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1-Benzazepines. The Synthesis and Reactivity of 2-Chloro-1,5-dimethyl-1*H*-1-benzazepines

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Abstract

Treatment of laevulinic acid with *N*-methylaniline yields 1,5-dimethyl-1*H*-1-benzazepin-2(3*H*)-one and 5-methyl-5-[4-(methylamino)phenyl]-1-phenylpyrrolidin-2-one. The structure of the latter is confirmed by a single-crystal X-ray study. The yield of benzazepinone is increased if either *m*-methoxy-*N*-methylaniline or *m*-methyl-*N*-methylaniline is allowed to react with laevulinic acid. Treatment of the benzazepinones with phosphoryl chloride in pyridine produces 2-chloro-1,5-dimethyl-1*H*-1-benzazepines in quantitative yields, but these compounds are highly reactive under acidic conditions, undergoing nucleophilic displacement at C2. In contrast, treatment of benzazepinones with neat phosphoryl chloride yields yellow dimers, assigned as 2′-chloro-1,1′,5,5′-tetramethyl-2,3′-bi-1*H*-1-benzazepines, and with stabilities only marginally greater than those of the 2-chloro-1,5-dimethyl-1*H*-1-benzazepines.

Introduction

The chemistry of 1-azepines and 1-benzazepines has been inadequately explored. Vogel[1] has reported that the ^{1}H n.m.r. spectrum of 1*H*-1-azepine can be measured at −78°C, but on warming, the molecule undergoes tautomerism and polymerizes.[1] Treatment of 1*H*-1-azepine with trimethylamine give the more stable 3*H*-1-azepine.[1] A number of substituted 1-benzazepines have been reported,[2–13] some of which are

[1] Vogel, E., Altenbach, H.-J., Drossard, J.-M., Schmickler, H., and Stegelmeier, H., *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 1016.
[2] Plieninger, H., and Wild, D., *Chem. Ber.*, 1966, **99**, 3070.
[3] Cromarty, A., and Proctor, G. R., *J. Chem. Soc., Chem. Commun.*, 1968, 842.
[4] Rautenstrauch, V., *J., Chem. Soc., Chem. Commun.*, 1969, 1122.
[5] Teuber, H. J., and Emmerich, G., *Tetrahedron Lett.*, 1970, 4069.
[6] Fried, F., Taylor, J. B., and Westwood, R., *J. Chem. Soc., Chem. Commun.*, 1971, 1226.
[7] Lin, M.-S., and Snieckus, V., *J. Org. Chem.*, 1971, **36**, 645.
[8] Acheson, R. M., Bridson, J. N., and Cameron, T. S., *J. Chem. Soc., Perkin Trans. 1*, 1972, 968.
[9] Gogte, V. N., More, K. M., and Tilak, B. D., *Indian J. Chem.*, 1974, **12**, 1237.
[10] Anastassiou, A. G., Reichmanis, E., Girgenti, S. J., and Schaefer-Ridder, M., *J. Org. Chem.*, 1948, **43**, 315.
[11] Hamada, Y., and Sugiura, M., *Yakugaku Zasshi*, 1980, **100**, 162.
[12] Davis, P. D., and Neckers, D. C., *J. Org. Chem.*, 1980, **45**, 456.
[13] Ikeda, M., Ohno, K., Uno, T., and Tamura, Y., *Tetrahedron Lett.*, 1980, 3403.

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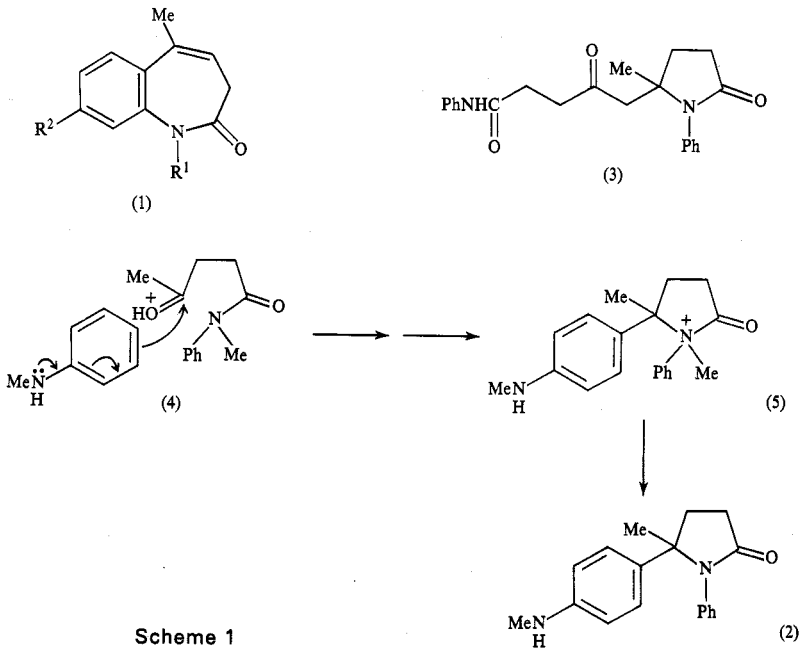
stable at room temperature but at *c.* 300°C undergo rearrangement.[13] The stability of neither the parent 1*H*-1-benzazepine nor of the isomeric 3*H*-1-benzazepine is known.

We chose 1*H*-1-benzazepin-2-ones as starting materials in previous attempts at the syntheses of 1*H*-1-benzazepines. One-step syntheses of (1; R^1 = H, R^2 = H, Me or MeO) may be effected by condensation of the appropriate aniline derivative with laevulinic acid or β-benzoylpropionic acid.[14] We expected that treatment of these compounds with phosphoryl chloride could yield chloro-1*H*-1-benzazepines (6; R^1 = H). This reaction did not result in the isolation of (6; R = H); instead condensation of two moles of (6; R^1 = H), or its 3*H*-isomer, gave complex rearrangement products.[15] A prerequisite for this rearrangement is a benzazepinone containing NH functionality. If, however, the nitrogen is blocked (e.g. with an NMe substituent) the required chloro product from the phosphoryl chloride reaction may be isolable. This paper describes the syntheses of appropriate 1-methyl-1*H*-1-benzazepin-2(3*H*)-ones and the course(s) of their subsequent reactions with phosphoryl chloride.

Results and Discussion

(a) The Syntheses of 1,5-Dimethyl-1H-1-benzazepin-2-ones

Treatment of laevulinic acid with *N*-methylaniline and *N*-methylaniline hydrochloride produced 1,5-dimethyl-1*H*-1-benzazepin-2(3*H*)-one (1; R^1 = Me, R^2 = H) in 5% yield, whose structure is confirmed by spectroscopic data (see Experimental section). A second product, 5-methyl-5-[4-(methylaminophenyl)]-1-phenylpyrrolidin-2-one (2) crystallized as its hydrochloride salt over a period of some weeks from the aqueous washings in an overall yield of 12%. The free base showed



Scheme 1

[14] Candeloro, V., and Bowie, J. H., *Aust. J. Chem.*, 1978, **31**, 2031.

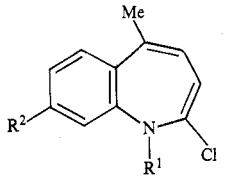
[15] Stringer, M. B., Candeloro, V., Bowie, J. H., Prager, R. H., Engelhardt, L. M., and White, A. H., *J. Chem. Soc., Perkin Trans. 1*, 1984, 2529.

an infrared carbonyl absorption at 1700 cm^{-1} (cyclic amide), and the presence of a quaternary carbon at δ 67·3 in the ^{13}C n.m.r. spectrum. The ^{1}H n.m.r. showed the presence of CMe, NMe, C_6H_5, *p*-disubstituted C_6H_4 and CH_2CH_2 units together with one exchangeable hydrogen. The mass spectrum showed the major decomposition channel $M^{+\bullet} \rightarrow (M^{+\bullet}-Me^{\bullet})^{+}$. Some of the data are consistent with the spectral data of (3), the major product formed from the reaction of laevulinic acid with aniline.[14] A plausible route (Scheme 1) to (2) is by way of nucleophilic attack of the *N*-methylaniline on the protonated anilide (4) to form (5), which then is demethylated[16] to form (2). The structure of (2) was confirmed by a single-crystal X-ray study, details of which are included in the Experimental section.

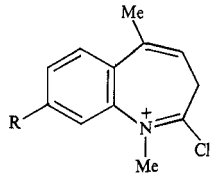
The formation of (1; R^1 = Me, R^2 = H) outlined above was achieved in only 5% yield. We found previously that *m*-methoxy or *m*-methylanilines effect the formation of benzazepinones in reasonable yield because of the activating properties of the electron-donating group at the cyclization site.[14] Similarly, 8-methoxy-1,5-dimethyl-1*H*-1-benzazepin-2-one (1; R^1 = Me, R^2 = OMe) and 1,5,8-trimethyl-1*H*-1-benzazepin-2-one (1; R^1 = Me, R^2 = Me) were prepared from *m*-methoxy-*N*-methylaniline and *m*-methyl-*N*-methylaniline in the respective yields 47 and 62%. In these cases no products analogous to (2) were isolated.

(b) Reactions of Benzazepinones with Phosphoryl Chloride

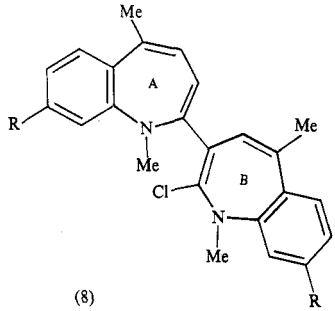
The reaction between (1; R^1 = Me, R^2 = H) and phosphoryl chloride (under nitrogen) was carried out under a variety of temperature conditions (−50 to 110°C) and reaction times (5 min to 20 h) by using various concentrations of phosphoryl chloride, neat or in dichloromethane. Only one isolable product, a bright yellow compound $C_{24}H_{23}ClN_2$, was obtained in optimal yield of 4% (1 h reflux in neat phosphoryl chloride). Considerable amounts of intractable polymer were also obtained. A corresponding yellow product, $C_{26}H_{27}ClN_2$, was obtained from (1; R^1 = R^2 = Me)



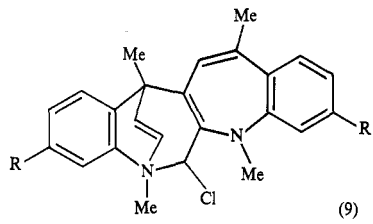
(6)



(7)



(8)



(9)

[16] Thermal dealkylations of quaternary ammonium salts are well known and are reviewed by Möller, F., in 'Methoden der Organischen Chemie (Houben–Weyl)' Vol 11/1, p. 961 (Georg Thieme: Stuttgart 1957).

in 40% yield, but only polymeric material was obtained from (1; R^1 = Me, R^2 = OMe). Both yellow products are unstable, and polymerize readily on standing.

When any one of the three compounds (1; R^1 = Me; R^2 = H, Me or OMe) is heated at reflux under nitrogen with phosphoryl chloride in pyridine, the reaction takes a quite different course. In each case, the respective 2-chloro-1,5-dimethyl-1*H*-1-benzazepine (6) is produced in quantitative yield as evidenced by the ^{1}H n.m.r. [in ($^2H_5$)pyridine] and mass spectra of the appropriate reaction mixture. The ^{1}H n.m.r. spectra are particularly diagnostic, and that of (6; R^1 = R^2 = Me) is shown in Fig. 1. Of particular note is the AB splitting pattern shown by the two 'olefinic' hydrogens of the azepine ring. Compounds (6) are stable under anhydrous conditions for 24 h if kept in pyridine at 0°. On further standing, polymerization occurs, and no 2-chloro-1,5-dimethyl-1*H*-benzazepine remains after one week. If water (or methanol) is added to the reaction mixture containing a 2-chloro-1,5-dimethyl-1*H*-benzazepine, the compound is immediately converted into the corresponding benzazepinone (1) in yields ranging from 41–98%. This reaction is so facile that exposure of the original reaction mixture [i.e. (6) dissolved in pyridine with some residual phosphoryl chloride] to the atmosphere results in total loss of the 2-chloro-1*H*-1-benzazepine, and formation of the benzazepinone (1) within a period of one hour. As a consequence of the reactivity of compounds (6), we were unable to isolate them in pure form by either crystallization or chromatographic separation. It appears that in the presence of acid 2-chloro-1,5-dimethyl-1*H*-1-benzazepines (6) react as enamines to form iminium salts (7), which then react readily with nucleophiles, namely with water at the α-position to form benzazepinones (1) or with a second molecule of (6) to initiate polymerization.*

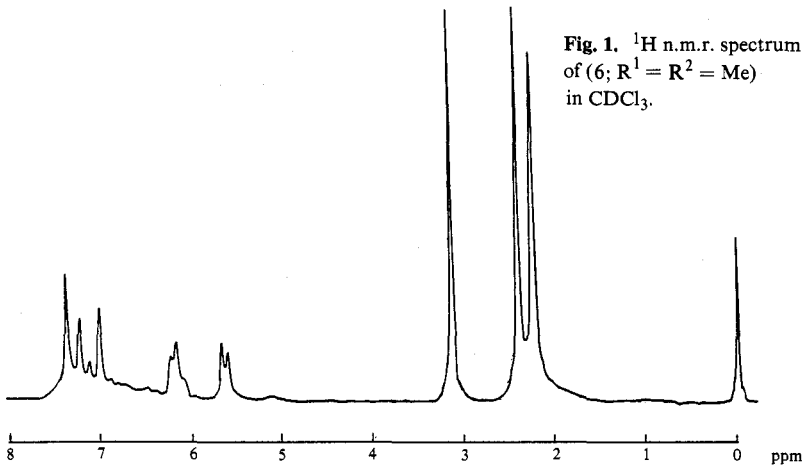


Fig. 1. ^{1}H n.m.r. spectrum of (6; R^1 = R^2 = Me) in $CDCl_3$.

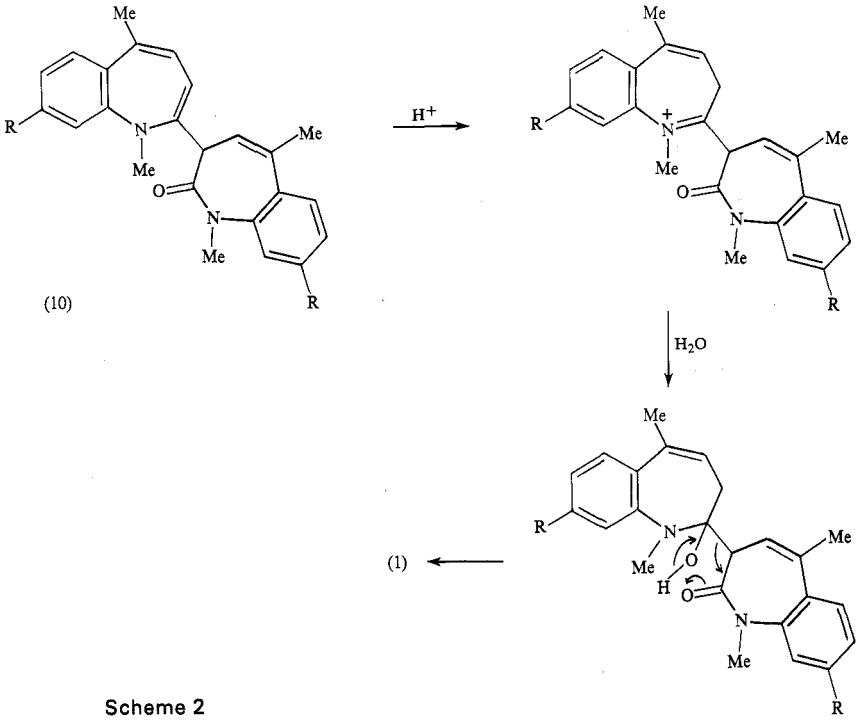
Two structural types suggest themselves for the yellow dimers produced by reaction of (1; R^1 = Me, R^2 = H and Me) with neat phosphoryl chloride. The first, represented by (8), may be formed by reaction of (6) with the iminium salt (7): this formulation is in accord with the described reactivity of (6). The second possibility involves a Diels–Alder reaction between two molecules of (6) followed by

* 1-Benzazepines, in the presence of hydrochloric acid, react readily at C 2 with methanol, indole or 1-methylindole.[8] The reaction observed with (6) is thus autocatalytic.

elimination of hydrogen chloride.* The addition may occur in two ways; one product, (9), is shown. The yellow dimers, while not being quite as reactive as compounds (6), polymerize on standing under anhydrous conditions and cannot be obtained in crystalline form. However, unlike compounds (6), they may be separated by flash chromatography on silica. The ^{13}C n.m.r. spectra of the two compounds do not contain resonances corresponding to quaternary carbons in the δ 30–50 region and thus formulation (9) is incorrect.

The spectroscopic data are in accord with structures (8; R = H and Me). In particular, the ^{1}H n.m.r. spectra show three olefinic hydrogens and the ^{13}C spectra [apart from CMe and NMe] only olefinic and aromatic carbons. The mass spectra exhibit peaks corresponding to $M^{+\bullet}$, $(M-Cl^{\bullet})^{+}$ and $[M-(HCl+Me^{\bullet})]$. We wished to obtain stable crystalline derivatives of the yellow dimers in order that an X-ray study could confirm their structures, but were unsuccessful in this venture. Catalytic reduction of (8; R = H) led to a plethora of unidentified products, while attempted reaction with $Fe_2(CO)_9$ [to form the $Fe(CO)_3$ complex] was not successful.

Since compounds (6) may be converted into stable benzazepinones (1) by reaction with water, reaction of (8) with water should yield (10), a structure which we



Scheme 2

* Although benzazepines, like 1-benzothiepin[17] and 1-benzoxepin,[18] undergo mainly valence tautomerism to naphthalene derivatives,[13] they, like the azepines,[19] do undergo Diels–Alder reactions with dimethyl acetylenedicarboxylate,[8] tetracyanoethylene and *N*-phenylmaleimide.

[17] Murata, I., Tatsuoka, T., and Sugihara, Y., *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 142.
[18] Igeta, H., Arai, H., Hasegawa, H., and Tsuchiya, T., *Chem. Pharm. Bull.*, 1975, **23**, 2791.
[19] Kende, A. S., Izzo, P. T., and Lancaster, J. E., *J. Am. Chem. Soc.*, 1965, **87**, 5044.

expected to be more stable than (8). The dimer (8; R = H) when allowed to stand in pyridine/water gave a low R_F product (on a silica t.l.c. plate) which could not be isolated but on attempted crystallization gave 1,5-dimethyl-1*H*-1-benzazepin-2-one (1; R^1 = Me, R^2 = H) in 70% yield overall. The other dimer (8; R = Me) gave, under the same conditions, a 78% yield of an unstable yellow brown oil, shown by mass measurement to be $C_{26}H_{28}N_2O$. It is suggested this product is (10; R = Me). This compound could not be crystallized and reacts instantaneously with water to yield two moles of benzazepinone (1; R^1 = R^2 = Me). The compound is even more prone to attack by water than its precursor (8; R = Me), as ^{1}H n.m.r. analysis (in $CDCl_3$ exposed to the atmosphere) showed quantitative conversion into the benzazepinone (1; R^1 = R^2 = Me) within 15 min. A suggested pathway for this reaction is shown in Scheme 2.

In conclusion, 2-chloro-1,5-dimethyl-1*H*-1-benzazepines may be produced in quantitative yield by reaction of the appropriate 1,5-dimethyl-1*H*-1-benzazepin-2-one with phosphoryl chloride in pyridine. These compounds are readily protonated (at C 3) to form iminium salts which undergo facile nucleophilic substitution at C 2. In contrast, reaction of 1,5-dimethyl-1*H*-1-benzazepin-2-ones with neat phosphoryl chloride gives yellow dimers, assigned as 2′-chloro-1,1′,5,5′-tetramethyl-2,3′-bi-1*H*-1-benzazepines, compounds only marginally less prone to nucleophilic substitution than the 2-chloro-1,5-dimethyl-1*H*-1-benzazepines themselves.

Experimental

Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Ultraviolet (in chloroform) and infrared spectra were recorded respectively on Pye Unicam SP 8-100 and Jasco A-102 spectrometers. ^{1}H n.m.r. were recorded at 60 MHz on a Jeol JMN-PMX 60 instrument (unless specifically indicated to the contrary); ^{13}C spectra with a Bruker WP 80 spectrometer. N.m.r. spectra were measured in anhydrous $CDCl_3$ under nitrogen, unless indicated to the contrary. Mass spectra were determined at 70 eV, by direct insertion, with an AEI MS 3074 instrument. Microanalyses were performed by the Australian Microanalytical Service, Melbourne, or by the Canadian Microanalytical Service, Vancouver. Light petroleum refers to the fraction b.p. 50–60°. *m*-Methoxy-*N*-methylaniline and *m*-methyl-*N*-methylaniline were prepared by the method of Crochet and Blanton.[20] Flash chromatography was performed by the method of Still, Kahn and Mitra,[21] silica gel 60 (230–400 mesh) being used.

The 1*H*-1-Benzazepin-2(3*H*)-ones

1,5-Dimethyl-1H-1-benzazepin-2(3H)-one (1; R^1 = Me, R^2 = H)

A mixture of laevulinic acid (10 g), *N*-methylaniline (50 ml) and *N*-methylaniline hydrochloride (20 g) was heated under reflux, in a nitrogen atmosphere, for 16 h. The excess of *N*-methylaniline was removed under reduced pressure, the residue acidified with 2 M hydrochloric acid (120 ml) and extracted with ether (3×60 ml). The organic extract was washed with 2 M hydrochloric acid (2×60 ml), water (60 ml), aqueous sodium carbonate (10%, 60 ml), water (60 ml), and saturated aqueous sodium chloride (60 ml), dried (K_2CO_3), and the solvent evaporated to give a yellow solid (1·42 g) which was crystallized from ether/light petroleum to yield *1,5-dimethyl-1H-1-benzazepin-2(3H)-one* (0·85 g, 5%) as colourless needles, m.p. 83–84° (Found: C, 76·9; H, 7·1. $C_{12}H_{13}NO$ requires C, 77·0; H, 7·5%). ν_{max} (CCl_4) 1675 cm^{-1}. ^{1}H n.m.r. δ: 7·48–7·07, 4H, m, aromatic H; 5·88, 1H, bt, *J* 7 Hz, H 4; 3·33, s, NMe; 3·03–2·85 2H, m, CH_2; 2·17, s, vinyl Me. Mass spectrum, *m/z* 187 ($M^{+\bullet}$, 41%), 172 ($M-CH_3^\bullet$, 18), 158 ($M-CHO^\bullet$, 59), 145 ($M-CH_2CO$, 100), 144 ($M-CH_3CO^\bullet$, 73). The aqueous extract was allowed to stand at 20° for 2 weeks, during which time a colourless hydrochloride salt

[20] Crochet, R. A., and Blanton, C. D., *Synthesis*, 1974, 55.
[21] Still, W. C., Kahn, M., and Mitra, A., *J. Org. Chem.*, 1978, **43**, 2923.

(3·26 g) precipitated. The solid was collected, dissolved in water (25 ml), neutralized with sodium carbonate, and extracted into diethyl ether (3×10 ml). Removal of the solvent gave *5-methyl-5-[4-(methylaminophenyl]-1-phenylpyrrolidin-2-one* (2) as a colourless solid (3·05 g) which crystallized from diethyl ether as colourless needles, m.p. 131–132° (Found: C, 77·1; H, 7·2. $C_{18}H_{20}N_2O$ requires C, 77·1; H, 7·2%). ν_{max} (CCl_4) 1700 cm^{-1}. ^1H n.m.r. (Bruker 300 MHz) δ: 7·23–7·04, 7H, m, aromatic H; 6·56, 2H, d, *J* 8·0 Hz, aromatic H; 3·94, broad s, NH; 2·77, s, MeN; 3·76–2·50, m, CH_2; 2·25–2·19, m, CH_2; 1·62, s, Me. ^{13}C n.m.r. δ ($CDCl_3$): 175·2 (C=O), 148·8 (C), 137·4 (C), 133·2 (C), 128·6 (CH), 126·7 (CH), 126·4 (CH), 112·4 (CH), 67·3 (C), 38·2 (CH_2), 30·6 (CH_3), 30·4 (CH_2) and 26·0 (CH_3). Mass spectrum, *m/z* 280 ($M^{+\bullet}$, 34%), 265($M-CH_3^\bullet$, 100), 160($M-C_7H_6NO^\bullet$, 37).

1,5,8-Trimethyl-1H-1-benzazepin-2(3H)-one (1; R^1 = R^2 = Me)

A mixture of laevulinic acid (10 g), *m*-methyl-*N*-methylaniline (50 ml) and *m*-methyl-*N*-methylaniline hydrochloride (20 g) was heated under reflux, in a nitrogen atmosphere, for 48 h. The excess aniline was removed under reduced pressure, and the residue worked up as with (1; R^1 = Me, R^2 = H), above. The crude product was crystallized from dichloromethane/light petroleum to yield *1,5,8-trimethyl-1H-1-benzazepin-2(3H)-one* (10·74 g, 62%) as colourless needles, m.p. 88·5–89·5° (Found: C, 77·4; H, 7·5. $C_{13}H_{15}NO$ requires C, 77·6; H, 7·5%). ν_{max} (CCl_4) 1660 cm^{-1}. ^1H n.m.r. δ: 7·0–7·4, 3H, m, H6, H7, H9; 5·7, 1H, bt, *J* 7 Hz, H4; 3·4, s, NMe; 2·5–2·9, m, CH_2; 2·4, s, ArMe; 2·2, s, vinyl Me. Mass spectrum, *m/z* 201 ($M^{+\bullet}$, 100%), 186 ($M-Me^\bullet$, 36), 172 ($M-CHO^\bullet$, 79), 159 ($M-CH_2CO$, 68), 158 ($M-CH_3CO^\bullet$, 73).

8-Methoxy-1,5-dimethyl-1H-1-benzazepin-2(3H)-one) (1; R^1 = Me, R^2 = OMe)

A mixture of laevulinic acid (10 g), *m*-methoxy-*N*-methylaniline (50 ml) and *m*-methoxy-*N*-methylaniline hydrochloride (20 g) was heated under reflux, in a nitrogen atmosphere, for 48 h. The reaction mixture was worked up as described for (1; R^1 = Me, R^2 = H). The resulting yellow oil (10·2 g) was crystallized from ether/light petroleum to yield *8-methoxy-1,5-dimethyl-1H-1-benzazepin-2(3H)-one* (8·70 g, 47%) as colourless needles, m.p. 76–77° (Found: C, 71·8; H, 6·9. $C_{13}H_{15}NO_2$ requires C, 71·9; H, 7·0%). ν_{max} (CCl_4) 1675 cm^{-1}. ^1H n.m.r. δ: 7·5–6·6, 3H, m, ArH; 5·75, 1H, bt, *J* 7 Hz, H4; 3·92, s, OMe; 3·35, s, NMe; 3·05–2·75, m, CH_2; 2·19, s, CMe. Mass spectrum, *m/z* 217 ($M^{+\bullet}$, 50%), 202 ($M-CH_3^\bullet$, 35), 188 ($M-CHO^\bullet$, 100), 175 ($M-CH_2CO$, 57), 174 ($M-CH_3CO^\bullet$, 61).

Reactions with Phosphoryl Chloride/Pyridine

2-Chloro-1,5-dimethyl-1H-1-benzazepine (6; R^1 = Me, R^2 = H)

A solution of 1,5-dimethyl-1,3-dihydro-2*H*-1-benzazepin-2-one (187 mg, 1·0 mmol) in phosphoryl chloride (3 ml) and pyridine (3 ml) was heated under reflux, in a nitrogen atmosphere, for 1 h. The reaction mixture was filtered under nitrogen, and the filtrate evaporated under vacuum to give *2-chloro-1,5-dimethyl-1H-1-benzazepine* as an unstable red oil (201 mg, 98%) (Found $M^{+\bullet}$ 205·0658. $C_{12}H_{12}{}^{35}ClN$ requires $M^{+\bullet}$ 205·0659). ^1H n.m.r. δ: 7·5–6·5, 4H, m, ArH; 5·9–5·6, 1H, m, H4; 5·3–5·2, 1H, bd, *J* 6 Hz; 2·9, s, NMe; 2·2, bs, vinyl Me.

2-Chloro-1,5,8-trimethyl-1H-1-benzazepine (6; R^1 = R^2 = Me)

A solution of 1,5,8-trimethyl-1*H*-1-benzazepin-2-one (201 mg, 1·0 mmol) in phosphoryl chloride (3 ml) and pyridine (3 ml) was heated under reflux, in a nitrogen atmosphere, for 1 h. The reaction mixture was filtered under nitrogen, and the filtrate evaporated under vacuum to give *2-chloro-1,5,8-trimethyl-1H-1-benzazepine* as an unstable red oil (210 mg, 96%) (Found $M^{+\bullet}$ 219·0816. $C_{13}H_{14}{}^{35}ClN$ requires $M^{+\bullet}$ 219·0815). ^1H n.m.r. δ: 7·1–6·7 3H, m, ArH; 6·0–5·4, 2H, AB quartet, *J* 5 Hz; 3·0, s, NMe; 2·3, s, ArMe; 1·8, bs, vinyl Me). ^{13}C n.m.r. δ: 20·36 (Me); 23·09 (Me); 36·82 (NMe); 113·58 (C3); 117·65 (C5); 120·02 (C4); 125·06 (C7); 125·36 (C9); 126·24 (C6); 127·36 (C8); 127·61 (C5a); 141·52 (C9a); 146·58 (C2).

2-Chloro-8-methoxy-1,5-dimethyl-1H-1-benzazepine (6; R^1 = Me, R^2 = OMe)

A solution of 8-methoxy-1,5-dimethyl-1*H*-1-benzazepin-2(3*H*)-one (217 mg, 1 mmol) in phosphoryl chloride (3 ml) and pyridine (3 ml) was heated under reflux, in a nitrogen atmosphere,

for 1 h. The reaction mixture was filtered under nitrogen, and the filtrate evaporated under vacuum to give *2-chloro-8-methoxy-1,5-dimethyl-1H-1-benzazepine* as an unstable red oil (227 mg, 97%) (Found: $M^{+\bullet}$ 235·0764. $C_{13}H_{14}{}^{35}ClNO$ requires $M^{+\bullet}$ 235·0764). ^1H n.m.r. δ: 7·2–7·0, d, *J* 10 Hz, H 6; 6·6–6·4, m, H 7, H 9; 5·8–5·7, m, H 4; 5·4–5·3, bd, *J* 6 Hz, H 3; 3·7, s, OMe; 3·0, s, NMe; 2·1, bs, vinyl Me.

Reactions with Neat Phosphoryl Chloride

2′-Chloro-1,1′,5,5′-tetramethyl-2,3′-bi-1H-benzazepine (8; R = H)

A solution of 1,5-dimethyl-1*H*-1-benzazepin-2(3H)-one (500 mg, 2·67 mmol) in phosphoryl chloride (5 ml) was heated under reflux, in a nitrogen atmosphere, for 1 h. The reaction mixture was cooled to 0°, poured into saturated aqueous sodium carbonate (100 ml), and extracted with dichloromethane (3×30 ml). The organic extract was washed with aqueous 10% sodium carbonate (30 ml), water (30 ml), and saturated aqueous sodium chloride (30 ml), dried (K_2CO_3), and the solvent evaporated to give a dark brown foam (549 mg). This foam was subjected to flash chromatography on silica gel (70 g) with ether/light petroleum (1 : 9) as eluent. The higher R_F fluorescent fraction gave *2′-chloro-1,1′,5,5′-tetramethyl-2,3′-bi-1H-benzazepine* (8; R = H) as a yellow oil (38 mg, 4%) (Found $M^{+\bullet}$, 374·1555. $C_{24}H_{23}{}^{35}ClN_2$ requires $M^{+\bullet}$ 374·1550); ^1H n.m.r. δ: 7·5–6·5, 8H, m, ArH; 6·1–5·8, bd, *J* 8 Hz, H 3; 5·2–5·1, m, H 4, H 4′; 3·0, s, NMe; 2·6, s, NMe; 2·2, 6H, bs, vinyl Me. Mass spectrum, *m/z* 376, 374 ($M^{+\bullet}$, 33 and 100%), 339 ($M-Cl^{\bullet}$, 94), 323 ($M-HCl-Me^{\bullet}$, 55).

2′-Chloro-1,1′,5,5′,8,8′-hexamethyl-2,3′-bi-1H-1-benzazepine (8; R = Me)

A solution of 1,5,8-trimethyl-1*H*-1-benzazepin-2(3*H*)-one (201 mg, 1·0 mmol) in phosphoryl chloride (5 ml) was heated under reflux, in a nitrogen atmosphere, for 1 h. The reaction mixture was cooled to 0°, poured into saturated aqueous sodium carbonate (100 ml), and worked up as above to give a dark brown foam (340 mg). This foam was subjected to flash chromatography on silica gel (70 g) with ether/light petroleum (3 : 7) as eluent. The higher F_F fluorescent fraction gave *2′-chloro-1,1′,5,5′,8,8′-hexamethyl-2,3′-bi-1H-1-benzazepine* as a yellow oil (160 mg, 40%) (Found: $M^{+\bullet}$ 402·1864. $C_{26}H_{27}{}^{35}ClN_2$ requires $M^{+\bullet}$ 402·1863). ^1H n.m.r. δ: 7·6–6·5, 6H, m, ArH; 6·2–5·8, 2H, m, H 4, H 4′; 5·3, d, *J* 5 Hz; 3·6, s, NMe; 3·1, s, NMe; 2·7, s, Me; 2·3, s, Me; 2·2, s, Me; 2·1, s, Me. Compound (8; R = Me) was insufficiently stable to allow the measurement of a satisfactory ^{13}C n.m.r. spectrum, but that obtained was totally consistent with the assigned structure. Mass spectrum, *m/z* 404, 402 ($M^{+\bullet}$, 28 and 84%), 367 ($M-Cl^{\bullet}$, 100), 351 ($M-HCl-CH_3{}^{\bullet}$, 56).

Reaction of 8-Methoxy-1,5-dimethyl-1H-1-benzazepin-2(3H)-one with Phosphoryl Chloride

A solution of 8-methoxy-1,5-dimethyl-1*H*-1-benzazepin-2(3*H*)-one (217 mg, 1 mmol) in phosphoryl chloride (3 ml) was heated under reflux, in a nitrogen atmosphere, for 1 h. The reaction mixture was cooled to 0°, poured into aqueous saturated sodium carbonate (80 ml), and extracted with dichloromethane (4×15 ml). The organic extract was washed with 10% aqueous sodium carbonate (15 ml), water (15 ml) and saturated aqueous sodium chloride (15 ml), dried (K_2CO_3), and the solvent evaporated to give a dark brown foam (241 mg). This foam was subjected to thick-layer chromatography on silica (35 g) with ether/light petroleum (4 : 1) as eluent. Gradient elution showed that only polymeric material was present.

Reactions with Water

Reactions of 2-Chloro-1,5-dimethyl-1H-1-benzazepines with Water

Each of the three compounds was allowed to react in the following manner. Isolated yields from (6; R^1 = Me; R^2 = H, Me and MeO), respectively, were 41, 98 and 70%.

A solution of 1,5,8-trimethyl-1*H*-1-benzazepin-2(3*H*)-one (201 mg, 1·0 mmol) in phosphoryl chloride (3 ml) and pyridine (3 ml) was stirred at 20° for 1 h. A ^1H n.m.r. spectrum showed quantitative conversion into 2-chloro-1,5,8-trimethyl-1*H*-1-benzazepine. Water (5 ml) was then added and the reaction mixture stirred at 20° for a further 10 min. The reaction mixture was extracted with dichloromethane (3×10 ml), the organic extract separated and washed with water (3×10 ml), dried (Na_2SO_4), and evaporated to give a yellow oil (195 mg) which crystallized on standing. The solid was recrystallized from ether/light petroleum to give 1,5,8-trimethyl-1*H*-1-benzazepin-2(3*H*)-one (182 mg, 98%), m.p. 88–89°.

Reaction of 2′-Chloro-1,1′,5,5′,8,8′-hexamethyl-2,3′-bi-1H-1-benzazepine with Water

A mixture of 2′-chloro-1,1′,5,5′,8,8′-hexamethyl-2,3′-bi-1*H*-1-benzazepine (8; R = Me) (432 mg, 1·1 mmol), pyridine (5 ml) and water (5 ml) was stirred at 20° for 2 h. The reaction mixture was extracted with dichloromethane (3×10 ml). The extract was dried (Na_2SO_4), and evaporated to give *1,5,8-trimethyl-3-(1,5,8-trimethyl-1H-1-benzazepin-2-yl)-1-benzazepin-2(3H)-one* (10; R = Me) (320 mg, 78%) as an unstable yellow-brown oil (Found $M^{+\bullet}$, 384·2198. $C_{26}H_{28}N_2O$ requires $M^{+\bullet}$ 384·2202). ^{1}H n.m.r. δ: 7·3–6·2, 6H, m, ArH; 6·0–5·7, 2H, m, H4, H4′; 5·1, bd, *J* 5 Hz, H3; 3·5, s, NMe; 3·0, s, NMe; 2·4, s, Me; 2·2, s, Me; 2·1, s, Me; 2·05, s, Me. Mass spectrum, *m/z* 384 ($M^{+\bullet}$, 100%), 368 (M − 16, 28) and 327 (M − MeNCO, 28).

Treatment of (10; R = Me) (320 mg, 0·83 mmol) with pyridine/water (as above) gave 1,5,8-trimethyl-1*H*-1-benzazepin-2(3*H*)-one (1; R^1 = R^2 = Me) (323 mg, 97%) which crystallized from diethyl ether as colourless needles, m.p. 88·5–89·5°.

Reaction of 2′-Chloro-1,1′,5,5′-tetramethyl-2,3′-bi-1H-1-benzazepine with Water

Treatment of 2′-chloro-1,1′5,5′-tetramethyl-2,3′-bi-1*H*-1-benzazepine (8; R = H) (83 mg, 0·2 mmol) with pyridine/water as outlined above gave a product (R_F 0·26 in ethyl acetate on Merck Kieselgel 60 F254) which could not be purified, but which from diethyl ether deposited 1,5-dimethyl-1*H*-1-benzazepin-2(3*H*)-one as colourless crystals, m.p. 83–84° (52 mg, 70%) (R_F 0·57 in ethyl acetate on Merck Kieselgel 60 F254).

Crystallography of (2)

Crystal data.—$C_{18}H_{20}N_2O$, *M* 280·4. Triclinic, space group $P\bar{1}$ (C_i^1, No. 2), *a* 12·005(4), *b* 10·248(4), *c* 6·533(3) Å, α 100·09(3), β 91·98(3), γ 95·07(3)°, *U* 787·2(5) Å^3. D_m 1·18(1), D_c (*Z* = 2) 1·18 g cm^{-3}. *F*(000) 300. Monochromatic Mo Kα radiation, λ 0·7106$_9$ Å, μ 0·80 cm^{-1}. Specimen: 0·40 by 0·30 by 0·25 mm (no absorption correction). *T* 295 K.

Structure determination.—1730 unique reflections were measured with the limit $2\theta_{max}$ 45° by using a Syntex $P2_1$ four-circle diffractometer in conventional $2\theta/\theta$ scan mode; 1436 with $I > 3\sigma(I)$ were used in the full-matrix least-squares refinement after solution of the structure by direct methods. Anisotropic thermal parameters were refined for the non-hydrogen atoms and (x, y, z, U_{iso}) for all hydrogen atoms. Residuals at convergence *R*, *R′* were 0·033, 0·040, reflection weights being $[\sigma^2(F)]^{-1}$. Neutral complex scattering factors were used;[22] computation used the XTAL 83 program system[23] implemented by S. R. Hall on a Perkin–Elmer 3240 computer. Results are shown in Fig. 2 and Tables 1–3; non-hydrogen atom numbering is given in the Figure. Material deposited comprises structure factor amplitudes, thermal and hydrogen atom parameters, and phenyl ring geometries.*

Structural Commentary

Stoichiometry and connectivity for (11) as proposed above are consistent with the results of the single-crystal X-ray structure determination. In regard to the five-membered ring, a good least-squares plane (χ^2, 6·9) is defined by C(11), N(1), C(4,5) O(5) (atom deviations, δ, −0·01, 0·00, 0·00, −0·01, 0·00 Å), with C(2,3) (δ, 0·12, −0·36 Å) disposed to either side. δC(21,27) are 1·58, −0·81 Å, with a dihedral angle for phenyl ring 1 of 46·4°, O(5)···H(12) being 2·56(2) Å. N(1) and C(5) are closely planar, with substituent angle sums of 359·9 and 360·0° respectively,

* Copies are available on application to the Editor-in-Chief, Editorial and Publications Service, CSIRO, 314 Albert Street, East Melbourne, Vic. 3002.

[22] Ibers, J. A., and Hamilton, W. C., (Eds) 'International Tables for X-Ray Crystallography' Vol. 4 (Kynoch Press: Birmingham 1974).

[23] Stewart, J. M., and Hall, S. R., (Eds) 'The XTAL System of Crystallographic Programs: User's Manual' Technical Report TR-901, Computer Science Center, University of Maryland, U.S.A. 1983.

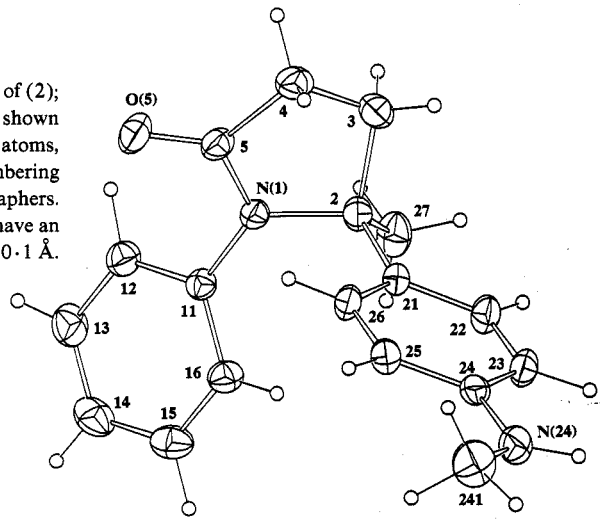


Fig. 2. A single molecule of (2); 20% thermal ellipsoids are shown for the non-hydrogen atoms, together with the atom numbering used by the crystallographers. Hydrogen atoms have an arbitrary radius of 0·1 Å.

Table 1. Non-hydrogen atom coordinates

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
N(1)	0·7517(1)	0·2331(1)	0·0676(2)	C(24)	0·6873(2)	0·7228(2)	0·3026(3)
C(11)	0·8547(2)	0·2171(2)	0·1693(3)	N(24)	0·6716(2)	0·8473(2)	0·4123(3)
C(12)	0·8855(2)	0·0905(2)	0·1699(4)	C(241)	0·6182(4)	0·8674(3)	0·6027(5)
C(13)	0·9848(2)	0·0723(3)	0·2703(4)	C(25)	0·6641(2)	0·6070(2)	0·3813(3)
C(14)	1·0537(3)	0·1806(3)	0·3687(4)	C(26)	0·6829(2)	0·4850(2)	0·2661(3)
C(15)	1·0250(2)	0·3057(3)	0·3646(4)	C(27)	0·8339(3)	0·3402(3)	−0·2102(4)
C(16)	0·9261(2)	0·3247(2)	0·2666(3)	C(3)	0·6262(2)	0·2802(2)	−0·1849(4)
C(2)	0·7386(2)	0·3366(2)	−0·0638(3)	C(4)	0·5631(2)	0·2043(3)	−0·0411(4)
C(21)	0·7251(2)	0·4716(2)	0·0706(3)	C(5)	0·6533(2)	0·1616(2)	0·0903(3)
C(22)	0·7482(2)	0·5893(2)	−0·0050(3)	O(5)	0·6412(1)	0·0779(1)	0·2028(3)
C(23)	0·7307(2)	0·7105(2)	0·1070(3)				

Table 2. Non-hydrogen molecular core distances (Å)

Atoms	Distance	Atoms	Distance
N(1)–C(11)	1·419(3)	C(2)–C(3)	1·552(3)
N(1)–C(2)	1·492(3)	C(3)–C(4)	1·504(4)
N(1)–C(5)	1·361(3)	C(4)–C(5)	1·501(4)
C(2)–C(21)	1·528(2)	C(5)–O(5)	1·226(3)
C(2)–C(27)	1·518(4)		

Table 3. Non-hydrogen molecular core angles (degrees)

Atoms	Angle	Atoms	Angle
C(11)–N(1)–C(2)	123·4(2)	C(21)–C(2)–C(3)	109·8(2)
C(11)–N(1)–C(5)	123·6(2)	C(27)–C(2)–C(3)	111·2(2)
C(2)–N(1)–C(5)	112·9(2)	C(2)–C(3)–C(4)	105·1(2)
N(1)–C(2)–C(21)	111·0(1)	C(3)–C(4)–C(5)	104·0(2)
N(1)–C(2)–C(27)	110·3(2)	N(1)–C(5)–C(4)	108·7(2)
N(1)–C(2)–C(3)	100·3(2)	N(1)–C(5)–O(5)	125·1(2)
C(21)–C(2)–C(27)	113·6(2)	C(4)–C(5)–O(5)	126·2(2)

with associated distances in the C(11)–N(1)–C(5)–O(5) string symptomatic of amide conjugation. The NMe substituent in phenyl ring 2 is closely coplanar, δN(24), C(241) from the C_6 ring plane (χ^2 7·5) being 0·02, −0·12 Å. N(24)–C(24,241) are 1·382(3), 1·411(4) Å, with C(24)–N(24)–C(241) 123·3(2), and N(24)–C(24)–C(23,25) 119·9(2), 122·8(2)°.

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