1,2,4-Benzoxadiazines[1]

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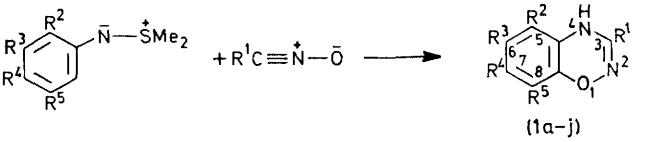
1,2,4-Benzoxadiazines (1) have been prepared by two new methods: (*a*) the reaction of *N*-aryl-*SS*-dimethylsulphimides with nitrile oxides, and (*b*) the oxidation of *N*-arylamidoximes. Both reactions are shown to involve the intermediacy of *N*-aryl-*C*-nitroso-imines, which can be reversibly intercepted in a Diels-Alder reaction with thebaine. Earlier publications on the synthesis of 1,2,4-benzoxadiazines have been re-assessed, and some of the structures proposed by previous workers have been revised.

N-ARYL-*SS*-DIMETHYLSULPHIMIDES are now available from the corresponding anilines by a variety of simple procedures.[2] During an investigation of their reactions with electrophiles we found that they combined readily with nitrile oxides, with the elimination of dimethyl sulphide, to give 1,2,4-benzoxadiazines in good yields.[1a] Details of this work are given here, together with evidence relating to the mechanism of the reaction. An alternative route to 1,2,4-benzoxadiazines is also described, and earlier work on the synthesis of this hitherto rare ring system is re-assessed.

N-Aryl-*SS*-dimethylsulphimides reacted with equimolar amounts of 4-toluonitrile oxide in dichloromethane at room temperature within 1—3 h; in most cases the reaction competed effectively with the slow dimerisation of the nitrile oxide. The adducts were isolated by evaporation of the reaction mixture followed either by crystallisation or by layer chromatography; yields of the products, which were not optimized, were in the range 27—89%. The structure of the products as 1,2,4-benzoxadiazines (1) was confirmed by an *X*-ray crystal structure determination of compound (1b).[3] This also showed that in the solid state the 4*H*-tautomer is preferred.

With *SS*-dimethyl-*N*-3-nitrophenylsulphimide and 4-toluonitrile oxide, both of the two possible 1,2,4-benzoxadiazines (1e and f) were formed; these were separated



(1a–j)

(1)	R^1	R^2	R^3	R^4	R^5
a;	4-MeC_6H_4	H	H	H	H
b;	4-MeC_6H_4	H	H	Cl	H
c;	4-MeC_6H_4	Ph	H	H	H
d;	4-MeC_6H_4	H	H	NO_2	H
e;	4-MeC_6H_4	H	NO_2	H	H
f;	4-MeC_6H_4	H	H	H	NO_2
g;	4-MeC_6H_4	Cl	H	H	NO_2
h;	CO_2Et	H	H	H	H
j;	CO_2Et	H	H	Cl	H
k;	CO_2Et	H	H	NO_2	H
m;	CO_2Et	Me	H	NO_2	H
n;	COPh	H	H	NO_2	H
o;	$COBu^t$	H	H	NO_2	H
p;	$CO{\cdot}NH_2$	H	H	NO_2	H
q;	CO_2H	H	H	NO_2	H
* r;	H	H	H	NO_2	H
* s;	Ph	H	NO_2	H	H
* t;	3-$NO_2{\cdot}C_6H_4$	H	NO_2	H	H
* u;	4-$NO_2{\cdot}C_6H_4$	H	NO_2	H	H
v;	Ph	H	H	NO_2	H
w;	3-$NO_2{\cdot}C_6H_4$	H	H	NO_2	H
x;	4-$NO_2{\cdot}C_6H_4$	H	H	NO_2	H

* Substances claimed in refs. 9 and 11, but now shown to be incorrectly formulated [see also structures (10)].

by layer chromatography and were isolated in approximately equal yields. The assignment of the 6-nitro structure (1e) to the less polar isomer is based mainly on

[1] Preliminary communications, (*a*) T. L. Gilchrist, C. J. Harris, and C. W. Rees, *J.C.S. Chem. Comm.*, 1974, 485; (*b*) T. L. Gilchrist, M. E. Peek, and C. W. Rees, *ibid.*, 1975, 913.

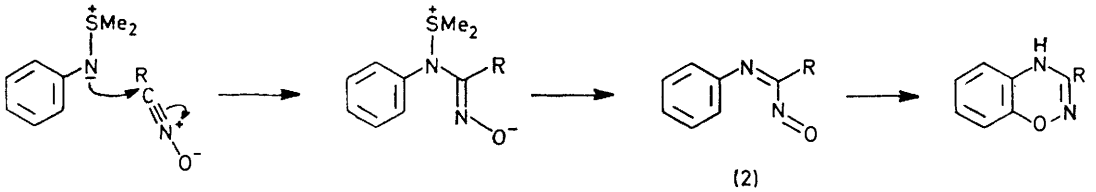
[2] (*a*) P. K. Claus, W. Rieder, P. Hofbauer, and E. Vilsmaier, *Tetrahedron*, 1975, **31**, 505; (*b*) P. K. Claus and W. Vycudilik, *Monatsh.*, 1970, **101**, 396; (*c*) A. K. Sharma, T. Ku, A. D. Dawson, and D. Swern, *J. Org. Chem.*, 1975, **40**, 2758; (*d*) U. Lerch and J. G. Moffatt, *ibid.*, 1971, **36**, 3861.

[3] A. F. Cameron and A. A. Freer, *Acta Cryst.*, 1976, **B32**, 1995.

the ^{1}H n.m.r. spectrum, which shows signals for the hydrogen atoms on C-7 and -8 as a pair of doublets (J 8 Hz) and for the hydrogen atom on C-5 as a singlet.

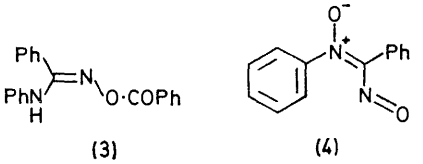
Ethyl cyanoformate N-oxide dimerises rapidly in solution at room temperature, and it was therefore generated *in situ* by adding the chloro-oxime precursor slowly to a solution containing the sulphimide and triethylamine below 0 °C. The reactions gave the 3-ethoxycarbonyl-1,2,4-benzoxadiazines (1 h and j) in moderate yields.

A mechanism which accounts for the formation of the 1,2,4-benzoxadiazines is shown in Scheme 1; it involves the nitroso-imines (2) as key intermediates. Such



SCHEME 1

nitroso-imines have not been described, although Boyer and Frints invoked the nitroso-imine (2; R = Ph) as an intermediate in the oxidation of N-phenylbenzamidoxime.[4] They obtained only compound (3) from these reactions, and we were also unable to detect the 3-phenyl-1,2,4-benzoxadiazine as a product of the oxidation of N-phenylbenzamidoxime with a range of oxidants. The



(3)

(4)

nitroso-imine N-oxide (4) has been isolated from the reaction of nitrosobenzene with benzonitrile oxide,[5] but it is reported to cyclise exothermically to 1-hydroxy-2-phenylbenzimidazole 3-oxide.†

In contrast to the results with the benzamidoximes, it was found that the amidoximes (5) bearing an ethoxycarbonyl group were oxidised by lead tetra-acetate, N-chlorobenzotriazole, and several other oxidants to give the 1,2,4-benzoxadiazines in good yields. The difference in behaviour of the two types of amidoxime may lie in the susceptibility of the nitroso-imines to nucleophilic attack: the C-aryl compounds appear to be very susceptible to attack by unchanged benzamidoxime, whereas the C-ethoxycarbonyl compounds preferentially cyclise. Only in the absence of nucleophiles (as in the sulphimide reactions) do the C-arylnitroso-imines cyclise.

Further evidence for the intermediacy of nitroso-imines in these reactions was provided by the oxidation of the amidoxime (5; R = Cl) in the presence of the nucleophilic diene thebaine. Kirby and Sweeny have shown that the structurally similar nitrosocarbonyl compounds can be intercepted in Diels–Alder reactions by dienes, nucleophilic dienes such as thebaine being particularly effective.[6] Similarly, thebaine proved to be a suitable reagent for intercepting the nitroso-imine (6; R = Cl), and a 1 : 1 adduct was isolated (64%). The compound is formulated as the Diels–Alder adduct (7): the 100 MHz n.m.r. spectrum shows a singlet (2H) at δ 6.21, assigned to the hydrogen atoms at C-7 and -8, and a singlet (1 H) at δ 4.56, assigned to the hydrogen at C-5.

An identical adduct was isolated (42%) from the reaction of N-4-chlorophenyl-SS-dimethylsulphimide with ethyl cyanoformate N-oxide and thebaine at −20 °C, indicating that the nitroso-imine is a common intermediate in the two reactions. It was also found that the retro-Diels–Alder reaction occurred when the thebaine adduct was heated in benzene at 80 °C for 3 h: 7-chloro-3-ethoxycarbonyl-1,2,4-benzoxadiazine and thebaine were isolated in good yield. These reactions are summarised in Scheme 2.

The benzoxadiazines prepared in this work are crystalline solids which are fairly stable in the solid state at ambient temperatures, but which decompose quite rapidly in solution when heated or exposed to light. Their thermal decomposition to benzoxazoles and other reactions will be discussed in a later paper. The mass spectra of the 3-(4-tolyl)-1,2,4-benzoxadiazines characteristically show a breakdown pattern containing a peak at $M^+ - 15$ (loss of NH) which parallels their thermal decomposition, but this was not observed in the mass spectra of the 3-ethoxycarbonyl compounds.

1,2,4-Benzoxadiazines were reported in the early German literature; the early work has been summarised by McKee.[7] As a result of our work some of the structures proposed in these papers need correction, whereas others are confirmed.

In a series of papers from 1897 to 1906, Jovitschitsch described the reaction of the amidoxime (5; R = H) with nitrous acid, but formulated the products incorrectly.[8] Semper and Lichtenstadt re-formulated the primary product of this reaction as 3-ethoxycarbonyl-

† We have since found that 3-phenyl-1,2,4-benzoxadiazine is also formed in this reaction (T. L. Gilchrist, P. Gordon, and C. W. Rees, unpublished observations). Related radical cyclisations are described by H. G. Aurich and K. Stork (*Chem. Ber.*, 1975, **108**, 2764).

[4] J. H. Boyer and P. J. A. Frints, *J. Org. Chem.*, 1968, **33**, 4554.

[5] F. Minisci, R. Galli, and A. Quilico, *Tetrahedron Letters*, 1963, 785.

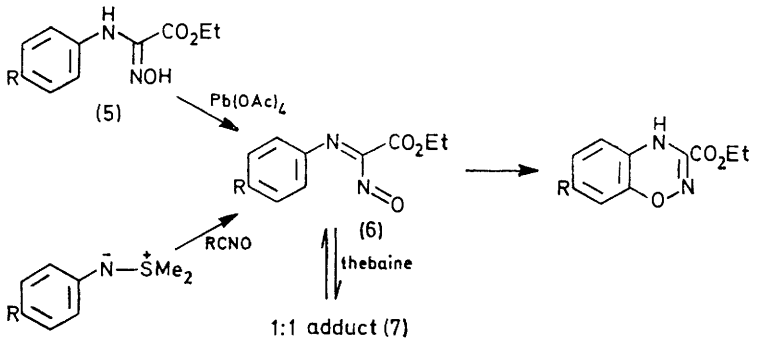
[6] G. W. Kirby and J. G. Sweeny, *J.C.S. Chem. Comm.*, 1973, 704.

[7] R. L. McKee, in 'The Chemistry of Heterocyclic Compounds. Five- and Six-membered Compounds with Nitrogen and Oxygen,' ed. A. Weissberger, Wiley–Interscience, New York, 1962, p. 454.

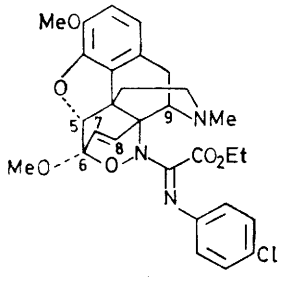
[8] M. Z. Jovitschitsch, *Ber.*, 1897, **30**, 2426; 1898, **31**, 3036; 1902, **35**, 151; 1906, **39**, 3821.

7-nitro-1,2,4-benzoxadiazine (1k) and proposed a mechanism for its formation which involved nitration of the benzene ring at the 2- and 4-positions, followed by displacement of the 2-nitro group by the oxime oxygen atom.[9] Other benzoxadiazine structures (1m—p) were proposed for compounds prepared in an analogous manner.[9,10] Mild basic hydrolysis of the ester (1k) was claimed to give the carboxylic acid (1q), which was readily decarboxylated to 7-nitro-1,2,4-benzoxadiazine (1r).

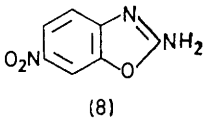
We have repeated the preparation of the ester (1k) by the method described;[9] the structure proposed by Semper and Lichtenstadt is supported by the n.m.r. and mass spectra. We thus confirm the structural assignment of the earlier workers, and, by analogy, the assignment of the structures (1m—p). Indeed these reactions may be closely analogous mechanistically to those we have observed, the nitrous acid acting as an oxidising agent to produce nitroso-imines from the amidoximes. Mild basic hydrolysis of the ester (1k) under the conditions described[9] gave a substance which had the properties associated with the benzoxadiazine (1r) by the earlier workers, but which must be reformulated as 2-amino-6-nitrobenzoxazole (8); the product was identical with a specimen of 2-amino-6-nitrobenzoxazole prepared by a standard route. We have no evidence to show at which stage of the reaction ring contraction occurs, and the mechanisms of this and related ring contractions are being investigated further. In summary, we find that all the structures proposed by Semper and Lichtenstadt are correct, except that of compound (1r).



SCHEME 2

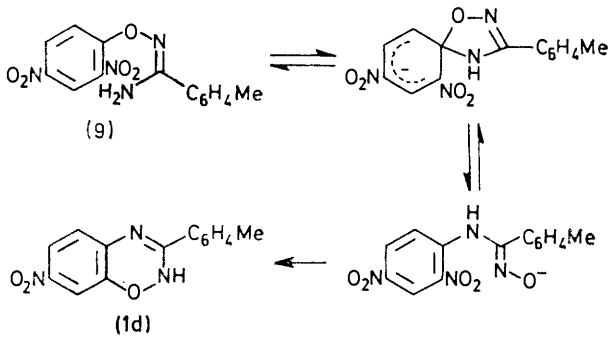


(7)



(8)

The only other report of the synthesis of 1,2,4-benzoxadiazines is by Werner and Herberger,[11] who found that the amidoxime (9) reacted with ethanolic potassium hydroxide to give a product which they formulated as 6-nitro-3-(4-tolyl)-1,2,4-benzoxadiazine (1e). A comparison of a specimen of the product prepared by this reaction with the 1,2,4-benzoxadiazine from *SS*-dimethyl-*N*-4-nitrophenyl sulphimide and 4-toluonitrile oxide showed that the two compounds were identical; thus, the substance is 7-nitro-3-(4-tolyl)-1,2,4-benzoxadiazine (1d). Since there is little doubt that the structure of the amidoxime (9) is correct (the i.r. spectrum in the 3000—3 500 cm^{-1} region being closely similar to that of *O*-acetyl- rather than that of *N*-acetyl-formamidoxine[12]) its reaction with ethanolic potassium hydroxide must involve a rearrangement. A likely mechanism, involving a spiro Meisenheimer complex as an intermediate, is shown in Scheme 3; somewhat analogous Smiles-type rearrangements have been reported.[13]

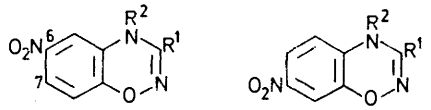


SCHEME 3

Werner and Herberger described the preparation of eight other 6-nitro-1,2,4-benzoxadiazines, (1s—u) and (10a—e), all involving the same type of ring closure.[11] It is likely, therefore, that these eight compounds have

[9] L. Semper and L. Lichtenstadt, *Annalen*, 1913, **400**, 302.
[10] H. Rheinboldt and O. Schmitz-Dumont, *Annalen*, 1925, **444**, 113.
[11] A. Werner and T. Herberger, *Ber.*, 1899, **32**, 2686.
[12] F. Eloy, R. Lenaers, and C. Moussebois, *Helv. Chim. Acta*, 1962, **45**, 437.
[13] C. F. Bernasconi, R. H. de Rossi, and C. L. Gehriger, *J. Org. Chem.*, 1973, **38**, 2838.

the 7-nitro-1,2,4-benzoxadiazine structures (1v—x), and (11a—e), respectively.



(10) (11)

a: $R^1 = R^2 =$ Ph, b: $R^1 =$ Ph, $R^2 = CH_2Ph$, c; $R^1 = 4\text{-}MeC_6H_4$, $R^2 =$ Ph, d; $R^1 = 3\text{-}NO_2C_6H_4$, R^2=Ph, e: $R^1 = 4\text{-}NO_2\text{-}C_6H_4$, R^2 = Ph

EXPERIMENTAL

N-Arylsulphimides were prepared by literature procedures involving the reaction of the aniline with dimethyl sulphoxide and P_4O_{10},[2b] or, preferably, by the reaction of the aniline with dimethyl sulphide and *N*-chlorosuccinimide.[2a] The crude sulphimides were examined by n.m.r. and were then used in subsequent reactions without further purification, with the exception noted below. 2-Chloro-5-nitroaniline gave, with dimethyl sulphide and *N*-chlorosuccinimide, the crystalline N-(2-*chloro*-5-*nitrophenyl*)-SS-*dimethylsulphimide* (71%), m.p. 127—128° (decomp.) (from toluene) (Found: C, 41.6; H, 4.1; N, 12.0. $C_8H_9ClN_2O_2S$ requires C, 41.3; H, 3.9; N, 12.0%); δ($CDCl_3$) 2.78(6H) and 7.2—7.7 (3 H, m).

1,2,4-*Benzoxadiazines from* 4-*Toluonitrile Oxide and* N-*Aryl*-SS-*dimethylsulphimides. General Procedure.*—4-Toluonitrile oxide [14] (2.0 mmol) in dichloromethane (10 ml) was added to the sulphimide (2.0 mmol) in dichloromethane (10ml) at room temperature. The reaction was monitored by t.l.c.; when no further change was observed (1—3 h) the mixture was evaporated and the crude benzoxadiazine was purified by crystallisation or by layer chromatography, as indicated below.

(*a*) *SS*-Dimethyl-*N*-phenylsulphimide and 4-toluonitrile oxide gave, by crystallisation of the crude product, 3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1a) (32%), m.p. 170° (decomp.) (from chloroform) (Found: C, 74.7; H, 5.45; N, 12.3. $C_{14}H_{12}N_2O$ requires C, 75.0; H, 5.4; N, 12.5%); $\nu_{max.}$ 3 150 cm^{-1} (NH); δ($CDCl_3$) 2.40 (3 H), 6.7—7.0 (4 H, m), 7.30 (2 H, d, *J* 8 Hz), and 7.72 (2 H, d, *J* 8 Hz); *m/e* 224 (M^+, base) and 209.

(*b*) *N*-4-Chlorophenyl-*SS*-dimethylsulphimide and 4-toluonitrile oxide gave, by crystallisation of the crude product, 7-*chloro*-3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1b) (64%) as pale yellow needles, m.p. 174—176° (decomp.) (from chloroform) (Found: C, 65.0; H, 4.2; N, 10.5. $C_{14}H_{11}ClN_2O$ requires C, 65.0; H, 4.3; N, 10.8%); $\nu_{max.}$ 3 150 cm^{-1} (NH); δ[$(CD_3)_2CO$] 2.41 (3 H), 6.8—7.0 (3 H, m), 7.38 (2 H, d, *J* 8 Hz), and 7.78 (2 H, d, *J* 8 Hz); *m/e* 260 and 258 (M^+, base), 245, and 243.

(*c*) *N*-Biphenyl-2-yl-*SS*-dimethylsulphimide and 4-toluonitrile oxide gave, by layer chromatography (silica; chloroform), 5-*phenyl*-3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1c) (50%) as pale yellow prisms, m.p. 102—104° (from ethanol) (Found: C, 79.8; H, 5.4; N, 9.25. $C_{20}H_{16}N_2O$ requires C, 80.0; H, 5.4; N, 9.3%); δ($CDCl_3$) 2.36 (3 H), and 6.7—7.6 (12 H, m); *m/e* 300 (M^+, base), and 285.

(*d*) *SS*-Dimethyl-*N*-4-nitrophenylsulphimide and 4-toluonitrile oxide gave, by layer chromatography (silica; chloroform–acetone, 19 : 1), 7-*nitro*-3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1d) (27%) as yellow crystals, m.p. 192—193° (decomp.) (from chloroform) (Found: C, 62.2; H, 4.3; N, 15.6. $C_{14}H_{11}N_3O_3$ requires C, 62.45; H, 4.1; N, 15.6%); $\nu_{max.}$ 3 350 cm^{-1} (NH); δ[$(CD_3)_2CO$] 2.40 (3 H) and 6.9—7.8 (7 H, m); *m/e* 269 (M^+, base), 254, 239, and 223.

(*e*) *SS*-Dimethyl-*N*-3-nitrophenylsulphimide and 4-toluonitrile oxide gave, by layer chromatography (silica; chloroform) two orange-red solids. The less polar component was identified as 6-*nitro*-3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1e) (41%), orange plates, m.p. 186—187° (decomp.) (from chloroform–hexane) (Found: C, 62.3; H, 4.2; N, 15.8. $C_{14}H_{11}N_3O_3$ requires C, 62.45; H, 4.1; N, 15.6%); ν_{max} 3 400 cm^{-1} (NH); δ[$(CD_3)_2CO$] 2.41 (3 H), 6.78 (1 H, d, *J* 8 Hz), 7.32 (2 H, d, *J* 8 Hz), 7.69 (1 H), 7.72 (2 H, d, *J* 8 Hz), 7.85 (1 H, d, *J* 8 Hz), and 8.7br (1 H); *m/e* 269, 254, 223, and 119 (base); *m** (269 ⟶ 223) 184.8.

The more polar component was identified as 8-*nitro*-3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1f) (48%), brick-red iridescent plates, m.p. 178—180° (decomp.) (from ethanol) (Found: C, 62.7; H, 4.4; N, 16.0%); $\nu_{max.}$ 3 370 cm^{-1} (NH); δ[$(CD_3)_2CO$] 2.40 (3 H), 7.0—7.2 (2 H, m), 7.45 (2 H, d, *J* 8 Hz), 7.4—7.6 (1 H, m), 7.76 (2 H, d, *J* 8 Hz), and 9.0br (1 H); *m/e* 269, 254, and 117 (base).

(*f*) *N*-(2-Chloro-5-nitrophenyl)-*SS*-dimethylsulphimide and 4-toluonitrile oxide gave, by layer chromatography (silica; chloroform–acetone, 19 : 1) 5-*chloro*-8-*nitro*-3-(4-*tolyl*)-4H-1,2,4-*benzoxadiazine* (1g) (40%), m.p. 172—173° (decomp.) (from ethanol) (Found: C, 55.55; H, 3.5; N, 13.7. $C_{14}H_{10}ClN_3O_3$ requires C, 55.4; H, 3.3; N, 13.8%); *m/e* 305 and 303 (M^+), 290, and 288.

Benzoxadiazines from Ethyl Cyanoformate N-*Oxide and* N-*Aryl*-SS-*dimethylsulphimides.*—(a) *Ethyl* 4H-1,2,3-*benzoxadiazine*-3-*carboxylate* Ethyl chloroglyoxylate oxime [15] (1.10 g, 7.3 mmol) in dichloromethane (50 ml) was added dropwise during 1 h to *SS*-dimethyl-*N*-phenylsulphimide (1.10 g, 7.3 mmol) and triethylamine (1.0 g) in dichloromethane (50 ml) at −60 °C. The mixture was stirred at −60 °C for 1 h, then at −20 °C for 1.5 h, and was then allowed to reach room temperature. It was washed with water and the organic phase was dried and evaporated. The residue was subjected to column chromatography (silica; chloroform) and to layer chromatography (silica; chloroform–hexane 7 : 3) giving yellow needles of *ethyl* 4H-1,2,4-*benzoxadiazine*-3-*carboxylate* (1h) (230 mg, 15%), m.p. 85—86° (from dichloromethane–hexane) (Found: C, 58.2; H, 5.0; N, 13.35. $C_{10}H_{10}N_2O_3$ requires C, 58.25; H, 4.9; N, 13.6%); $\nu_{max.}$ 3 350 (NH) and 1 709 (CO) cm^{-1}; δ($CDCl_3$) 1.36 (3 H, t, *J* 7 Hz), 4.43 (2 H, q, *J* 7 Hz), and 6.45—7.05 (4 H, m); *m/e* 206 (M^+) and 120 (base).

(b) *Ethyl* 7-*chloro*-4H-1,2,4-*benzoxadiazine*-3-*carboxylate*. Ethyl chloroglyoxylate oxime (180 mg, 1.2 mmol) in dichloromethane (8 ml) was added dropwise to *N*-4-chlorophenyl-*SS*-dimethylsulphimide (190 mg, 1.0 mmol) and triethylamine (150 mg) in dichloromethane (8 ml) at −25 °C. The mixture was allowed to reach room temperature and the organic phase was washed, dried, and evaporated. The residue gave, by layer chromatography (silica; chloroform–acetone, 19 : 1), *ethyl* 7-*chloro*-4H-1,2,4-*benzoxadiazine*-3-*carboxylate* (1j) (74 mg, 31%), m.p. 133—134° (decomp.) (from ethanol) (Found: C, 49.85; H, 3.7; N, 11.4. $C_{10}H_9ClN_2O_3$ requires C, 49.9; H, 3.7; N, 11.6%); $\nu_{max.}$ 3 350 (NH) and 1 709 (CO) cm^{-1}; δ($CDCl_3$) 1.38 (3 H, t, *J* 7 Hz), 4.41 (2 H, q, *J* 7 Hz), 6.49 (1 H, d, *J* 8 Hz), 6.70 (1 H, d, *J* 2 Hz), and 6.87 (1 H, dd, *J* 2 and 8 Hz); *m/e* 242/240 (M^+) and 168 (base).

[14] A. Dondoni and F. Taddei, *Boll. sci. Fac. Chim. ind. Bologna*, 1967, **25**, 155.

[15] G. S. Skinner, *J. Amer. Chem. Soc.*, 1924, **46**, 731.

Benzoxadiazines by Oxidation of Amidoximes.—(a) *Ethyl-4H-1,2,4-benzoxadiazine-3-carboxylate.* (i) Ethyl (phenylamino)glyoxylate oxime was prepared (90%) by addition of ethyl chloroglyoxylate oxime (0.01 mol) to aniline (0.01 mol) and triethylamine (2 ml) in benzene (20 ml) at room temperature, and had m.p. 105—106° (from ethanol) (lit.,[9] 107—108°); $\nu_{max.}$ 3 320, 3 150, and 1 705 cm^{-1}.

(ii) The oxime (120 mg, 0.58 mmol) was dissolved in dichloromethane (20 ml) at 0 °C and lead tetra-acetate (255 mg, 0.58 mmol) was added in portions. The mixture was filtered through Celite and the yellow filtrate was evaporated. The residue gave, by layer chromatography, the benzoxadiazine (1 h) (62 mg, 53%), identical (i.r.) with that prepared from the sulphimide.

(b) *Ethyl 7-chloro-4H-1,2,4-benzoxadiazine-3-carboxylate.* (i) *Ethyl (4-chlorophenylamino)glyoxylate oxime.* Ethyl chloroglyoxylate oxime (0.1 mol) and 4-chloroaniline (0.2 mol) in ether (8 ml) at room temperature gave the *oxime* (70%), m.p. 131—132° (from ethanol) (Found: C, 49.3; H, 4.8; N, 11.55. $C_{10}H_{11}ClN_2O_3$ requires C, 49.5; H, 4.5; N, 11.55%); $\nu_{max.}$ 3 340, 3 200, 3 080, and 1 705 cm^{-1}; $\delta(CDCl_3)$ 1.22 (3 H, t, *J* 7 Hz), 4.30 (2 H, q, *J* 7 Hz), 6.82 (2 H, d, *J* 8.5 Hz), and 7.23 (2 H, d, *J* 8.5 Hz).

(ii) Lead tetra-acetate (250 mg, 0.56 mmol) was added to the oxime (120 mg, 0.50 mmol) in dichloromethane (20 ml) at 0 °C. The mixture was filtered through Celite and evaporated. Layer chromatography of the residue (silica; chloroform–acetone, 19 : 1) gave the benzoxadiazine (1j) (105 mg, 88%), m.p. 130° (decomp.), identical (i.r.) with that obtained from the sulphimide.

Interception of Ethyl 2-(4-Chlorophenylimino)-2-nitrosoacetate by Thebaine.—(*a*) *N*-4-Chlorophenyl-*SS*-dimethylsulphimide (1.94 g, 12.3 mmol) and thebaine (3.2 g, 10.3 mmol) were dissolved in dichloromethane (30 ml) at −20 °C. Ethyl chloroglyoxylate oxime (1.7 g, 11.2 mmol) in dichloromethane (20 ml) was mixed with triethylamine (1.5 ml) at −20 °C and the solution was added to that containing the sulphimide and thebaine during 5 min. The mixture was stirred at −20 °C for 20 min and at room temperature for 20 min. Column chromatography (silica) gave ethyl 7-chloro-1,2,4-benzoxadiazine-3-carboxylate (307 mg, 13%) and the *thebaine adduct* (7) (2.40 g, 42%), m.p. 158—160° (from ethanol) (Found: C, 62.7; H, 5.45; N, 7.6. $C_{29}H_{30}ClN_3O_6$ requires C, 63.1; H, 5.5; N, 7.6%); $\nu_{max.}$ 1 708 (CO) and 1 637 (CN) cm^{-1}; δ (100 MHz; $CDCl_3$) 1.03 (3 H, *J* 7 Hz), 2.45 (3 H, NMe), 2.0—3.5 (6 H, m), 3.48 (3 H, OMe), 3.80 (3 H, OMe), 4.04 (2 H, q, *J* 7 Hz), 4.56 (1 H, H-5); 4.94 (1 H, d, *J* 6.5 Hz, H-9),* 6.21 (2 H, H-7 and -8), 6.56 (1 H, d, *J* 8.5 Hz), 6.70 (1 H, d, *J* 8.5 Hz), 6.76 (2 H, d, *J* 8.5 Hz), and 7.17 (2 H, d, *J* 8.5 Hz); *m/e* 553/551 (M^+), 536/534, and 311 (thebaine, base).

(*b*) Ethyl (4-chlorophenylamino)glyoxylate oxime (120 mg, 0.50 mmol) and thebaine (150 mg, 0.48 mmol) were dissolved in dichloromethane, and to the stirred solution at −20 °C was added lead tetra-acetate (250 mg, 0.56 mmol). The mixture was stirred for 20 min at −20 °C and for 20 min at room temperature. It was filtered through Celite and the filtrate was examined by t.l.c.; no benzoxadiazine was detected. Layer chromatography (silica; chloroform–acetone, 4 : 1) gave the thebaine adduct (7) (170 mg, 64%). Heating the adduct (235 mg, 0.43 mmol) in boiling benzene (30 ml) for 3 h gave ethyl 7-chloro-1,2,4-benzoxadiazine-3-carboxylate (84 mg, 82%) and thebaine (120 mg, 90%).

4-Methylbenzamide O-(2,4-Dinitrophenyl)oxime (9).—4-Methylbenzamidoxime [16] (1.50 g, 10 mmol) in absolute ethanol (20 ml) was treated with sodium ethoxide (10 mmol) in ethanol (5 ml) at room temperature, and 1-chloro-2,4-dinitrobenzene (2.02 g, 10 mmol) in ethanol (60 ml) was added. A precipitate rapidly appeared. After 2 h the solid was filtered off and crystallised, giving the 2,4-dinitrophenyl derivative (1.56 g, 51%), m.p. 173—174° (from ethanol) (lit.,[11] 174°); $\nu_{max.}$ 3 440 and 3 350 (NH), 1 643 (C=N), and 1 605.

Reaction of the Amidoxime (9) *with Ethanolic Potassium Hydroxide.*—The amide *O*-(2,4-dinitrophenyl)oxime (306 mg, 1 mmol) was added to a boiling solution of potassium hydroxide (2 g) in ethanol (10 ml); a blue colouration developed. The solution was cooled and hydrochloric acid (30%) was then added to bring the pH to 5—6. A suspension of an orange solid in an orange solution was produced. The solid was filtered off and washed with ethyl acetate. Layer chromatography (silica; chloroform–acetone, 9 : 1) gave yellow crystals (95 mg, 37%), m.p. 193° (decomp.) (from chloroform) (lit.,[11] 185°). A mixture of the substance with 6-nitro-3-(4-tolyl)-1,2,4-benzoxadiazine had m.p. 168—170° (decomp.); a mixture with the 8-nitro isomer had m.p. 168—170° (decomp.); a mixture with the 7-nitro isomer had m.p. 193° (decomp.). The n.m.r. and i.r. spectra of the product were identical with those of the 7-nitro isomer, and the n.m.r. spectrum was different from those of the 6- and 8-nitro compounds.

Reaction of Ethyl 7-Nitro-1,2,4-benzoxadiazine-3-carboxylate with Sodium Hydroxide.—The benzoxadiazine (1k) was prepared by the reported procedure [9] and gave yellow plates (1.76 g, 57%), m.p. 182° (from ethanol) (lit.,[9] 181.5°), δ[$(CD_3)_2CO$] 1.32 (3 H, t, *J* 7 Hz), 4.35 (1 H, t, *J* 7 Hz), 6.99 (1 H, d, *J* 8 Hz), 7.38 (1 H, d, *J* 2 Hz), and 7.80 (1 H, dd, *J* 2 and 8 Hz).

The benzoxadiazine (250 mg) was stirred for 1.5 h in aqueous sodium hydroxide (0.2M; 10 ml) at room temperature. A purple colour appeared at first, but faded to grey-green. The mixture was neutralised (HCl) and the solution was shaken with dichloromethane (5 × 10 ml) to give yellow needles (170 mg, 95%), m.p. 245° (from ethanol); $\nu_{max.}$ 3 430 and 1 700 cm^{-1}; *m/e* 179 (M^+). The literature gives m.p. 240° for the product of this reaction; as reported,[9] the product gives a deep red solution with aqueous sodium hydroxide.

A specimen of 2-amino-6-nitrobenzoxazole prepared by the method of Acheson and Taylor [17] from 2-amino-5-nitrophenol and cyanogen bromide had m.p. 244° (lit.,[18] 244°). It was identical (i.r. spectrum and mixed m.p.) with the product obtained from the action of sodium hydroxide on the benzoxadiazine (1k).

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* In the n.m.r. spectrum of thebaine the H-9 signal appears as a doublet (*J* 6.5 Hz) at δ 3.52 (T. Rüll and D. Gagnaire, *Bull. Soc. chim. France*, 1963, 2180). Models indicated that this proton would be deshielded in the adduct by the ester carbonyl group, and that H-8 would also be deshielded.

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