An Analysis of the ^1H and ^{13}C Nuclear Magnetic Resonance Spectra of 3-t-Butylaminoacrolein and of Glyoxal t-Butylhydrazone

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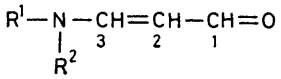
^1H N.m.r. spectra have confirmed that 3-t-butylaminoacrolein exists as the *E-s-E* configuration in polar solvents, and as a mixture of *Z-s-Z* and *E-s-E* isomers in non-polar solvents. The spectra of glyoxal t-butylhydrazone are independent of solvent and are thought to indicate *Z-s-E* structure for this compound. The fully coupled ^{13}C n.m.r. spectra of both compounds have been completely assigned using specifically labelled derivatives where necessary. The long-range ^{13}C–^1H coupling constants of 3-t-butylaminoacrolein are strongly dependent on the shape of the conjugated system.

CONSIDERABLE interest has been shown in the structure and spectra of the enaminone (1) [1] and azaenaminone (2) (α-dicarbonyl hydrazone) [2] systems. 3-Dialkylaminoacrolein derivatives (1; R^1,R^2 = alkyl) represent the simplest case, in which the *E-s-E* structure is favoured in all solvents, though even a trivial substitution at



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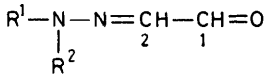
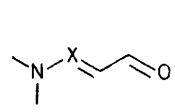


(2)

carbon may cause a change in the configuration.[3] A further complication is introduced with 3-alkylamino- and 3-amino-acroleins, in which intramolecular hydrogen-bonding may be possible.[4,5] Indeed, u.v. and ^1H n.m.r. spectra indicate that the *Z-s-Z* structure is favoured in non-polar solvents, though the *E-s-E* configuration dominates in polar solvents. The present work has two objectives. First, to extend the earlier studies of aza-



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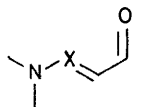

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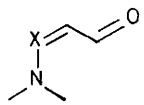

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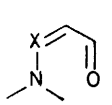
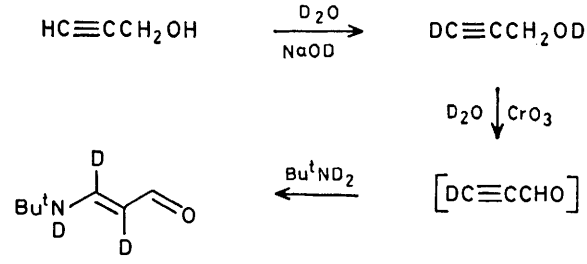


Z—*s*—*Z*

enaminones to an example where intramolecular hydrogen bonding is possible, and, secondly, to study the effect of the configuration of the enaminone and azaenaminone systems on the ^{13}C n.m.r. parameters, in particular on the long-range ^{13}C–^1H coupling constants.

No examples of glyoxal mono-*N*-alkylhydrazones are known, and indeed preliminary reactions of glyoxal with simple alkylhydrazines were not encouraging. However, treatment of glyoxal with t-butylhydrazine smoothly gave the monohydrazone (2; R^1 = Bu^t, R^2 = H) together with an unidentified amorphous product. For comparison, 3-t-butylaminoacrolein [6] (1; R^1 = Bu^t, R^2 = H) was synthesised by standard methods. A number of specifically deuteriated derivatives of this compound were also required. Exchange at the NH and at the 2-position is possible under mild conditions (see Experimental section): a label was introduced to the 3-position by the sequence shown in the Scheme.



SCHEME

The ^1H n.m.r. spectrum of 3-t-butylaminoacrolein (1; R^1 = Bu^t, R^2 = H) recorded in [$^2H_4$]methanol (Table 1) is characteristic of the *E-s-E* isomer. In particular, the vicinal coupling constants are similar in size to those quoted for 3-dimethylaminoacrolein.[3] Two isomers of (1; R^1 = Bu^t, R^2 = H) are apparent in [^2H]chloroform solution, of which the minor constituent (30%) is clearly the *E-s-E* isomer by analogy with the above spectrum. The major isomer (70%) showed a more complex coupling pattern. Assignment of the 1- and 2-H couplings was possible by inspection, which gave two of the three couplings in the eight-line 3-H pattern. The remaining coupling (10 Hz) was identified by deuterium exchange of the NH. 3-H gave a broad unresolved peak under these conditions, which collapsed to a clean quartet on deuterium decoupling. The *Z-s-Z* structure is assigned to this major isomer because of the small value of the vicinal couplings $^3J_{1,2}$ and $^3J_{2,3}$, the large value of $^3J_{3,NH}$ which indicates a transoid arrangement around this bond, and the large value of the allylic coupling $^4J_{1,3}$ which suggests a planar W arrangement of these atoms.

In contrast to these results, the ^1H n.m.r. spectrum of the azaenaminone (2; R^1 = Bu^t, R^2 = H) is unchanged in polar or non-polar solvents (Table 1). The *Z-s-Z* structure is excluded by the low-frequency position of NH. The vicinal coupling constant $^3J_{1,2}$ is similar in

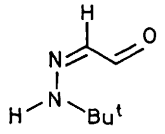
TABLE 1

^{1}H N.m.r. spectra of 3-t-butylaminoacrolein and glyoxal t-butylhydrazone [a]

Compound	Solvent	Isomer	δ(Bu^t)	δ(1-H)	δ(2-H)	δ(3-H)	δ(NH)	$^3J_{1,2}$	$^4J_{1,3}$	$^3J_{2,3}$	$^4J_{2,NH}$	$^3J_{3,NH}$
(1; R^1 = Bu^t, R^2 = H)	[$^2H_4$]MeOH	*E-s-E*	1.30	8.76	5.34	7.53		9.2		12.1		
	C^2HCl_3	*E-s-E*	1.30	8.97	5.34	7.17 [b]	*ca.* 7.0	8.5		12.0		
		Z-s-Z	1.30	9.03	4.95	6.91	10.2	2.3	3.3	7.0		10.0
(2; R^1 = Bu^t, R^2 = H)	[$^2H_4$]MeOH		1.27	9.20	7.04			7.8				
	C^2HCl_3		1.29	9.34	7.00		7.44	7.8			1.2	

[a] Coupling constants are quoted in Hz. [b] Broad, observable only after shaking with deuterium oxide.

size to that of the *NN*-disubstituted compound (2; R^1 = R^2 = Me) for which an *s-E* geometry has been proposed.[2] Although unusual long-range couplings through two nitrogen atoms have been noted,[7] the observation of a significant allylic coupling $^4J_{2,NH}$ which is *not* present in the acrolein (1; R^1 = Bu^t, R^2 = H) suggests a W configuration. Only the *Z-s-E* structure (A) is consistent with these observations. Additional



(A)

evidence that the structure is not *E-s-E* is obtained from its u.v. spectrum which shows a molar absorption coefficient *ca.* 20% lower than might be expected by comparison with enaminone [4] and azaenaminone [2] model compounds.

The configurational independence of glyoxal t-butylhydrazone is confirmed by the similarity of its ^{13}C n.m.r. spectra in [$^2H_4$]methanol and in [^{2}H]chloroform (Table 2). The assignment of the minor coupling constants is possible by inspection: deuterium exchange confirmed that the 4.1 Hz coupling in the C(2) signal is due to interaction with the NH.

As expected, the ^{13}C n.m.r. spectra of 3-t-butylaminoacrolein show considerable complexity (Table 2). The spectrum of the *E-s-E* isomer in [$^2H_4$]methanol is similar to that quoted for the parent 3-aminoacrolein (1; R^1 = R^2 = H) in deuterium oxide.[8,9] The C-1, -2, and -3 signals show one, two, and zero long-range J_{CH}, respectively, whether the spectrum is recorded in [$^1H_4$]- or in [$^2H_4$]-methanol, which shows that no coupling with NH takes place. The multiplicity of the C-1 resonance is unchanged in the spectrum of the [2,*N*-$^2H_2$]-derivative, but collapses to a $^1J_{CH}$ doublet in the spectrum of the [3-^{2}H]-compounds, which allows the long-range coupling to be assigned as $^3J_{C\text{-}1,3\text{-}H}$. In view of this result, the earlier assignment of the corresponding coupling in 3-aminoacrolein, may need to be revised.[9] The assignment of the coupling at C-2 also follows since only the larger coupling (20.9 Hz) is maintained in the spectrum of the [3-^{2}H]-derivative.

In [^{2}H]chloroform solution, only the *Z-s-Z* isomer gave

TABLE 2

^{13}C N.m.r. spectra of 3-t-butylaminoacrolein and glyoxal t-butylhydrazone [a]

Compound	Solvent	Isomer	δ(C*Me*$_3$)	δ(*C*Me$_3$)	δ(C-1)	δ(C-2)	δ(C-3)	^1J	^2J	^3J
(1; R^1 = Bu^t, R^2 = H)	[$^2H_4$]MeOH	*E-s-E*	29.75	53.68	190.63	102.98	160.23	C(1)H(1) 162.8 C(2)H(2) 157.1 C(3)H(3) 160.9	C(1)H(2) C(2)H(1) 20.9 C(2)H(3) 2.2 C(3)H(2) C(3)NH	C(1)H(3) 5.9 C(2)NH C(3)H(1)
	C^2HCl_3	*E-s-E* [b]	29.37	52.02	188.74	102.61	155.74			
		Z-s-Z	29.56	52.33	186.95	94.00	149.00	C(1)H(1) 166.3 C(2)H(2) 163.8 C(3)H(3) 161.5	C(1)H(2) 4.9 C(2)H(1) 20.0 C(2)H(3) 3.2 C(3)H(2) 4.2 C(3)NH	C(1)H(3) 9.1 C(2)NH 3.2 C(3)H(1) 7.4
(2; R^1 = Bu^t, R^2 = H)	[$^2H_4$]MeOH		28.60	56.12	192.31	133.18		C(1)H(1) 172.6 C(2)H(2) 164.9	C(1)H(2) 8.5 C(2)H(1) 21.7	C(2)NH
	C^2HCl_3		28.29	55.41	190.49	133.06		C(1)H(1) 174.6 C(2)H(2) 163.7	C(1)H(2) 7.8 C(2)H(1) 23.0	C(2)NH 4.1

[a] Chemical shifts are in p.p.m. to high frequency of Me_4Si. Coupling constants are quoted in Hz: the error is generally within ±0.5 Hz. [b] Coupling constants not measured.

signals which were sufficiently intense for a full analysis of the coupling pattern, which was much richer than for the *E-s-E* isomer. The C-1, -2, and -3 signals show two, three, and two long-range J_{CH}, respectively. Deuterium exchange of the NH removed only one 3.2 Hz coupling from the signal due to C-2, but the additional exchange of 2-H left only the interactions between C-1 and 3-H (^3J 9.1 Hz) and between C-3 and 1-H (^3J 7.4 Hz). The couplings which have been removed by this operation must represent interactions with 2-H ($^2J_{C-1,2-H}$ 4.9, $^2J_{C-3,2-H}$ 4.2 Hz). Unambiguous assignment of the remaining couplings to C-2 was possible using the spectrum of the [3-^{2}H] derivative. The C-2 signal in this material shows minor couplings of 3.2 (to NH) and of 20.0 Hz, which must represent interaction with 1-H: the coupling removed by the deuterium label ($^2J_{C-2,3-H}$) is 3.2 Hz.

It is apparent from Table 2 that the ^{13}C n.m.r. parameters of 3-t-butylaminoacrolein (1; R^1 = Bu^t, R^2 = H) are strongly dependent on the shape of the molecule: even the chemical shifts can differ by >8 p.p.m. in the *E-s-E* and *Z-s-Z* geometry. The one-bond coupling constants $^1J_{CH}$ are slightly larger in the *Z-s-Z* than the *E-s-E* configuration, with the effect again being greatest for C-2 (>6 Hz). The rather larger $^1J_{CH}$ values observed in the azaenaminone series (2; R^1 = Bu^t, R^2 = H) may be an electronegativity effect [*cf.* benzene, $^1J_{CH}$ 159 Hz; pyridine, $^1J_{CH}$ (average) 164 Hz].[10]

Two- and three-bond coupling constants $^2J_{CH}$ and $^3J_{CH}$ vary from 0 to 23 Hz in these systems. Only $^2J_{C-2,1-H}$ (= 21.5 ± 1.5 Hz) and $^2J_{3,NH}$ (= 0 Hz) are insensitive to the relative positions of the interacting atoms, but the influence of secondary structural features precludes the general use of these parameters in structure determinations. Thus $^2J_{C-1,2-H}$ is not observable in the spectrum of the *E-s-E* isomer of the enaminone (1; R^1 = Bu^t, R^2 = H), though it is significant (8 Hz) in the spectrum of the azaenaminone (2; R^1 = Bu^t, R^2 = H) which is also thought to have an *s-E* conformation about the C-1–C-2 bond.

Despite these reservations, the pattern of the ^{1}H-coupled ^{13}C n.m.r. spectrum of enaminones is reproducibly dependent on configuration, and can be used in empirical analysis provided that a sufficiently good model compound is known. Thus the ^{13}C spectrum of 3-dimethylaminoacrolein (1; R^1 = R^2 = Me) in [^{2}H]chloroform, δ 187.86 ($^1J_{CH}$ 162.0,[3] $J_{C-1,3-H}$ 6.5 Hz, C-1), 100.11 ($^1J_{CH}$ 157.5,[2] $J_{C-2,1-H}$ 22.8,[2] $J_{C-2,3-H}$ *ca.* 1.0 Hz, C-2), and 159.68 p.p.m. ($^1J_{CH}$ 162.1 Hz, C-3) is consistent with that of the *E-s-E* configuration by comparison with the data in Table 2.

EXPERIMENTAL

^{1}H and ^{13}C n.m.r. spectra were recorded at 100 and 20 MHz, respectively.

3-*t-Butylaminoacrolein*.—Prepared by the standard addition of t-butylamine to propynal, this derivative was purified by sublimation at 10^{-1} Torr, and had m.p. 79—81 °C (lit.,[6] 85—86 °C), *m/e* 127 (M^+, 24%), 112 (17), 94 (12), 71 (12), 70 (20), 57 (33), 44 (17), 43 (38), 42 (38), 41 (100), and 39 (29).

Propynal for these experiments was made by the recent method of Veliev and Guseinov.[11] Although this was convenient for the preparation of a solution of propynal (b.p. 55—57 °C), in our hands it was not possible to isolate it from the mixed solvents of ether, b.p. 37 °C, and ethyl methyl ketone, b.p. 80 °C, by simple distillation.

Glyoxal Mono-t-butylhydrazone.—A solution of t-butylhydrazine [from t-butylhydrazine hydrochloride (6.24 g, 50 mol)] in water (10 ml) containing sodium hydroxide (2.0 g, 50 mmol) was added to a solution of glyoxal (40%, 6 ml) in water (200 ml). After 15 min at room temperature, the amorphous solid which had precipitated was filtered, and the filtrate was set aside for 1 h. The filtrate was then extracted with methylene chloride (4 × 40 ml) and the organic extracts were dried (Na_2SO_4), and concentrated. Flash distillation of the residue at 120° and 16 Torr gave the *hydrazone* (2.61 g, 41%), *m/e* 128 (M^+, 23%), 113 (7), 71 (18), 57 (100), 41 (26), $\lambda_{max.}$($CHCl_3$) 293 nm (ε 20 600) (Found: C, 56.45; H, 9.6; N, 21.9. $C_6H_{12}N_2O$ requires C, 56.25; H, 9.4; N, 21.9%).

[2,3,N-$^2H_3$]-3-*t-Butylaminoacrolein*.—(a) [3-^{2}H]*Propyn*-[^{2}H]*ol*. Propynol (6.0 g) was dissolved in deuterium oxide (15 ml) containing sodium deuterioxide [from sodium (50 mg)]. Exchange was complete within 1 min (^{1}H n.m.r.). The solution was extracted eight times with methylene chloride, the combined organic extracts were dried (Na_2SO_4), and the solvent was evaporated. The crude [3-^{2}H]propyn[^{2}H]ol (5.6 g, 93%) was used directly for the oxidation.

(b) [3-^{2}H]*Propynal* (cf. *ref.* 11). A solution of chromium trioxide (9.2 g) in [$^2H_2$]sulphuric acid (6.4 ml) and deuterium oxide (18 ml) was added over 1 h to a stirred and cooled solution of [3-^{2}H]propyn[^{2}H]ol (5.6 g, 0.1 mol) in ethyl methyl ketone (15 ml). The mixture was stirred for 5 h at 20°, diluted with deuterium oxide (5 ml), and extracted with ether (20 ml). After it had been dried (Na_2SO_4), the organic layer was distilled through a short Vigreux column: the fraction of b.p. ≤70° was used for the next stage.

(c) [NN-$^2H_2$]-*t-Butylamine*. t-Butylamine (7.0 g) was shaken with deuterium oxide (10 ml). The solution was saturated with sodium chloride and extracted with ether (3 × 20 ml). The combined ether extracts were dried (Na_2SO_4) and used without further work-up.

(d) [2,3,N-$^2H_3$]-3-*t-Butylaminoacrolein*. The ethereal solution of [*NN*-$^2H_2$]-t-butylamine from (c) above, was added to the solution of [3-^{2}H]propynal from (b) above, and the mixture was set aside for 1.5 h. Evaporation of the solvents gave a dark residue which was sublimed to give the *aminoacrolein* as crystals (0.61 g, 4.7%). Analysis by ^{1}H n.m.r. confirmed the sites of deuteriation.

In situ *Generation of Other Deuteriated* 3-*t-Butylaminoacroleins*.—(a) [N-^{2}H]-3-*t-Butylaminoacrolein*. The *E*-isomer was obtained when the undeuteriated derivative was dissolved in [$^2H_4$]methanol. (Spectra of the *N*-^{1}H derivative were therefore recorded in [$^1H_4$]methanol, using a capillary lock of deuterium oxide.) The *Z*-isomer was *N*-deuteriated in deuteriochloroform, by shaking with deuterium oxide.

(b) [2,N-$^2H_2$]-3-*t-Butylaminoacrolein*. A solution of the undeuteriated compound in [$^2H_4$]methanol containing a trace of sodium methoxide was monitored by ^{1}H n.m.r. After 24 h, complete exchange at the 2-position had taken

place to give the *E*-isomer, whose spectra were recorded *in situ*. To obtain the *Z*-isomer, the solution was neutralised with methanolic hydrogen chloride and the solvent was evaporated. The resultant partially crystalline material was dissolved in deuteriochloroform, filtered, and shaken with deuterium oxide.

(c) [3-^{2}H]-3-*t-Butylaminoacrolein*. This derivative was made by the same procedure as in (b) above, only [2,3,*N*-$^2H_3$]-3-t-butylaminoacrolein was used as starting material, and [$^1H_4$]methanol was employed to accomplish the back-exchange. The *N*-^{1}H and *N*-^{2}H derivatives of the *Z*-isomer were obtained by shaking the deuteriochloroform solution with water and with deuterium oxide, respectively.

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