Nitrenes Generated from Nitro-compounds by Various Phosphorus Reagents in Heterocyclic Synthesis. A Convenient Route to Substituted 3*H*-Azepines †

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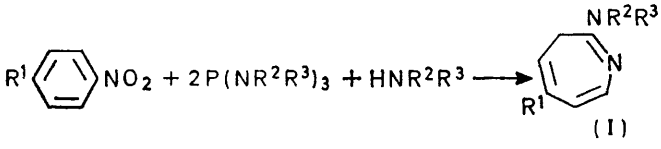
Reductions of substituted nitrobenzenes with various trivalent phosphorus reagents in the presence of an excess of primary or secondary amine lead to substituted azepines by addition to the nitrene intermediate followed by ring expansion. Azepines substituted with functional groups are thus readily available for further synthesis. Where ring expansion does not occur, typical nitrene reactions such as proton abstraction from the amine solvent, insertion into the N–H bond, and trapping by the phosphorus reagent are observed.

In 1966 Odum and Brenner [1] reported the reduction of nitrosobenzene by triphenyl- and tributyl-phosphines in the presence of diethylamine to give 2-diethylamino-3*H*-azepine (I; $R^1 = H$, $R^2 = R^3 = Et$). Reduction of nitrobenzene with trivalent phosphorus reagents in diethylamine under more drastic conditions subsequently also gave this compound (I; $R^1 = H$, $R^2 = R^3 = Et$).[2,3] To our knowledge only two substituted nitrobenzenes (2-nitrobiphenyl and *o*-nitrotoluene) have been similarly reduced to give substituted 2-diethylamino-3*H*-azepines (in low yields). We now report the extension of this reaction to various substituted nitro-compounds to give a general synthesis of azepines. Initial results are shown in Table 1.

TABLE 1

Reduction of nitrobenzenes by alkylphosphorous triamides in the presence of amines to give azepines



(I)

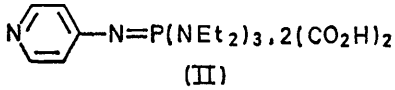
R^1	NR^2R^3	Yield of (I) (%)
H	Piperidino	60
Me	NMe_2	42
Ph	NEt_2	56
4-Pyridyl	NEt_2	47

Reaction temperatures were *ca.* 120°

Tris(monoalkylamino)phosphines gave poor yields of azepines (I), probably because of their instability under the reaction conditions.[4]

Reactions with 1-nitronaphthalene did not give the desired benzazepine but instead 1-naphthylamine (6%) and the *N'*-substituted 1-naphthylhydrazine (*ca.* 10%) were isolated (NR^2R^3 = piperidino). These are typical nitrene proton abstraction and insertion products. Irradiation of *p*-cyanophenyl azide in dimethylamine had given the corresponding hydrazine (70%) and *p*-cyanoaniline (5%). In the presence of a triplet sensitiser, product yields were reversed (6 and 70%, respectively).[5] The intermediacy of a singlet nitrene in the absence of a sensitiser was implied.

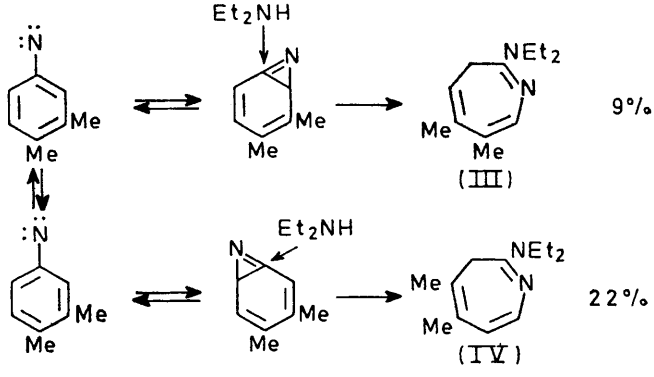
Reactions with 3- or 4-nitropyridines and with 6-nitroquinoline gave only intractable tars and not the desired diazepines. 4-Nitropyridine *N*-oxide reacted



(II)

with hexaethylphosphorous triamide in diethylamine but the only product isolated was the trapped nitrene (II), obtained as the oxalate in 10% yield.

Azepines from ortho- *and* meta-*Substituted Nitrobenzenes.*—Previously proposed mechanisms [1,6] for nitrene ring expansions imply that 2- and 3-substituted nitrobenzenes should form mixtures of isomers, whereas symmetrically substituted nitrobenzenes (*e.g.* 3,5- and 3,4,5-) would give a single product. In the case of 3,4-dimethylnitrobenzene, isomeric products were obtained as shown in Scheme 1.



SCHEME 1

The n.m.r. spectra of compounds (III) and (IV) were consistent with the 3*H*-azepine structure.[1,2,7,8] Reduction of 2,4-dimethylnitrobenzene gave 2-diethylamino-5,7-dimethyl-3*H*-azepine (7%) and 2-diethylamino-3,5-dimethyl-3*H*-azepine (2%). The lower total

† Previously communicated in part at the Joint Annual Meeting of The Chemical Society and the Royal Institute of Chemistry, University of Edinburgh, April 1970.

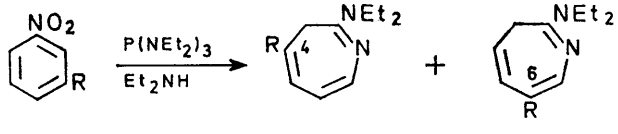
[1] R. A. Odum and M. Brenner, *J. Amer. Chem. Soc.*, 1966, **88**, 2074.
[2] J. I. G. Cadogan and M. J. Todd, *Chem. Comm.*, 1967, 178.
[3] F. R. Atherton and R. W. Lambert, unpublished results.
[4] G. M. Kosolapoff, 'Organophosphorus Compounds,' Wiley, New York, 1950, p. 278.
[5] R. A. Odum and A. M. Aaronson, *J. Amer. Chem. Soc.*, 1969, **91**, 5680.
[6] R. Huisgen and M. Appl, *Chem. Ber.*, 1958, **91**, 12; 1959, **92**, 2961.
[7] W. von E. Doering and R. A. Odum, *Tetrahedron*, 1966, **22**, 81.
[8] (*a*) J. I. G. Cadogan and M. J. Todd, *J. Chem. Soc.* (*C*), 1969, 2808; (*b*) J. I. G. Cadogan, D. J. Sears, D. M. Smith, and M. J. Todd, *ibid.*, p. 2813; (*c*) J. I. G. Cadogan and R. K. Mackie, *ibid.*, p. 2819.

yield may be due to insertion of the nitrene into the C–H bond of the *ortho*-methyl group,[9] or proton abstraction therefrom.[8a,10] Rearrangement to a substituted pyridine may be a competing reaction; Sundberg [11] and his co-workers have reported the isolation of no less than 37% of *N*-(*o*-tolyl)-2-acetimidoylpyridine from the nitrene formed on irradiation of *o*-nitrotoluene in triethyl phosphite. Reduction of 3,5-dimethylnitrobenzene gave 2-diethylamino-4,6-dimethyl-3*H*-azepine in 46% yield.

The results shown in Table 2 suggest that electron-withdrawing groups in the *meta*-position of nitrobenzenes favour the production of 6-substituted 3*H*-azepines (VII) and electron-releasing groups favour formation of the 4-isomers (VI). The results for diethylcarbamoyl and

TABLE 2

Reduction of *m*-nitrobenzenes to 4- and 6-substituted 3*H*-azepines



(V) (VI) (VII)

R	4-Isomer (%)	6-Isomer (%)
Cl	5	28
Ph	18	31
4-Pyridyl	19	30
Me	28	19
OMe	30	
Et_2NCO	17	3 [a]
Ac	14	3 [b]

[a] Isolated as amides (XI). [b] Isolated as methiodides.

acetyl substituents are then anomalous, but the low total yield of isomers suggests that these 6-isomers may have reacted further to give products which were not isolated.

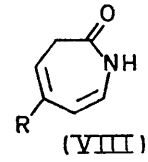
Isomers were usually readily separated by crystallisation as oxalates (prepared as described in the Experimental section) and yields quoted are those of pure isolated isomer. In two cases [(III) + (IV) and (VI) + (VII) (R = Me)] separation was difficult and the amount of each isomer was calculated from the n.m.r. spectrum of the total oxalate fraction. Occasionally (VII; R = Ph or 4-pyridyl) most of the 6-isomer (VII) could be crystallised as the free base prior to oxalate separation.

N.m.r. Spectra.—The structure of 2-diethylamino-3*H*-azepines is now firmly established on the basis of spectral evidence including detailed n.m.r. studies.[7,8c] Chemical shifts and coupling constants for substituted 2-dialkylamino-3*H*-azepines prepared during the present work were consistent with these studies.* N.m.r. data for derivatives of substituted 3*H*-azepines, described below, were consistent with the proposed structures; details are given in the Experimental section.

* These n.m.r. data are available as Supplementary Publication No. SUP 20674 (7 pp.). For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

[9] R. J. Sundberg, *Tetrahedron Letters*, 1966, 477; G. Smolinsky and B. I. Feuer, *J. Org. Chem.*, 1966, **31**, 3882.
[10] G. Smolinsky, *J. Org. Chem.*, 1961, **26**, 4108.

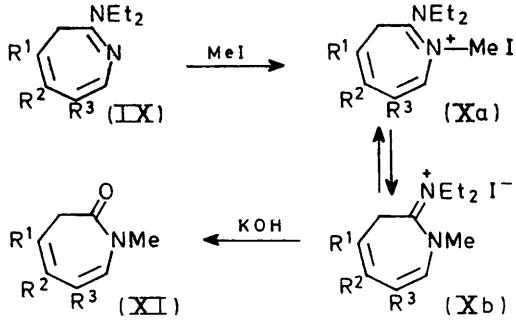
Hydrolysis of 2-Diethylamino-3H-azepines.—Hydrolysis of 2-diethylamino-3*H*-azepines in water, aqueous 2-methoxyethanol, or aqueous 2-ethoxyethanol to 1,3-dihydro-2*H*-azepin-2-ones was slow. Yields of compounds (VIII; R = H, Ph, or 4-pyridyl) were 52, 41, and 53%, respectively. The unsubstituted azepinone (VIII;



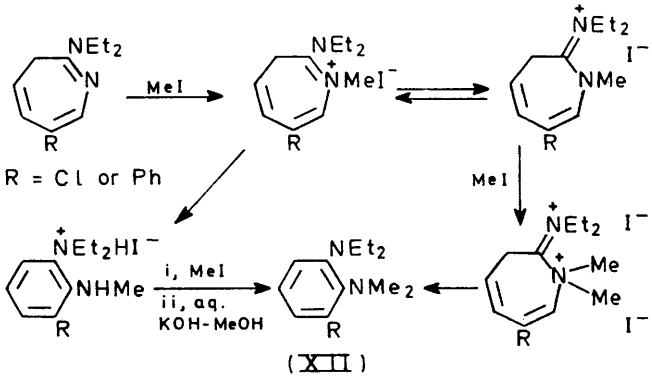
(VIII)

R = H) had the same m.p. and u.v. and n.m.r. spectra as material previously described.[7,12]

Quaternisation of 2-Diethylamino-3H-azepines.—The quaternisation of the 2-diethylamino-3*H*-azepines (IX) with methyl iodide followed by hydrolysis was a convenient route to 1,3-dihydro-1-methyl-2*H*-azepin-2-ones (XI) (Scheme 2). Yields varied between 14 and 83% but were usually greater than 50%. In two cases (X; R^1 = MeO, R^2 = R^3 = H; R^1 = AcO, R^2 = R^3 = H) crystalline quaternary salts were isolated in high yield and fully characterised.



SCHEME 2



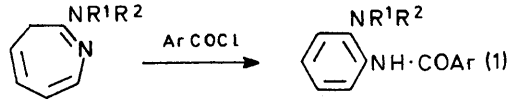
SCHEME 3

Ring contraction had occurred in by-products isolated from two C-6 substituted azepines (IX; R^1 = R^2 = H, R^3 = Cl; R^1 = R^2 = H, R^3 = Ph), their aromatic nature (XII) being revealed by the changed n.m.r.

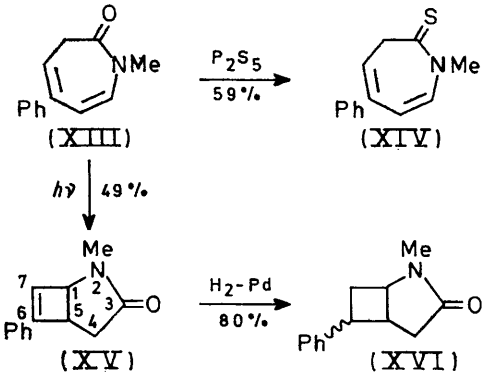
[11] R. J. Sundberg, W. G. Adams, R. H. Smith, and D. E. Blackburn, *Tetrahedron Letters*, 1968, 777.
[12] E. Vogel, R. Erb, G. Lenz, and A. A. Bothner-By, *Annalen*, 1965, **682**, 1.

spectrum. The formation of (XII) may be rationalised as shown in Scheme 3. Similar ring contractions of unsubstituted azepines (Equation 1) have been reported.[7,13]

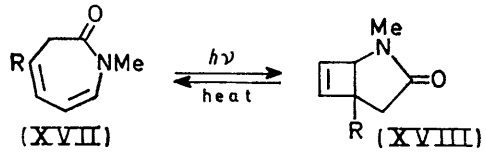
Further transformations of some of the foregoing azepinones are outlined in Schemes 4 and 5. Photo-



isomerisations similar to (XIII) ⟶ (XV) have been described previously.[14–17] Simple 5-substituted 2-azabicyclo[3.2.0]hept-6-enes (XVIII) shown in Scheme 5, have been synthesised for the first time; carbocyclic analogues such as (XX) and (XXI) are known.[18] The chemical shifts of the vinyl protons of various compounds (XVIII) (τ 3·28—3·5) are close both to those found for the vinyl protons of (XXII) (τ 3·6—3·89) [19] and to those for the cyclobutene protons of other similar compounds [*e.g.* (XXI), τ 3·40—3·92].[12,14–16,20] Coupling constants were 2·8—2·9 Hz, further supporting the



SCHEME 4



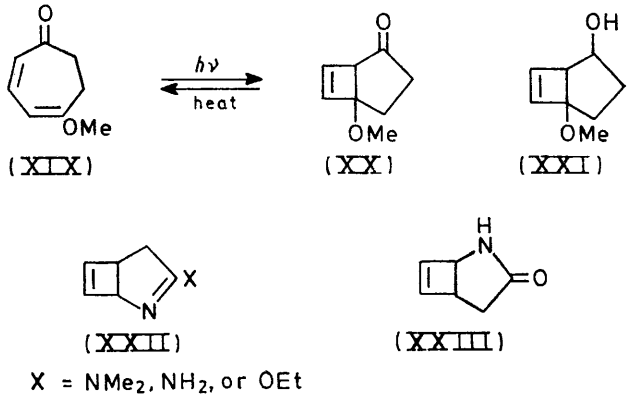
R :	Ph	Et_2NCO	OMe
Yield (%)	65	63	—

SCHEME 5

cyclobutene structure for which values of 2·5—3·7 Hz have been reported.[19,21]

That photoisomerisation of (XVII; R = OMe) gave two products was shown by analytical g.l.c. A small amount of one product was isolated by preparative g.l.c. and its n.m.r. spectrum was consistent with structure (XVIII; R = OMe).

The chemical shifts of the olefinic protons of (XVIII; R = OMe) and (XXI) [18b] are very similar (complex multiplets at τ 3·49 and 3·85, respectively). Attempted separation on a larger scale partly isomerised (XVIII; R = OMe) back to (XVII; R = OMe). The instability of (XVIII; R = OMe) may be compared to that found for (XX), which underwent ring expansion back to (XIX) on warming to 50° in ethanol.[18c] In contrast, ring expansion of the parent azabicyclo-compound (XXIII) to (VIII; R = H) required a temperature of 500°.[12]



EXPERIMENTAL

Spectrophotometers used were the Perkin-Elmer 137 (u.v.) and the Unicam SP 200 (i.r.). N.m.r. spectra were measured for solutions in deuteriochloroform (unless otherwise stated) with a Varian A60 instrument (tetramethylsilane as internal standard). Mass spectra were determined with an A.E.I. MS9 spectrometer.

The terms light petroleum and petroleum refer to the fractions of b.p. 40—60 and 60—80°, respectively.

2-Piperidino-3H-azepine (I; R^1 = H, NR^2R^3 = piperidino).—Hexamethylphosphorous triamide [22] (HMPT) (8·2 g, 50 mmol) and piperidine (42 g, 500 mmol) were heated under nitrogen until the reflux temperature rose to 107°. Nitrobenzene (3·1 g, 25 mmol) was added and the mixture was refluxed for 29 h. Piperidine was evaporated off and the residue was distilled; yield 3·25 g (74%), b.p. 114—116° at 0·7 mmHg. G.l.c. (QF1; 125°) showed a single peak (>97%). Spectra (i.r., u.v., n.m.r.) were in agreement with literature precedents [1,7] and the material was converted into the crystalline *oxalate*, m.p. 155° (decomp.) (from propan-2-ol) (60% yield from nitrobenzene) (Found: C, 58·6; H, 6·9; N, 10·55. $C_{13}H_{18}N_2O_4$ requires C, 58·6; H, 6·8; N, 10·5%).

2-Dimethylamino-5-methyl-3H-azepine (I; R^1 = R^2 = R^3 = Me).—*p*-Nitrotoluene (21 g, 150 mmol), HMPT (49 g, 300 mmol), and dimethylamine were heated in an autoclave at 125° for 18 h. Work-up as above gave the base, b.p. 68° at 0·9 mmHg, n_D^{20} 1·5573, which was converted into the

[13] R. Huisgen, D. Vossius, and M. Appl, *Chem. Ber.*, 1958, **91**, 1, 12.
[14] (*a*) O. L. Chapman and E. D. Hoganson, *J. Amer. Chem. Soc.*, 1964, **86**, 498; (*b*) L. A. Paquette, *ibid.*, p. 500.
[15] L. A. Paquette and W. C. Farley, *J. Org. Chem.*, 1967, **32**, 2725.
[16] L. A. Paquette, *J. Amer. Chem. Soc.*, 1964, **86**, 4092.
[17] G. V. Smith and H. Kriloff, *J. Amer. Chem. Soc.*, 1963, **85**, 2016.
[18] (*a*) O. L. Chapman and D. J. Pasto, *Chem. and Ind.*, 1961, 53; (*b*) O. L. Chapman, D. J. Pasto, A. A. Griswold, *J. Amer. Chem. Soc.*, 1962, **84**, 1213; (*c*) O. L. Chapman, D. J. Pasto, G. W. Borden, and A. A. Griswold, *ibid.*, p. 1220.
[19] R. A. Odum and B. Schmall, *Chem. Comm.*, 1969, 1299.
[20] G. W. Borden, O. L. Chapman, R. Swindell, and T. Tzeuka, *J. Amer. Chem. Soc.*, 1967, **89**, 2979.
[21] O. L. Chapman, *J. Amer. Chem. Soc.*, 1963, **85**, 2014.
[22] A. Michaelis, *Annalen*, 1903, **326**, 129; *Org. Synth.*, 1966, **46**, 42.

oxalate (15·3 g, 42%), m.p. 158—160° (Found: C, 54·6; H, 6·7; N, 11·7. $C_{11}H_{16}N_2O_4$ requires C, 55·0; H, 6·7; N, 11·7%).

2-*Diethylamino*-3H-*azepines*.—*General method*. A mixture of the nitrobenzene, hexaethylphosphorous triamide (HEPT) (2 mol. proportions), and diethylamine (10 mol. proportions) was heated in an autoclave at 120° for 18 h. Work-up involved distillation, precipitation of oxalate, basification, extraction, and redistillation; then purification by recrystallisation of the oxalate or chromatography of the base on alumina. Azepine-containing fractions were monitored by u.v. and i.r. spectroscopy. Details of products are shown in Table 3. N.m.r. data concerning products in Table 3 and earlier examples support the proposed structures.*

2-*Isopropylamino*-3H-*azepine* (I; $R^1 = R^2 = H$, $R^3 = CHMe_2$).—Phosphorus trichloride (16 ml, 180 mmol) in light petroleum (300 ml) was treated with isopropylamine (69 g, 1·2 mol) at 20°. Base hydrochloride was filtered off and the filtrate was evaporated *in vacuo*. The residue was treated with isopropylamine (250 ml) and nitrobenzene (11 g, 90 mmol) and heated in an autoclave at 115° for 18 h. Distillation gave two fractions: (A), 5·2 g, b.p. 58° at 1·6 mmHg, a *ca.* 1 : 1 mixture of nitrobenzene and aniline from which the latter was isolated as oxalate, m.p. 165—166° (9% based on PCl_3); (B), 13·7 g, b.p. 126—142° at 1·4 mmHg containing an ether-insoluble product, *NN'N''*-tri-isopropylphosphoramide (6·8 g, 17%), m.p. 123—124° (lit.,[23] 124·5—125°). The filtrate on treatment with oxalic acid yielded the desired azepine (1·2 g, 5·5%), m.p. 96—97° (decomp.) (from propan-2-ol–ethyl acetate) (Found: C, 55·0; H, 6·6; N, 11·6. $C_{11}H_{16}N_2O_4$ requires C, 55·0; H, 6·7; N, 11·7%).

Reduction of 1-*Nitronaphthalene by Tripiperidinophosphine*.—HMPT (8·15 g, 50 mmol) and piperidine (42·5 g, 500 mmol) were heated at 107° for 15 min. 1-Nitronaphthalene (4·3 g, 25 mmol) was added and the mixture was refluxed for 23 h. Distillation, then precipitation from ether with dry hydrogen chloride, yielded a mixture of two salts which was separated by fractional crystallisation. Salt A was 1-naphthylamine hydrochloride (6%). Salt B was *N-naphthyl-N'N'-pentamethylenehydrazine* (*ca.* 10%), m.p. 219—224° (from ethanol–ethyl acetate) (Found: C, 68·4; H, 7·5; Cl, 13·5; N, 10·4. $C_{15}H_{19}ClN_2$ requires C, 68·6; H, 7·3; Cl, 13·5; N, 10·7%). The n.m.r. spectrum (D_2O) showed only aromatic and piperidine protons.

Reduction of 4-*Nitropyridine* N-*Oxide by HEPT*.—4-Nitropyridine *N*-oxide (5·9 g, 42 mmol), HEPT (34 g, 140 mmol), and diethylamine (61 g, 840 mmol) were heated in an autoclave at 120° for 18 h. Evaporation, followed by chromatography on alumina, first with benzene–chloroform as eluant then with chloroform–methanol, gave a base which was characterised as *trisdiethylamino-(4-pyridylimino)-phosphorane dioxalate* (2·3 g, 10%), m.p. 115—116° (from propan-2-ol–ethyl acetate) (Found: C, 48·4; H, 7·4; N, 13·6; P, 5·7. $C_{21}H_{38}N_5O_8P$ requires C, 48·55; H, 7·4; N, 13·5; P, 6·0%), $\lambda_{max.}$ (EtOH) 295 (ε 24,600). The n.m.r. spectrum (D_2O) was consistent with structure (II).

Aqueous Hydrolysis of 2-*Diethylamino*-3H-*azepines*.—(a) 1,3-*Dihydro*-2H-*azepin*-2-*one* (VIII; R = H). 2-Diethylamino-3*H*-azepine (16 g, 100 mmol) in a mixture of 2-methoxyethanol (80 ml) and water (20 ml) was refluxed for 22 h. Solvents were evaporated off and the residue was acidified and extracted with chloroform. Combined extracts were dried (Na_2SO_4), evaporated, and distilled; yield 6·3 g, b.p. 90—92° at 0·7 mmHg, m.p. 44—48°. The product (VIII; R = H) was sublimed to give material (5·7 g, 52%) of m.p. 48—50° (lit.,[12,24] 48—50°) (Found: C, 65·9; H, 6·6; N, 12·75. Calc. for C_6H_7NO: C, 66·0; H, 6·5; N, 12·8%). Spectral values agreed with the literature.[7,12,24]

(b) 1,3-*Dihydro*-5-*phenyl*-2H-*azepin*-2-*one* (VIII; R = Ph). Similarly, 2-diethylamino-5-phenyl-3*H*-azepine (12 g, 50 mmol), after being refluxed for 36 h in aqueous 2-ethoxyethanol gave, after purification by chromatography on alumina in benzene–chloroform and recrystallisation from benzene–petroleum, then from ethyl acetate, the *product* (VIII; R = Ph) (3·8 g, 41%), m.p. 141—142° (Found: C, 77·8; H, 6·1; N, 7·5. $C_{12}H_{11}NO$ requires C, 77·8; H, 6·0; N, 7·6%), $\lambda_{max.}$ (EtOH) 240 nm (ε 22,500).

(c) 1,3-*Dihydro*-5-(4-*pyridyl*)-2H-*azepin*-2-*one* (VIII; R = 4-pyridyl).—Similarly, 2-diethylamino-5-(4-pyridyl)-3*H*-azepine (10 g, 41 mmol) after being refluxed for 50 h as above gave, after chromatography, the *product* (VIII; R = 4-pyridyl) (4·1 g, 53%), m.p. 163—165° (from ethyl acetate–light petroleum) (Found: C, 71·0; H, 5·6; N, 15·1. $C_{11}H_{10}N_2O$ requires C, 71·0; H, 5·4; N, 15·0%), $\nu_{max.}$ (Nujol) 1670 cm^{-1} (amide), $\lambda_{max.}$ (EtOH) 244 nm (ε 20,600).

Quaternisation of 2-*Diethylamino*-3H-*azepines and Hydrolysis of Salts so formed to Azepinones* (XI).—(a) 1,3-*Dihydro*-1-*methyl*-2H-*azepin*-2-*one* (XI; $R^1 = R^2 = R^3 = H$). A mixture of 2-diethylamino-3*H*-azepine (16 g, 100 mmol), methyl iodide, and acetonitrile (100 ml) was refluxed for 2 h. Volatile materials were evaporated off; the residue was treated with 2N-potassium hydroxide (50 ml) and methanol (35 ml) and kept at 20° for 72 h. The mixture was evaporated and the residue was partitioned between dilute acid and chloroform; the solvent extract was dried (Na_2SO_4), evaporated, and distilled; yield 7·2 g (58%), b.p. 50—54° at 0·6 mmHg (lit.,[12] 94—95° at 12 mmHg) g.l.c. (LAC IR 296; 145°) showed this product to be >99% pure (Found: C, 67·9; H, 7·3; N, 11·1. Calc. for C_7H_9NO: C, 68·3; H, 7·4; N, 11·4%). Spectral values agreed with the literature.[12]

(b) Other 1,3-dihydro-1-methyl-2*H*-azepin-2-ones were similarly prepared. Details are summarised in Table 4. N.m.r. data supported the proposed structures.*

2-*Diethylamino*-4-*methoxy*-1-*methyl*-3H-*azepinium Iodide* (X; R^1 = MeO, $R^2 = R^3 = H$).—Quaternisation of (IX; R^1 = MeO, $R^2 = R^3 = H$) with methyl iodide in acetonitrile gave the *salt* (93%), m.p. 146—148° (from acetone–ethyl acetate) (Found: C, 43·0; H, 5·9; I, 37·8; N, 8·3. $C_{12}H_{21}IN_2O$ requires C, 42·9; H, 6·3; I, 37·8; N, 8·3%), $\lambda_{max.}$ (EtOH) 227 (ε 23,500) and 309 nm (6950).

4-*Acetyl*-2-*diethylamino*-1-*methyl*-3H-*azepinium Iodide* (X; R^1 = Ac, $R^2 = R^3 = H$).—Similarly, quaternisation of (IX; R^1 = Ac, $R^2 = R^3 = H$) gave the *salt* (58%), m.p. 154—156° (Found: C, 44·9; H, 5·9; I, 36·9; N, 8·0. $C_{13}H_{21}IN_2O$ requires C, 44·8; H, 6·1; I, 36·5; N, 8·05%), $\lambda_{max.}$ 237 (ε 18,900) and 368 nm (6790).

3-*Chloro*-N^1,N^1-*diethyl*-N^2,N^2-*dimethyl*-o-*phenylenediamine Hydrochloride* (XII; R = Cl).—The azepine (IX; $R^1 = R^2 = H$, R^3 = Cl) was quaternised and hydrolysed as above. Extraction from acid gave the azepinone (XI;

* See footnote, p. 1080.

[23] A. B. Foster, E. F. Martlew, M. Stacey, P. J. M. Taylor, and J. M. Webber, *J. Chem. Soc.*, 1961, 1204.

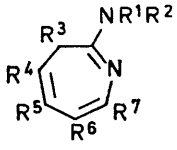
[24] E. Vogel and R. Erb, *Angew. Chem. Internat. Edn.*, 1962, **1**, 53.

$R^1 = R^2 = H$, $R^3 = Cl$). The acid layer slowly deposited a crystalline *solid* (8%), m.p. 205—206° (Found: C, 54·5; H, 7·7; Cl, 26·9; Cl^-, 13·4; N, 10·6. $C_{12}H_{20}Cl_2N_2$ requires C, 54·8; H, 7·7; Cl, 26·9; Cl^-, 13·5; N, 10·6%), $\lambda_{max.}$ (EtOH) 253 nm (ε 680), τ 2·1 (1H, 2d, Ar) and 2·52 (2H, m, Ar).

1,3-*Dihydro*-1-*methyl*-5-*phenyl*-2H-*azepine*-2-*thione* (XIV). —The azepinone (XIII) (4 g, 20 mmol) in pyridine (30 ml) was treated in portions with phosphorus pentasulphide (5·2 g, 23 mmol). After being refluxed for 3 h the mixture was poured into water and the product extracted with chloroform and purified by chromatography on alumina to give the *thione* (XIV) (2·5 g, 59%), m.p. 115° (from petroleum) (Found: C, 72·4; H, 6·1; N, 6·4; S, 14·9. acetone–ether) (Found: C, 70·5; H, 8·5; Cl, 11·6; N, 9·4. $C_{18}H_{25}ClN_2$ requires C, 70·9; H, 8·3; Cl, 11·6; N, 9·2%), $\lambda_{infl.}$ (EtOH) 230 nm (ε 8110), τ 2·57 (8H, m, Ar).

TABLE 3

Substituted 2-diethylamino-3*H*-azepines (XXIV; $R^1 = R^2 = Et$)



(XXIV)

R^3	R^4	R^5	R^6	R^7	M.p. (°C) [B.p. (°C) /mmHg]	Oxalate m.p. (°C)	Formula	Found (%) C	H	N	Hal	Reqd. (%) C	H	N	Hal	U.v. (EtOH) $\lambda_{max.}$/nm	ε	U.v. (0·1N-NaOH EtOH) $\lambda_{max.}$/nm	ε
H	H	Ph	H	H	78—79		$C_{16}H_{20}N_2$	80·2	8·5	11·6		80·0	8·4	11·65		252	20·200		
H	H	4-Py*	H	H	62—63		$C_{15}H_{19}N_3$	74·9	8·2	17·25		74·7	7·9	17·4		268	16,900		
H	Me	Me	H	H		119—120	$C_{14}H_{22}N_2O_4$	59·3	7·7	10·0		59·6	7·9	9·9					
H	H	Me	H	Me		140—141	$C_{14}H_{22}N_2O_4$	59·4	7·8	9·9		59·6	7·9	9·9		263	7460	294	7440
Me	H	Me	H	H		85—86	$C_{15}H_{23}N_2O_6$	55·1	7·0	8·9		55·0	7·1	8·6		281	6640	303	7510
H	Me	H	Me	H	[96—99/ 1·3]		$C_{12}H_{20}N_2$	74·3	10·7	14·5		75·0	10·5	14·6		285	8560		
H	Cl	H	H	H		108—110	$C_{12}H_{17}ClN_2O_4$	49·8	6·0	9·6	11·7	49·9	5·9	9·7	12·3	280	6630	300	8510
H	H	H	Cl	H		119—120	$C_{12}H_{17}ClN_2O_4$	50·1	6·1	9·7	11·7	49·9	5·9	9·7	12·3	270	7300	269	6850
																		309	7700
H	Ph	H	H	H		171—172	$C_{18}H_{22}N_2O_4$	65·6	6·7	8·7		65·4	6·7	8·5		240	18,300		
																310	8700		
H	H	H	Ph	H		137—138	$C_{18}H_{22}N_2O_4$	65·3	6·7	8·5		65·4	6·7	8·5		293	12,900		
H	H	H	Ph	H	75—76		$C_{16}H_{20}N_2$	79·9	8·3	11·6		80·0	8·4	11·65		318	17,100		
H	4-Py	H	H	H	76—78	165—172	$C_{15}H_{19}N_3$	74·6	7·9	17·1		74·7	7·9	17·4		253	20,600		
																378	7900		
H	H	H	4-Py	H	97—99		$C_{15}H_{19}N_3$	74·4	7·7	17·2		74·7	7·9	17·4		228	12,800		
																340	21,600		
H	Me	H	H	H		139	$C_{13}H_{20}N_2O_4$	58·3	7·8	10·65		58·2	7·5	10·4					
H	H	H	Me	H		120—125 [b]	$C_{13}H_{20}N_2O_4$	58·7	7·6	10·4		58·2	7·5	10·4		266	8800	296	7180
H	OMe	H	H	H		125—127	$C_{13}H_{20}N_2O_5$	55·3	7·2	9·8		54·9	7·1	9·85		257	4940	288	9210
																289	4850		
H	Ac	H	H	H		115—117	$C_{14}H_{20}N_2O_5$	56·5	6·9	9·5		56·8	6·8	9·45		227	22,500 [c]	241	25,000
																320	5840	398	7790
H	H	H	Ac	H	134—137 [d]		$C_{13}H_{21}IN_2O$	44·9	6·2	8·1	36·8	44·8	6·1	8·05	36·5	301	15,100		

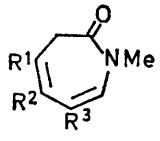
[a] 5,6-Isomer was identified and estimated by n.m.r. [b] Base obtained by preparative g.l.c. (APL; 185°) was converted into oxalate. [c] Values in 0·1N-HCl–EtOH. [d] Methiodide.

* For the preparation of 4-*p*-nitrophenylpyridine, see A.R. Katritzky and P. Simmons, *J. Chem. Soc.*, 1960, 1511.

Py = Pyridyl.

TABLE 4

Substituted 1,3-dihydro-1-methyl-2*H*-azepin-2-ones



(XI)

R^1	R^2	R^3	M.p. (°C) [B.p. (°C)/ mmHg]	Formula	Found (%) C	H	N	Hal	Required (%) C	H	N	Hal	U.v. (EtOH) $\lambda_{max.}$/nm	ε
Me	H	Me	[69—71/1·1]	$C_9H_{13}NO$	71·0	8·7	9·15		71·5	8·7	9·3		256	5070
H	H	Cl	[68—72/0·2]	C_7H_8ClNO	53·6	5·5	8·8	22·3	53·4	5·1	9·0	22·5	274	3850
Ph	H	H	42—44	$C_{13}H_{13}NO$	78·0	6·7	6·9		78·4	6·6	7·0		228	14,100
													301	10,900
H	Ph	H	92—93	$C_{13}H_{13}NO$	78·2	6·8	7·1		78·4	6·6	7·0		242	23,100
H	H	Ph	75—76	$C_{13}H_{13}NO$	78·5	6·7	7·1		78·4	6·6	7·0		282	9660
MeO	H	H	[82·3/0·3]	$C_8H_{11}NO_2$	63·0	7·3	9·5		62·7	7·2	9·1		263	5310
Ac	H	H	54—56	$C_9H_{11}NO_2$	65·3	6·8	8·2		65·4	6·7	8·5		220	15,500
													322	6140
$Et_2N{\cdot}CO$	H	H	71—73	$C_{12}H_{18}N_2O_2$	64·7	8·2	12·5		64·8	8·2	12·6		284	5270
H	H	$Et_2N{\cdot}CO$	87—89	$C_{12}H_{18}N_2O_2$	64·8	8·3	12·5		64·8	8·2	12·6		274	5410

N^3,N^3-*Diethyl*-N^2,N^2-*dimethylbiphenyl*-2,3-*diamine Hydrochloride* (XII; R = Ph).—The azepine (IX; $R^1 = R^2 = H$, R^3 = Ph) similarly afforded the azepinone (XI; $R^1 = R^2 = H$, R^3 = Ph). An impurity isolated during chromatographic purification was converted into the *hydrochloride* (XII; R = Ph) (8%), m.p. 208—210° (from

$C_{13}H_{13}NS$ requires C, 72·5; H, 6·1; N, 6·5; S, 14·9%), $\lambda_{max.}$ (EtOH) 242 (ε 12,800), 266 (15,800), and 313 nm (9860).

2-Methyl-6-phenyl-2-azabicyclo[3.2.0]*hept-6-en-3-one* (XV).—The azepinone (XIII) (24 g, 120 mmol) in dry methanol (800 ml) was irradiated with a Hanovia medium-pressure lamp for 168 h. The solution was evaporated and the residue was chromatographed on alumina with benzene–chloroform as eluant [starting material (10·5 g) was recovered]. The *product* (XV) was recrystallised from benzene; yield 6·7 g (49% based on material consumed), m.p. 147—148° (Found: C, 78·5; H, 6·7; N, 7·0. $C_{13}H_{13}NO$ requires C, 78·4; H, 6·6; N, 7·0%), $\lambda_{max.}$ (EtOH) 217 (ε 11,500), 257 (16,000), and 291 nm (4450), τ 2·65 (5H, m, Ph), 3·35 (s, 1H on C-7), 5·65 (d, 1H on C-1), 6·26 (m, 1H on C-5), 7·08 (3H, s, NMe), 7·38 (d, 1H on C-4), 7·48 (s, 1H on C-4), $J_{4,5}$ 4·2, $J_{1,5}$ 4·4, $J_{1,7}$ <2 Hz, *m/e* 199 (M^+), 198 (M − 1), 170 (M − CO − H), 157 (M − CH_2O), and 97 (M − PhC≡CH).

2-Methyl-5-phenyl-2-azabicyclo[3.2.0]*hept-6-en-3-one* (XVIII; R = Ph).—The azepinone (XVII; R = Ph) was irradiated as above for 28 h. After chromatography on alumina the *product* (XVIII; R = Ph) was crystallised from petroleum; yield 4·8 g (65%), m.p. 71·5—73° (Found: C, 78·7; H, 6·7; N, 7·1. $C_{13}H_{13}NO$ requires C, 78·4; H, 6·6; N, 7·0%), $\lambda_{max.}$ 260 nm (ε 217) (benzene tail peaks), τ 2·70 (5H, m, Ph), 3·27 (2d, 1H on C-7), 3·46 (d, 1H on C-6), 5·75 (d, 1H on C-1), 7·05 (3H, s, NMe), and 7·19 (s, 2H on C-4), $J_{1,7}$ 1·8, $J_{6,7}$ 2·9 Hz.

NN-*Diethyl-2-methyl-3-oxo-2-azabicyclo*[3.2.0]*hept-6-ene-5-carboxamide* (XVIII; R = Et_2N·CO).—The azepinone (XVII; R = Et_2N·CO) was irradiated as above for 24 h and the *product* (XVIII; R = Et_2N·CO) was purified by chromatography; yield 5·3 g (63%), m.p. 79—81·5° (from cyclohexane–petroleum (Found: C, 64·5; H, 8·0; N, 12·85. $C_{12}H_{18}N_2O_2$ requires C, 64·8; H, 8·2; N, 12·6%), τ 3·37 (d, 1H on C-6), 3·50 (2d, 1H on C-7), 5·19 (d, 1H on C-1), 6·66 (4H, 2q, NEt_2), 7·08 (3H, s, NMe), 7·37 (s, 2H on C-4), and 8·83 (6H, 2t, NEt_2), $J_{1,7}$ 1·8, $J_{6,7}$ 2·9 Hz; no u.v. maximum above 206 nm.

5-Methoxy-2-methyl-2-azabicyclo[3.2.0]*hept-6-en-3-one* (XVIII; R = MeO).—The azepinone (XVII; R = MeO) was irradiated as above for 3 h and the product was partially purified by chromatography on silica gel. Analytical g.l.c. (Triton X-100; 180°) showed the presence of starting material and two other compounds. A small amount of pure product (XVIII; R = MeO) was isolated by preparative g.l.c. (APL; 165°); $\nu_{max.}$ 1680 cm^{-1} (C=O), τ 3·48 (m, 2H on C-6 and C-7), 5·68 (s, 1H on C-1), 6·64 (3H, s, OMe), 7·02 (3H, s, NMe), and 7·36 (s, 2H on C-3), *m/e* 153 (M^+) but fragmentation pattern identical with that of starting material, rearrangement probably taking place in the spectrometer; no u.v. maximum above 210 nm. The olefinic protons of carbocyclic analogue (XXI) (multiplet at τ 3·85) are comparable to those of (XVIII; R = MeO) (multiplet at τ 3·48).

2-Methyl-6-phenyl-2-azabicyclo[3.2.0]*heptan-3-one* (XVI).—The bicycloheptene (XV) (1·0 g, 5 mmol) in dry ethanol (25 ml) was hydrogenated over 5% palladium–charcoal (0·1 g). Catalyst and solvent were removed and the residue was crystallised from light petroleum to give the *bicycloheptanone* (0·8 g, 80%), m.p. 47—48° (Found: C, 77·3; H, 7·5; N, 7·1. $C_{13}H_{15}NO$ requires C, 77·6; H, 7·5; N, 7·0%), $\lambda_{max.}$ 260 nm (ε 207) (benzene tail peaks).

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