b	NMe	CO·NMe·CO	Aromatic
(V)	4.5—4.7 (1 H, m)	3.9—4.1 (1 H, m)	2.09 or 2.23	2.23 or 2.09	7.15—7.85 (6 H, m)
(VI)	4.6—4.8 (1 H, m)	4.05—4.25 (1 H, m)	2.29 (3 H, s)		5.9—6.15 (2 H, m) 7.0—7.9 (9 H, m)
(VII)	5.55—5.75 (1 H, m)	4.2—4.4 (1 H, m)			5.9—6.2 (2 H, m) 6.65—7.9 (15 H, m)
(VIII)	5.45—5.7 (1 H, m)	4.0—4.25 (1 H, m)		2.14 (3 H, s)	6.6—7.8 (11 H, m)
(IX)	5.49 (1 H, s)	3.41 (1 H, s)		3.02 (3 H, s)	6.55—7.8 (11 H, m)
(XIII)	4.97 (1 H, s)	3.56 (1 H, s)		3.04 (3 H, s)	7.25—7.9 (6 H, m)
(XIV)	4.9—5.1 (1 H, m)	4.1—4.3 (1 H, m)		2.18 (3 H, s)	7.25—7.85 (6 H, m)

2,3-*Dihydro*-2-*methyl*-1H-*benz*[de]*isoquinoline* N-*Oxide* (IIIa).— To a solution of the benzisoquinoline (IIa) [2] (2.86 g) in methanol (20 ml) was added 30% hydrogen peroxide (7.0 g), and the mixture was kept at room temperature for 1 day. The excess of hydrogen peroxide was decomposed with platinum oxide, methanol was removed *in vacuo*, and the residue was diluted with saturated sodium chloride solution and extracted with chloroform. The extract was washed with saturated sodium chloride solution, dried ($MgSO_4$), and concentrated to give *plates* (1.77 g, 57%) which were recrystallised from ethyl acetate; m.p. 170—172° (Found: C, 72.1; H, 7.0; N, 6.5. $C_{13}H_{13}NOH_2O$ requires C, 71.9; H, 7.0; N, 6.45%); δ ($CDCl_3$) 3.17 (3 H, s, N·CH_3), 4.85 (4 H, ABq, *J* 12 Hz, benzylic), and 7.2—7.9 (6 H, m, aromatic).

2,3-*Dihydro*-2-*phenyl*-1H-*benz*[de]*isoquinoline* N-*Oxide* (IIIb).—To a solution of the benzisoquinoline (IIb) [6] (700 mg) in acetic acid (10 ml) was added 30% hydrogen peroxide (1 ml). The mixture was kept at room temperature for 1 day, then poured into water (10 ml) and extracted with chloroform. The extract was washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and concentrated to give crystals (530 mg, 68%), m.p. 150—152° (from methanol–ether) (Found: C, 79.7; H, 6.2; N, 5.0. $C_{18}H_{15}NO,0.5H_2O$ requires C, 80.0; H, 6.0; N, 5.2%); δ ($CDCl_3$) 5.15 (4 H, ABq, *J* 12 Hz) and 7.2—8.0 (11 H, m, aromatic).

Dimethyl 7,10-*Dihydro*-11-*methyl*-7,10-*iminocyclohepta*[de]*naphthalene*-8,9-*dicarboxylate* (IV).—To a solution of dimethyl acetylenedicarboxylate (100 mg) and triethylamine (100 mg) in acetic anhydride (5 ml) was added in portions the *N*-oxide (IIIa) (105 mg) at −10 °C. The mixture was stirred at −10 °C for 30 min, then acetic anhydride was removed *in vacuo*. The residue was diluted with water and extracted with chloroform. The extract was dried ($MgSO_4$) and concentrated. The residue was submitted to p.l.c. (chloroform) to give the *adduct* (IV) (137 mg, 83%), m.p. 133—134° (from ethanol) (Found: C, 70.6; H, 5.3; N, 4.3. $C_{19}H_{17}NO_4$ requires C, 70.6; H, 5.3; N, 4.3%); $\nu_{max.}$ ($CHCl_3$) 1 715 cm^{-1} (C=O); δ ($CDCl_3$) 2.55 (3 H, s, N·CH_3), 3.86 (6 H, s, 2 × CO_2Me), 4.96 (2 H, s, bridgehead), and 7.3—7.9 (6 H, m, aromatic).

endo-7,8,9,10-*Tetrahydro*-11-*methyl*-7,10-*iminocyclohepta*[de]*naphthalene*-8,9-N-*methyldicarboximide* (V).—A similar procedure to that for the preparation of (IV) gave the *adduct* (V) [from (IIIa) (100 mg) and *N*-methylmaleimide (60 mg)] (117 mg, 80%), m.p. 217—219° (from ethanol), as cubes (Found: C, 73.9; H, 5.5; N, 9.4. $C_{18}H_{16}N_2O_2$ requires C, 73.95; H, 5.5; N, 9.6%); $\nu_{max.}$ ($CHCl_3$) 1 770 and 1 695 cm^{-1} (C=O).

endo-7,8,9,10-*Tetrahydro*-11-*methyl*-7,10-*iminocyclohepta*[de]*naphthalene*-8,9-N-*phenyldicarboximide* (VI).—By a similar procedure the *adduct* (VI) (105 mg, 59%) was obtained [from (IIIa) (100 mg) and *N*-phenylmaleimide (84 mg)], m.p. 176—178° (from ethanol) as prisms (Found: C, 77.9; H, 5.2; N, 8.0. $C_{23}H_{18}N_2O_2$ requires C, 77.95; H, 5.1; N, 7.9%); $\nu_{max.}$ ($CHCl_3$) 1 770 and 1 710 cm^{-1} (C=O).

endo-7,8,9,10-*Tetrahydro*-11-*phenyl*-7,10-*iminocyclohepta*[de]*naphthalene*-8,9-N-*phenyldicarboximide* (VII).—To a solution of *N*-phenylmaleimide (50 mg) and triethylamine (50 mg) in acetic anhydride (3 ml) was added in portions the *N*-oxide (IIIb) (65 mg) at −10 °C. The mixture was stirred at the same temperature for 30 min and kept in a refrigerator for 5 days. Work-up as described for (IV) gave the *adduct* (VII) (67 mg, 61%), m.p. 260—262° [from benzene–light petroleum (b.p. 60—80 °C)] as plates (Found: C, 80.7; H, 4.9; N, 6.5. $C_{28}H_{20}N_2O_2$ requires C, 80.7; H, 4.8; N, 6.7%); $\nu_{max.}$ ($CHCl_3$) 1 775 and 1 710 cm^{-1} (C=O).

endo- *and* exo-7,8,9,10-*Tetrahydro*-11-*phenyl*-7,10-*iminocyclohepta*[de]*naphthalene*-8,9-N-*methyldicarboximides* (VIII) *and* (IX).—By a procedure similar to that for the preparation of (VII), a mixture consisting of two products was obtained, which was submitted to p.l.c. (benzene) to give the adducts (VIII) (192 mg, 52%) and (IX) (32 mg, 9%). The endo-*adduct* (VIII) had m.p. 291—292° [from ethyl acetate–light petroleum (b.p. 60—80 °C)] (Found: C, 77.9; H, 5.1; N, 7.9. $C_{23}H_{18}N_2O_2$ requires C, 77.95; H, 5.1; N, 7.9%); $\nu_{max.}$ ($CHCl_3$) 1 775 and 1 695 cm^{-1} (C=O). The exo-*adduct* (IX), afforded needles, m.p. 280—282° (from ethanol) (Found: C, 77.9; H, 5.1; N, 7.8%); $\nu_{max.}$ ($CHCl_3$) 1 780 and 1 700 cm^{-1} (C=O).

exo- *and* endo-7,8,9,10-*Tetrahydro*-7,10-*epithiocyclohepta*[de]*naphthalene*-8,9-N-*methyldicarboximides* (XIII) *and* (XIV).—A solution of the sulphoxide (X) [4] (101 mg) and *N*-methylmaleimide (60 mg) in acetic anhydride (5 ml) was refluxed for 1 h. Acetic anhydride was evaporated off *in vacuo* and the residue was diluted with water and extracted

[5] J. E. Shields, D. Gavrilovic, J. Kopecky, W. Hartmann, and H.-G. Heine, *J. Org. Chem.*, 1974, **39**, 515.

[6] E. Höft, A. Rieche, and H. Schultze, *Annalen*, 1966, **697**, 181.

with chloroform. The dried extract was concentrated to yield two products which were separated by p.l.c. [benzene–light petroleum (b.p. 30—60 °C) (1 : 1)] to give the adducts (XIII) (70 mg, 52%) and (XIV) (24 mg, 17%). The *exo-adduct* (XIII) formed prisms, m.p. 187—189° [from benzene–light petroleum (b.p. 60—80 °C)] (Found: C, 69.4; H, 4.5; N, 4.6. $C_{17}H_{13}NO_2S$ requires C, 69.1; H, 4.4; N, 4.7%); $\nu_{max.}$ ($CHCl_3$) 1 780 and 1 695 cm^{-1} (C=O). The endo-*adduct* (XIV) gave pale yellow prisms, m.p. 235—236° [from acetone–light petroleum (b.p. 60—80 °C)] (Found: C, 69.3; H, 4.5; N, 4.7%); $\nu_{max.}$ ($CHCl_3$) 1 770 and 1 695 cm^{-1} (C=O).

Quaternisation of the Adducts (V) *and* (VI).—A solution of the adduct (V) (100 mg) and methyl iodide (1 ml) in ethyl acetate was kept at room temperature for 1 day. The precipitate was collected and recrystallised from methanol to give the *methiodide* (XVa) (126 mg, 83%), m.p. 248—250° (decomp.) (Found: C, 50.7; H, 4.3; N, 5.8. $C_{19}H_{19}IN_2O_2$, H_2O requires C, 50.5; H, 4.6; N, 6.2%). Similarly the *methiodide* (XVb) was obtained from (VI) (150 mg) and an excess of methyl iodide (2 ml) in 85% yield (178 mg) as needles, m.p. 261—262° (decomp.) (from methanol) (Found: C, 57.9; H, 4.3; N, 5.6. $C_{24}H_{21}IN_2O_2$ requires C, 58.0; H, 4.3; N, 5.6%).

Cyclohepta[de]*naphthalene*-8,9-N-*methyldicarboximide* (XVIa).—A solution of the methiodide (XVa) (250 mg) in methanolic 5% potassium hydroxide (20 ml) was refluxed for 30 h. The precipitated red crystals were collected and recrystallised from benzene to give the *imide* (XVIa) (140 mg, 93%) as red needles, m.p. 268—269° (Found: C, 78.1; H, 4.4; N, 5.5. $C_{17}H_{11}NO_2$ requires C, 78.15; H, 4.2; N, 5.4%); $\nu_{max.}$ ($CHCl_3$) 1 745 and 1 700 cm^{-1} (C=O); $\lambda_{max.}$ (EtOH) 249 (log ε 3.81), 312sh (2.94), 316sh (2.92), 336 (2.91), 343sh (2.86), 357sh (3.04), 373 (3.18), 392 (3.11), and 412sh nm (2.66); δ ($CDCl_3$) 3.10 (3 H, s, N·CH_3), 6.95 (2 H, s), and 7.0—7.5 (6 H, m).

Cyclohepta[de]*naphthalene*-8,9-N-*phenyldicarboximide* (XVIb).—Compound (XVb) (50 mg) was dissolved in methanolic 5% potassium hydroxide (5 ml) with slight warming on a water-bath and the resulting solution was kept at room temperature for 1 day. The precipitated red crystals were collected and recrystallised from benzene to give red *needles* (XVIb) (24 mg, 74%), m.p. >300° (Found: C, 81.65; H, 4.1; N, 4.3. $C_{22}H_{13}NO_2$ requires C, 81.7; H, 4.05; N, 4.3%); $\nu_{max.}$ ($CHCl_3$) 1 750 and 1 700 cm^{-1} (C=O); $\lambda_{max.}$ ($CHCl_3$) 253 (log ε 4.75), 260 (4.75), 300sh (4.15), 312 (4.18), 320sh (4.15), 335 (4.07), 340sh (4.05), 362 (4.01), 379 (4.15), 398 (4.11), 416 (3.73), 469 (2.97), and 503 nm (2.98); δ ($CDCl_3$) 6.9—7.8 (m).

[6/929 *Received*, 14*th May*, 1976]