Azepinones. Part 3.[1,2] Reactions of Simple 1*H*-Azepin-3(2*H*)-ones with Electrophiles

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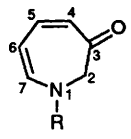
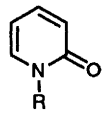
The dienaminone conjugated system of 1*H*-azepin-3(2*H*)-ones (**1**) and (**2**) is active towards electrophiles at either oxygen or carbon centres. Analysis of ^{1}H and ^{13}C NMR spectra shows that *O*-protonation (trifluoroacetic acid) and *O*-alkylation (triethyloxonium tetrafluoroborate) take place. Sequential deuterium exchange at the 4-, 6- and 2-positions of (**1**) occurs *via* the free base. Treatment of (**1**) or (**2**) with *N*-halogenosuccinimides gives 4-halogeno and 4,6-dihalogeno products. The X-ray crystal structure of the 4-chloro derivative (**11**) shows that the halogen substituent has little effect on the geometry of the ring.

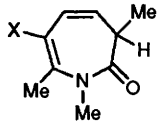
The 1*H*-azepin-3(2*H*)-one system *e.g.* (**1**)[3] contains a planar[4] electron-rich dienaminone system, which is potentially active towards electrophiles at carbon and oxygen centres (Fig. 1). The



(**1**) R = Me
(**2**) R = Ph



(**3**)



(**4**) X = H
(**5**) X = Cl

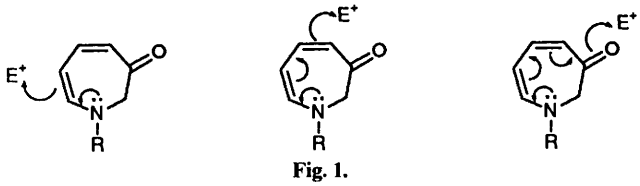
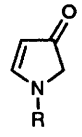


Fig. 1.

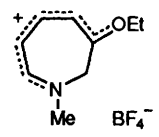
former reactions are well known for the related pyridin-2-ones (**3**),[5,6] which give 3- and/or 5-substituted products by nitration,[7] diazo-coupling,[8] halogenation[9] or deuteriation under acid conditions.[10] Similarly, the 1*H*-azepin-2(3*H*)-one (**4**) gives the 6-chloro compound (**5**) on treatment with *N*-chlorosuccinimide.[9] Our recent studies of the 1*H*-pyrrol-3(2*H*)-one system (**6**) have included *O*-protonation and alkylation,[11] and electrophilic substitution;[12] in this paper we report the behaviour of their vinylogues: azepinones *viz.* (**1**) and (**2**) under corresponding conditions.

The 1-methylazepinone (**1**) is smoothly protonated in trifluoroacetic acid to give a solution which is stable at room temperature for several weeks. Because of the unexpected[11] spectroscopic changes which accompany protonation (see below), an authentic *O*-substituted azepinium derivative was synthesised by treatment of a methylene dichloride solution of compound (**1**) with triethyloxonium tetrafluoroborate. When this reaction was carried out in the presence of anhydrous potassium carbonate, the salt (**7**) was obtained as an uncontaminated oil which nevertheless could not be crystallised. It showed closely similar NMR spectra to those of the azepinone (**1**) in acid solution, which we therefore conclude has undergone *O*-protonation to give compound (**8**).

Assignment of the ^{1}H NMR spectra of the salts (**7**) and (**8**) (Table 1) is possible by inspection. The electron-rich sites (4-H and 6-H) occur in relatively shielded positions as a doublet and



(**6**)



(**7**)

doublet of doublets, respectively, whereas the electron-deficient sites (C-7 and C-5) occur as a deshielded doublet and doublet of doublets, respectively (*cf.* ref. 1). Unambiguous identification of the ^{13}C NMR peaks of the protonated azepinone (**8**) (Table 2) was made by specific decoupling of each of the above proton signals; assignment of the corresponding spectrum of (**7**) clearly follows by analogy.

The major effects of protonation on the NMR spectra of model enaminones[13]—which are also found in the 1*H*-pyrrol-3(2*H*)-one system[11]—include: (*a*), equalisation of vicinal coupling constants ($^3J_{HH}$) across the conjugated system due to bond order effects; (*b*), increase in the magnitude of $^1J_{CH}$ associated with the positive charge;[13] (*c*), a similarly induced high frequency shift of all signals in the ^{1}H NMR spectrum and of the signal due to the carbon atom α to the nitrogen in the ^{13}C NMR spectra though the position of the β-carbon atom signal is relatively unaffected; and (*d*) a *low* frequency shift of the signal due to the carbonyl carbon atom, owing to reduction of the anisotropic effect of the carbonyl group. In general terms, effects (*b*)–(*d*) are also followed in the 1*H*-azepin-3(2*H*)-one series (Tables 1 and 2) though the deshielding effect on the carbon α to the nitrogen (C-7) is also felt at the other electron deficient site (C-5), and the shielding of the carbonyl signal (C-3; 26.5 ppm shift) is massive by comparison with that of the enaminones[11,13] (*ca.* 10 ppm). However, the dramatic effects on $^3J_{HH}$ (Table 1) and the divergence of the ^{13}C NMR shifts of the electronically similar sites C-4 and C-6 (Table 2) are clearly abnormal. It is possible that these may be explained by varying contributions from the canonical forms (**8A–E**) (Fig. 2). In particular the large size of $^3J_{5,6}$ indicates a large bond order across these positions, as found in the resonance structures (**8D**) and (**8E**), and the observed trends in chemical shifts are consistent with this picture.

An indication of the relative reactivity of the electrophilic sites of the 1*H*-azepin-3(2*H*)-one system was obtained by the observation of the rate of deuterium incorporation in [^{2}H]trifluoroacetic acid solution. ^{1}H NMR spectroscopy showed immediate changes in the signal of the 5-position and less rapid change of the signal corresponding to the 7-position,

Table 1. ^{1}H NMR parameters of the cations (7) and (8).

Compound	Parameter	2-H	4-H	5-H	6-H	7-H	$^3J_{4,5}$	$^3J_{5,6}$	$^3J_{6,7}$
(8a)[a]	δ_H.J_{HH}	4.12	6.50	7.67	6.63	8.04	7.7	11.5	5.0
	Δ[c]	+0.55	+0.33	+0.83	+1.46	+1.32	−3.3	+2.4	−2.2
(7)[b]	δ_H.J_{HH}	4.17	6.38	7.70	6.69	8.41	7.7	11.3	4.7
	Δ[c]	+0.60	+0.21	+0.86	+1.52	+1.69	−3.3	+2.2	−2.5

[a] TFA solution. [b] [$^2H_6$]acetone. [c] δ or ^3J of cation minus δ or ^3J of free base.

Table 2. ^{13}C NMR parameters of the cations (7) and (8).

Compound	Parameter	C-2	C-3	C-4	C-5	C-6	C-7
(8)[a]	δ_C	56.47	153.70	109.07	151.21	115.67	159.63
	$\Delta\delta_C$[c]	−6.18	−26.51	−14.26	+9.20	+16.26	+12.44
	^1J	147.8	—	164.1	161.8	170.8	175.2
	Δ^1J[d]	+6.4	—	+4.5	+10.1	+9.1	+5.4
(7)[b]	δ_C	56.40	*b*	104.49	148.93	115.91	160.31
	$\Delta\delta_C$[c]	−6.25	*b*	−18.84	+6.92	+16.50	+13.12

[a] TFA solution. [b] [$^2H_6$]acetone, DEPT. [c] δ (7) or (8) − δ (1). [d] ^1J (8) − ^1J(1).

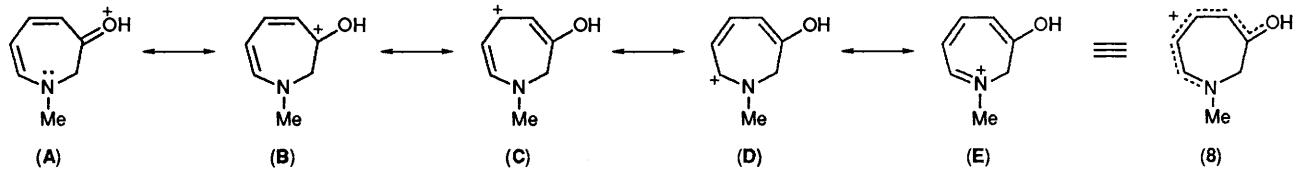
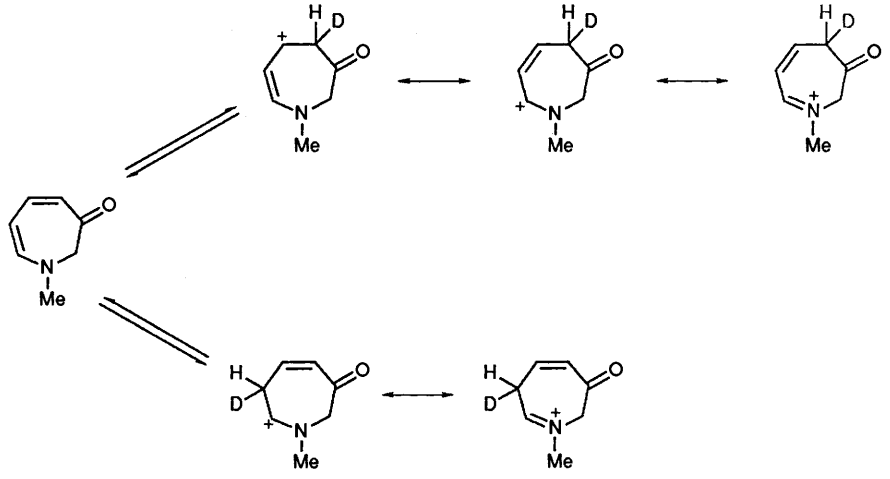


Fig. 2.



Scheme 1.

thus clearly indicating loss of coupling to the 4- and 6-positions. Since the signals for the 4- and 6-positions were superimposed it was difficult to monitor accurately the rate of deuterium incorporation at each site, but the change in the coupling pattern of the 5- and 7-signals over an hour showed clearly that exchange was considerably more rapid at the 4-position. By assuming exchange at this position was complete after 20 min, an approximate half-life for reaction at the 6-position was found and used as a correction factor in the calculation of the half-life for reaction at the 4-position. Exchange at the 2-position could be readily monitored and was found to be considerably slower than at either position on the conjugated system. The trend shown by the half-lives [4 (2.5 min) < 6 (15 min) < 2 (250 min)] is similar to that found in open-chain dienaminones[14] and pyridin-2-ones.[15]

Since the salt (7) shows no evidence of deuterium incorporation at either the 2-, 4- or 6-positions, even after a number of weeks in solution in [^{2}H]trifluoroacetic acid, it would appear that the exchange observed above must take place *via* the free base form of the azepinone. Although NMR studies suggest that the most electron-rich site is position 6,[1] the relative reactivity of positions 4 and 6 is readily explained in terms of the stability of the intermediate cations (Scheme 1). The absence of exchange at the 2-position of the salt (7) is understandable since 2-deprotonation would generate the counter-Hückel alkoxyazepine (**9**) (*cf.* ref. 16). The gradual exchange observed at this site of azepinone (**1**) must occur by some alternative mechanism.

In order to study the relative reactivity of positions 4 and 6 towards electrophiles under non-acidic conditions, a series of

Table 3. ^{1}H NMR parameters for halogenoazepin-3(2*H*)-ones (**10**)–(**13**).

Azepin-3-one	R	2-H	5-H	6-H	7-H	R	$^3J_{5,6}$	$^3J_{6,7}$
(**13**)	Me	3.71	7.12	—	7.72	3.19	—	—
(**12**)	Ph	4.29	7.46[a]	—	7.29[a]	7.1–7.4	—	—
(**11**)	Ph	4.27	7.10	5.51	*b*	7.1–7.4	7.5	9.8
(**10**)	Me	3.63	6.83	5.20	7.20	3.20	6.9	10.0

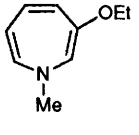
[a] Identified from aromatic signals by presence of long-range coupling $^4J_{5,7}$ and $^4J_{2,7}$ (both 0.9 Hz). [b] Superimposed on aromatic signals.

Table 4. ^{13}C NMR chemical shifts for chloroazepin-3(2*H*)-ones (**10**)–(**12**).

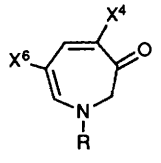
Azepin-3-one	C-2	C-3	C-4	C-5	C-6	C-7
(**12**)	58.55 (−0.13)[a]	175.44 (−0.6)	130.08 (+0.28)	139.54[b] (+0.66)	109.49 (+6.42)	139.08[b] (−2.82)
(**11**)	58.68 (−0.7)	176.06 (−6.81)	129.80 (+3.09)	138.88[b] (−1.39)	103.07 (−0.79)	141.90[b] (+0.46)
(**10**)	61.31 (−1.34)	173.42 (−6.79)	125.84 (+2.51)	140.62 (−1.39)	98.81 (−0.69)	147.22[c] (+0.63)

[a] Figures in brackets refer to shifts observed for unsubstituted azepinones for (**10**) and (**11**) and to shifts from monochloro compound in (**12**). [b] Assigned by consideration of the fully coupled spectra. [c] Tentatively assigned by comparison with *N*-phenyl example (**11**).

halogenation reactions was carried out. Numerous attempts to isolate the products of halogenation failed because of the sensitivity of these compounds; thus it was found that heating to above *ca.* 40 °C in order to remove solvent resulted in decomposition, as did distillation, and if the compounds were left on silica columns for any length of time the product appeared to react with the stationary phase. However, treatment of the 1-methyl- and 1-phenyl-azepinones (**1**) and (**2**) with one equivalent of *N*-chlorosuccinimide at 0 °C for 45 min, afforded the 4-chloro compounds (**10**) and (**11**) in 51 and 41% yields, respectively, after washing with sodium hydrogen



(**9**)



	R	X^4	X^6
(**10**)	Me	Cl	H
(**11**)	Ph	Cl	H
(**12**)	Ph	Cl	Cl
(**13**)	Me	Br	Br
(**14**)	Me	Br	H

carbonate solution and dry flash chromatography. The compounds could be purified by recrystallisation from methanol at −20 °C, and in the solid state they were stable for many months at room temperature. The site of reaction follows from the ^{1}H NMR spectra (which show 5-H and 7-H as doublets and 6-H as a doublet of doublets) and from the X-ray crystal structure of compound (**11**) (see below). When two equivalents of *N*-chlorosuccinimide were used (or if the monochloro derivative was treated with one equivalent of *N*-chlorosuccinimide) the 4,6-dichloro compound (**12**) (44%) could be isolated. In all cases, other significant components were present, but these could not be obtained cleanly owing to decomposition. As found for the deuterium exchange reactions, it is clear that position 4 remains the most reactive to electrophiles (*cf.* Scheme 1) and that a 4-chloro substituent does not significantly deter subsequent reaction at the 6-position.

Treatment of the 1-methylazepinone (**1**) with either one or two equivalents of *N*-bromosuccinimide resulted in the isolation only of the dibrominated species (**13**) in 8 and 60% yield, respectively. Two equivalents of the succinimide yielded the product as a crystalline compound without chromatography on one occasion, but this purity could not be attained reproducibly, and generally chromatography and recrystallisation from a methanol solution at −20 °C was necessary. The compound decomposed in chloroform solution over a period of hours to give a black, insoluble precipitate, and therefore a ^{13}C NMR spectrum was not obtained. The NMR spectrum of the crude mixture of products obtained by reaction with one equivalent of *N*-bromosuccinimide suggested that the major components were the unchanged azepinone (**1**) and the monobromo compound (**14**), together with some of the dibromo compound (**13**). However, only compound (**13**) (8%) could be isolated in pure form after chromatography; identification of compound (**14**) followed by comparison of the ^{1}H NMR spectrum of a (contaminated) minor component with that of the monochloro derivative (**10**) (see Experimental section).

The NMR parameters of the fully characterised halogenoazepinones (**10**)–(**13**) are given in Tables 3 and 4. In the ^{1}H NMR spectra (Table 3) the expected deshielding on substitution by halogen is particularly marked for the dihalogeno compounds (**12**) and (**13**) (*cf.* ref. 1). For the monosubstituted examples, the effect of the halogen is to reduce $^3J_{5,6}$ and increase $^3J_{6,7}$ (from *ca.* 9 to 7 and from 7.5 to 10 Hz, respectively) though the reason for this trend is unclear at this stage.

The C-5 and C-7 resonances in the ^{13}C NMR spectra have very similar chemical shifts, as is found in those azepinones with no halogen substituents.[1] However, it was noted earlier[1] that the C-7 resonance of 1*H*-azepin-3(2*H*)-ones gave rise to a doublet of complex signals due to long-range coupling whereas the C-5 resonance was a simple doublet of doublets, and since the same pattern was found in the chloro-substituted derivatives (**11**) and (**12**) (Table 4) these resonances could be unambiguously distinguished. In addition, the one-bond coupling for the signal of the carbon atom at the position next to nitrogen is expected to be larger and, in agreement with the assignment made above, $^1J_{C\text{-}7,7\text{-}H}$ is *ca.* 180 Hz while $^1J_{C\text{-}5,5\text{-}H}$ is *ca.* 160 Hz in both examples. The marked shielding of the carbonyl carbon atom on substitution of the adjacent atom (6.8 ppm) is similar to that observed in 1*H*-pyrrol-3(2*H*)-ones[12] and it seems probable that this is due to an electronic effect, as is observed across single bonds in a number of α-chloro ketones.[17] This is postulated as being a result of the electronegativity of the chlorine atom countering the effect of the carbonyl oxygen atom. The substituent effects in the remainder of the conjugated system might have been anticipated to be comparable with those observed in benzene and the conjugated systems of heteroaromatics, but with the exception of a consistent high frequency shift at the site of substitution no such trends are observed.

The X-ray crystal structure of the monochloro derivative (**11**) was obtained to confirm the above NMR interpretations and to find the effect of the substituent on the geometry of the ring. Bond lengths, angles and torsion angles are given in Tables 5–7 and fractional co-ordinates in Table 8; ORTEP diagrams are shown in Fig. 3, and selected data for compounds (**2**) and (**11**) are displayed in Fig. 4. The C–Cl bond length [1.743(3) Å] is

Table 5. Bond lengths with standard deviations.

Bond	Length (Å)	Bond	Length (Å)
N(1)–C(2)	1.452(4)	C(3)–C(4)	1.444(4)
N(1)–C(7)	1.356(4)	C(4)–Cl(4)	1.743(3)
N(1)–C(8)	1.415(3)	C(4)–C(5)	1.352(4)
C(2)–C(3)	1.518(4)	C(5)–C(6)	1.420(5)
C(3)–O(3)	1.222(4)	C(6)–C(7)	1.356(5)

Table 6. Angles with standard deviations.

Atoms	Angle (°)	Atoms	Angle (°)
C(2)–N(1)–C(7)	118.46(24)	C(3)–C(4)–C(5)	126.7(3)
C(2)–N(1)–C(8)	121.09(21)	Cl(4)–C(4)–C(5)	118.35(23)
C(7)–N(1)–C(8)	120.38(22)	C(4)–C(5)–C(6)	129.1(3)
N(1)–C(2)–C(3)	109.68(23)	C(5)–C(6)–C(7)	127.1(3)
C(2)–C(3)–O(3)	120.9(3)	N(1)–C(7)–C(6)	124.5(3)
C(2)–C(3)–C(4)	114.69(25)	N(1)–C(8)–C(9)	120.89(17)
O(3)–C(3)–C(4)	124.4(3)	N(1)–C(8)–C(13)	119.11(17)
C(3)–C(4)–Cl(4)	114.74(21)		

Table 7. Torsion angles with standard deviations.

Atoms	Torsion angle (°)
C(7)–N(1)–C(2)–C(3)	82.0(3)
C(8)–N(1)–C(2)–C(3)	−100.9(3)
C(2)–N(1)–C(7)–C(6)	−26.8(4)
C(8)–N(1)–C(7)–C(6)	156.1(3)
C(2)–N(1)–C(8)–C(9)	−38.9(3)
C(2)–N(1)–C(8)–C(13)	141.80(22)
C(7)–N(1)–C(8)–C(9)	138.11(24)
C(7)–N(1)–C(8)–C(13)	−41.2(3)
N(1)–C(2)–C(3)–O(3)	112.8(3)
N(1)–C(2)–C(3)–C(4)	−68.7(3)
C(2)–C(3)–C(4)–Cl(4)	−163.31(21)
C(2)–C(3)–C(4)–C(5)	11.1(4)
O(3)–C(3)–C(4)–Cl(4)	15.1(4)
O(3)–C(3)–C(4)–C(5)	−170.5(3)
C(3)–C(4)–C(5)–C(6)	19.9(5)
Cl(4)–C(4)–C(5)–C(6)	−165.9(3)
C(4)–C(5)–C(6)–C(7)	5.9(6)
C(5)–C(6)–C(7)–N(1)	−20.4(5)
N(1)–C(8)–C(9)–C(10)	−179.33(18)
N(1)–C(8)–C(13)–C(12)	179.35(17)

Table 8. Atomic co-ordinates with e.s.d.s.

Atom	*x*	*y*	*z*	U_{iso}
N(1)	0.109 5(3)	0.313 01(12)	0.316 8(3)	0.052 2(15)
C(2)	0.210 0(4)	0.249 06(15)	0.398 7(3)	0.054 9(19)
C(3)	0.205 6(4)	0.185 47(15)	0.285 7(3)	0.051 6(19)
O(3)	0.358 4(3)	0.163 16(12)	0.253 8(3)	0.072 9(16)
C(4)	0.011 1(4)	0.153 95(16)	0.225 4(3)	0.050 6(18)
Cl(4)	0.012 32(13)	0.066 95(4)	0.139 92(10)	0.070 4(6)
C(5)	−0.164 8(4)	0.182 23(17)	0.240 0(3)	0.062 1(22)
C(6)	−0.212 1(5)	0.255 94(18)	0.274 9(4)	0.073 7(24)
C(7)	−0.091 6(4)	0.316 09(17)	0.288 9(4)	0.065 4(22)
C(8)	0.218 37(25)	0.372 58(8)	0.273 19(21)	0.049 5(18)
C(9)	0.394 20(25)	0.397 17(8)	0.371 48(21)	0.057 7(19)
C(10)	0.498 24(25)	0.456 48(8)	0.327 06(21)	0.067 3(23)
C(11)	0.426 48(25)	0.491 20(8)	0.184 33(21)	0.071 3(24)
C(12)	0.250 65(25)	0.466 61(8)	0.086 04(21)	0.068 2(22)
C(13)	0.146 59(25)	0.407 30(8)	0.130 47(21)	0.056 7(19)

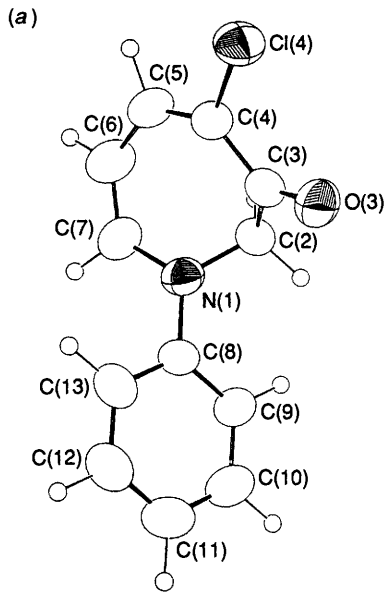


Fig. 3. (*a*), ORTEP diagram of the azepinone (**11**) showing crystallographic numbering system; (*b*), side view of the azepinone (**11**).

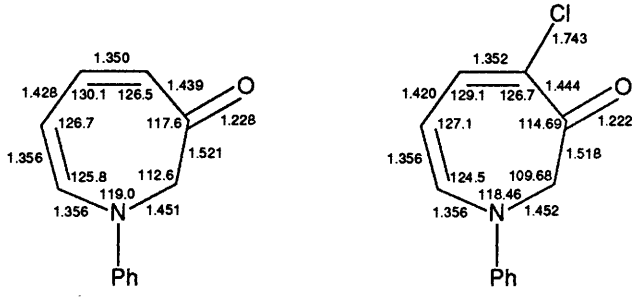


Fig. 4. Selected bond lengths and bond angles for the azepinones (**2**) and (**11**).

typical of that in aromatic chloro compounds[18] [1.739(10) Å] but surprisingly there is no significant change in the bond lengths of the seven-membered ring as a result of the substituent (Fig. 4). The bulk of the chlorine atom is apparently accommodated by a reduction in the ring bond angles at C-2 and C-3 (Fig. 4); the dihedral angle Cl–C(4)–C(3)–O(3) is just 15°. Clearly the geometry remains controlled by the dienaminone conjugated system and the substitution causes a relatively small perturbation.

Experimental

^{1}H and ^{13}C NMR spectra were recorded at 200 and 50 MHz respectively for solutions in [^{2}H]chloroform, unless otherwise stated.

Protonation of 1H-*Azepin*-3(2H)-*ones with Trifluoroacetic Acid.*—The appropriate azepinone was dissolved in trifluoroacetic acid, and spectra were recorded using an external [$^2H_2$]water lock. Deuterium exchange reactions were observed using neat [^{2}H]trifluoroacetic acid. Results are shown in Tables 1 and 2.

3-Ethoxy-1-methyl-1,2-dihydroazepinium Tetrafluoroborate.—1-Methyl-1*H*-azepin-3-(2*H*)-one (60 mg, 0.50 mmol) was dissolved in methylene dichloride and a solution of freshly prepared triethyloxonium tetrafluoroborate in methylene dichloride (0.67M; 0.53 mmol) was added. Solid potassium carbonate (75 mg, 0.55 mmol) was also added and the solution was stirred at room temperature overnight. The reaction mixture was then filtered and the solvent was evaporated from the filtrate under reduced pressure to give the alkylated salt as an orange oil which could not be obtained in crystalline form but was characterised by its NMR spectra. In the absence of potassium carbonate, a small amount of the protonated salt was also observed. Thus, 3-ethoxy-1-methyl-1,2-dihydroazepinium tetrafluoroborate was prepared (100 mg, 79%); δ_H([$^2H_6$]-acetone) 8.41 (1 H, d, ^3J, 4.7 Hz), 7.70 (1 H, dd, ^3J, 11.3 and 7.7 Hz), 6.69 (1 H, dd, ^3J, 11.3 and 4.8 Hz), 6.38 (1 H, d, ^3J 7.7 Hz), 4.19 (2 H, q, ^3J 7.0 Hz), 4.17 (2 H, s), 3.86 (3 H, s) and 1.37 (3 H, t, ^3J 7.0 Hz); δ_C(DEPT) 160.31, 148.93, 115.91, 104.49, 66.81, 56.40, 46.41 and 12.64; no reasonable electron impact mass spectrum could be obtained.

Reaction of 1H-*Azepin*-3(2H)-*ones with* N-*Halogenosuccinimides.*—A number of reactions were carried out with *N*-halogenosuccinimides (NXS). All reactions were carried out by addition of a solution of the appropriate NXS in methanol (8 ml) to a solution of the azepinone (1 mmol) in methanol (10 ml) cooled on an ice bath. The reaction mixtures were stirred at 0 °C in all cases and further reaction conditions are listed with individual examples. The reaction mixture was then poured into methylene dichloride (20 ml) and washed with sodium hydrogen carbonate solutions (20%; 3 × 20 ml). The organic layer was then dried ($MgSO_4$) and the solvent was removed under reduced pressure at room temperature. Chlorinated products were then purified by dry-flash column chromatography using methylene dichloride as eluant. The dibromo compound was similarly purified or was obtained as a crystalline solid when two equivalents of NBS were used. All products were very sensitive to heat, and solvent was therefore removed at room temperature; the products could not be purified by distillation or conventional recrystallisation. However, if the solids were dissolved in the minimum possible quantity of methanol and kept at −20 °C overnight, crystalline, analytically pure materials could be obtained. The dibromo compound was particularly sensitive and decomposed to a black insoluble material even when left in solution at *ca.* 30 °C.

The following *halogeno*-1H-*azepin*-3(2H)-*ones* were obtained: *4,6-dichloro-1-phenyl* (from the 1-phenyl azepinone and 2.1 equiv. NCS, room temperature for 45 min) (110 mg, 44%), m.p. 105–108 °C (decomp.) (from methanol) (Found: C, 55.7; H, 3.5; H, 5.45. $C_{12}H_9Cl_2NO{\cdot}0.25H_2O$ requires C, 55.7; H, 3.65; N, 5.4%); δ_H 7.46 (1 H, d, ^4J 0.9 Hz), 7.25 (1 H, q, ^4J and ^5J 0.9 Hz), 7.1–7.45 (5 H, m) and 4.29 (2 H, d, ^5J 0.9 Hz); δ_C 175.44 (q), 142.60 (q), 139.55, 139.08, 130.08 (q), 129.66, 126.06, 120.13, 109.49 (q), and 58.55; *m/z* 257, 255, 253 (M^+, 10, 33, and 50%), 226 (17), 224 (25) and 105 (100); *4-chloro-1-phenyl* (from the 1-phenyl azepinone and 1 equiv. NCS, 0 °C for 45 min (90 mg, 41%), m.p. 66–67 °C (from methanol) (Found: C, 64.6; H, 4.6; N, 6.25. $C_{12}H_{10}ClNO{\cdot}0.25H_2O$ requires C, 64.3; H, 4.7; N, 6.25%); δ_H 7.1–7.4 (6 H, m) (olefinic proton superimposed on aromatics) 7.10 (1 H, d, ^3J 7.5 Hz), 5.52 (1 H, dd, ^3J 7.5 and 9.8 Hz) and 4.27 (2 H, s); δ_C 176.06 (q), 143.74 (q), 141.90, 138.88, 129.80 (q), 129.57, 125.71, 120.36, 103.07 and 58.68; *m/z* 221, 219 (M^+, 29 and 70%), 192 (18), 190 (47), 156 (35), 105 (100) and 77 (47); *4-chloro-1-methyl* (from 1-methylazepinone and 1 equiv. NCS, 0 °C for 45 min) (80 mg, 51%) (Found: M^+, 157.0288. $C_7H_8{}^{35}ClNO$ requires M^+, 157.0294); δ_H 7.21 (1 H, d, ^3J 10.0 Hz), 6.83 (1 H, d, ^3J 6.9 Hz), 5.20 (1 H, dd, ^3J 6.9 and 10.0 Hz), 3.63 (2 H, s) and 3.20 (3 H, s); δ_C 173.42 (q), 147.37, 140.62, 125.85 (q), 98.15, 61.31 and 43.88; *m/z* 159, 157 (M^+, 26 and 79%), 130 (30), 128 (100) and 94 (72); *4,6-dibromo-1-methyl* [from 1-methylazepinone and 2.1 equiv. NBS, 5 min at 0 °C (also from 1-methylazepinone and 1 equiv. NBS, 5 min at 0 °C)], [168 mg, 60% (23 mg, 8%)], m.p. 140–141 °C (decomp.) (from methanol) (Found: C, 30.4; H, 2.7; N, 5.15. $C_7H_7Br_2NO$ requires C, 29.9; H, 2.5; N, 5.0%); δ_H 7.72 (1 H, s), 7.12 (1 H, s), 3.71 (2 H, s) and 3.19 (3 H, s); (^{13}C NMR spectrum could not be obtained due to the facile decomposition of the compound in solution); *m/z* 283, 281, 279 (M^+, 36, 71 and 36%), 254 (16), 252 (32), 250 (16), 202 (50), 200 (50), 174 (18), 172 (18), 159 (20), 157 (20) and 40 (100).

From the reaction with one equiv. of NBS and the 1-methylazepinone, a fraction was collected (11 mg) which consisted of the 4-bromo derivative [δ_H 7.46 (1 H, d, ^3J 10.0 Hz), 6.87 (1 H, d, ^3J 6.9 Hz), 5.19 (1 H, dd, ^3J 10.0 and 6.9 Hz), 3.71 (2 H, s) and 3.22 (3 H, s)], together with an equal amount of an unidentified impurity.

Crystal Data.—$C_{12}H_{10}ClNO$, M = 219.67. Monoclinic, a = 6.909 6(3), b = 18.046 4(7), c = 0.845 0(4) Å, β = 103.210(4)°, V = 1073.7 Å^3 [from 2θ values of 32 reflections measured at ±ω (2θ = 40–45°, $\bar{\lambda}$ = 1.541 84 Å), T = 298 K], space group $P2_1/c$ (No. 14), Z = 4, D_c = 1.359 g cm^{-3}, $F(000)$ = 456, yellow-brown plate 0.12 × 0.27 × 0.52 mm, μ(Cu-K$_\alpha$) = 2.94 mm^{-1}.

Data Collection and Processing.—Stoë STADI-4 four-circle diffractometer, T = 298 K, graphite-monochromated Cu-K$_\alpha$ X-radiation ($\bar{\lambda}$ = 1.541 84 Å), ω–2θ mode with ω scan width (0.66 + 0.347tanθ)°, 1656 unique reflections ($2\theta_{max}$ 120°, ±h,k,l), of which 1211 with $F \geqslant 6\sigma(F)$ were used in all calculations, absorption correction by means of ψ scans (min. and max. transmission factors 0.177 and 0.293, respectively), no significant crystal decay or movement.

Structure Analysis and Refinement.—Automatic direct methods[19] located all non-H atoms and the structure was refined by full-matrix least-squares on F,[20] with anisotropic thermal parameters for all non-H atoms; the phenyl ring was refined as an idealised hexagon and H atoms were included in fixed, calculated positions. At final convergence, R = 0.0383, wR = 0.0441, S = 1.239 for 125 parameters, with the weighting scheme $w^{-1} = \sigma^2(F) + 0.000\,053F^2$ giving satisfactory agreement analyses. The final ΔF synthesis showed no feature above 0.15 or below −0.16 e Å^{-3} and in the final least-squares cycle $(\Delta/\sigma)_{max}$ was 0.02. Molecular geometry calculations utilised CALC[21] and the Figures were produced using ORTEPII.[22] Supplementary material deposited with the Cambridge Crystallographic Data Centre comprises H-atoms positions and thermal parameters.

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