Tetrahedron Letters Vol. 21, pp 223 - 226
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0040-4039/80/0108-0223$02.00/0

SYNTHESIS OF 5-DIALKYLAMINO-1,2,3-TRIAZOLES AND 2-AMINO-1-AZIRINES FROM TERTIARY AMIDES

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Summary : The reaction of sodium azide with β-monosubstituted-α-chloroenamines (generated from tertiary amides) yields either 5-dialkylamino-1,2,3-triazoles or 2-amino-1-azirines according to the basicity of the amine substituent.

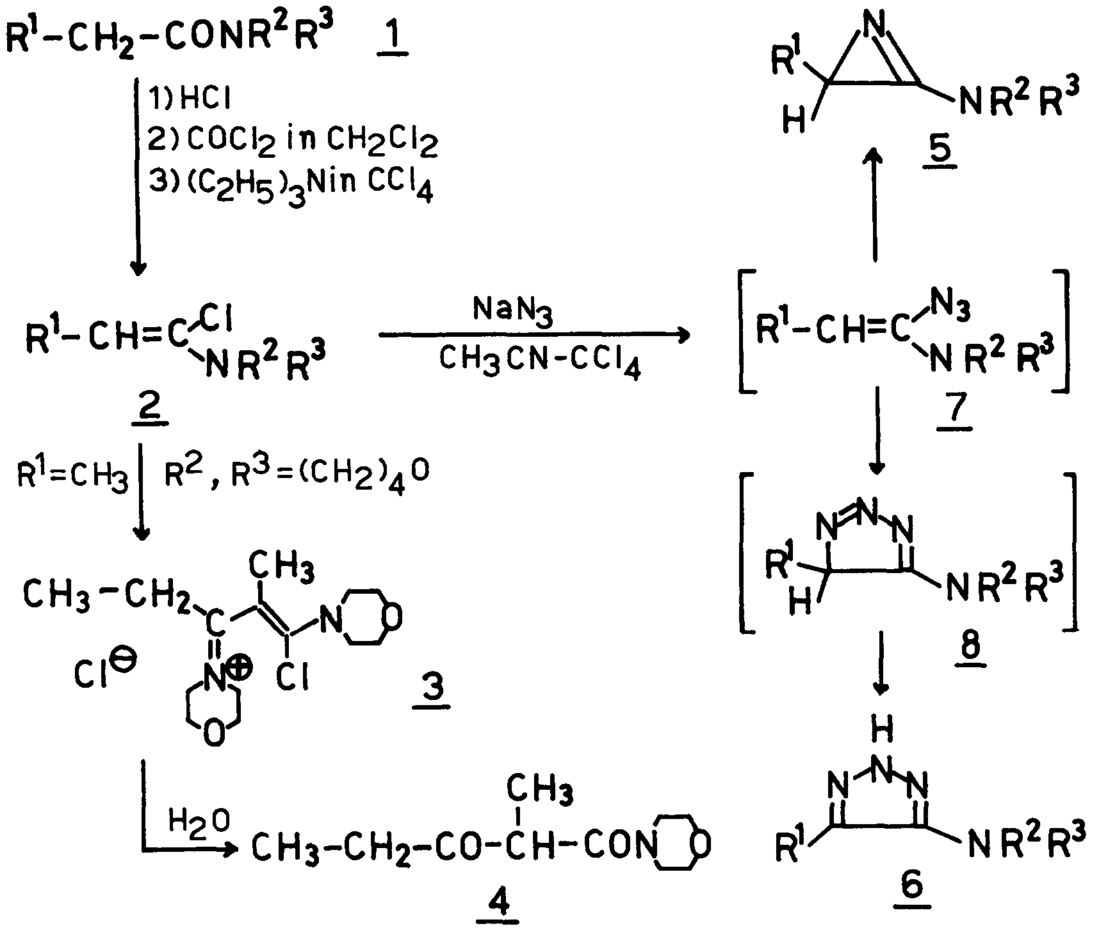
Previous studies (1,2) of this laboratory have led to the development of a practical route to 2-amino-1-azirines bearing two substituents at position-3. This novel class of cyclic amidines has aroused much interest (3) as potential starting material for the preparation of functionalized heterocyclic compounds. However the unavailability of the 3-monosubstituted-1-azirines was a serious limitation to the general applicability of these new heterocyclic reagents.

We wish to describe briefly experimental conditions allowing for the preparation of solutions of the unstable β-monosubstituted-α-chloroenamines (4,5) which can be conveniently used for the synthesis of 3-monosubstituted-2-amino-1-azirines and 5-dialkylamino-1,2-3-triazoles (Scheme 1).

A solution of tertiary amide 1 in CH_2Cl_2 saturated with HCl was treated with a 3 to 5 fold excess of $COCl_2$ for 5 to 7 days at 20°. Removal of the solvent in vacuo (no moisture !) left a solid residue which was finely ground and covered with enough CCl_4 or petroleum ether (b.p. < 70°) to yield a 0.2-1.0 molar solution of α-chloroenamine. Triethylamine (1.5 equiv.) was added to the vigorously stirred suspension of the amide chloride. After 2-3 hrs at 20° the mixture was filtered off rapidly under a stream of dry nitrogen or argon. Yields (6) were determined by nmr with an added standard (Table 1).

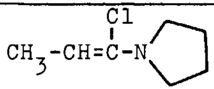
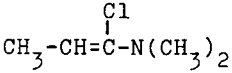
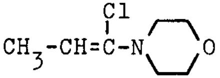
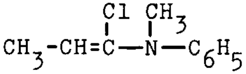
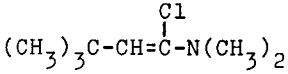
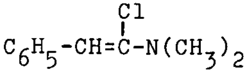
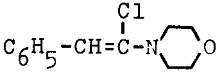
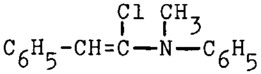
The less basic α-chloroenamines 2d and 2h are stable enough to be distilled and kept in pure form. 2c can be distilled but solidifies on standing overnight to give 3 which yields 4 on hydrolysis. More basic α-chloroenamines autocondense even more readily and can be kept only for a few hours in solvents like CCl_4, ether or petroleum ether. Solvents like CH_2Cl_2 or $CHCl_3$ were found to accelerate dramatically the condensation reactions. Preliminary studies suggest that these solvents accelerate the ionisation of 2 to the highly electrophilic keteniminium salts which react with 2 to give 3.

Scheme 1



Slow addition of the solutions of 2 in CCl_4 to a suspension of NaN_3 (1.2 equiv. based on 1) in dry CH_3CN produce 2-amino-1-azirines only with the less basic α-chloroenamines 2d and 2h (Table 2). The more basic α-chloroenamines do not give 5 (no absorption at 1750-1770 cm^{-1}) but rather the triazoles 6. Thus, in these systems, the cyclisation of the intermediate α-azidoenamines 7 occurs much faster than the loss of N_2. The primary cyclisation products 8 are expected to isomerise fast to their aromatic tautomers 6.

Table 1 α-Chloroenamines derived from 2-Monosubstituted-Acetamides

	α-chloroenamine	Yields[a] %
2a		53 (in 0,2M CCl_4)
2b	 $CH_3-CH=\overset{Cl}{C}-N(CH_3)_2$	40-49 (in 0,5M CCl_4)
2c		50, neat (b.p. 85-95°C/20 Torr)
2d	 $CH_3-CH=\overset{Cl}{C}-\overset{CH_3}{N}-C_6H_5$	59-62, neat (b.p. 65°C/1.5 Torr)
2e	 $(CH_3)_3C-CH=\overset{Cl}{C}-N(CH_3)_2$	62-65, neat (b.p. 50-54°C/12 Torr)
2f	 $C_6H_5-CH=\overset{Cl}{C}-N(CH_3)_2$	60-70 (in 1M CCl_4)
2g		50-60, neat
2h	 $C_6H_5-CH=\overset{Cl}{C}-\overset{CH_3}{N}-C_6H_5$	45-52, neat (b.p. 160°C/0.02 Torr)

[a] based on the amide 1

Table 2 Products from α-chloroenamines and NaN_3

Product (Yields %)[a]		m.p.(°C) or b.p.(°C/Torr)
6a	(80)	136 - 138
6b	(60)	63-65/0.1
6c	(58)	120 - 122
5d	(74)	71-74/0.2
6e	(84)	147 - 148
6f	(66)	85 - 87
6g	(62)	114 - 117
5h	(71)	94 - 96

[a] based on 2

In conclusion, our goal has been only partly reached : 3-monosubstituted 2-amino-1-azirines are now available but only with a weakly basic amine group at C-2. On the other hand the sequence 1 → 2 → 6 represents a new and convenient route toward functionalized triazoles (8). The mechanistic meaning of our findings will be discussed in the full report of our results.

Acknowledgement

We thank the "Institut pour l'Encouragement de la Recherche Scientifique dans l'Industrie et l'Agriculture" for according Ph.D. fellowships to three of us (M.H., M.Ho. and B.T.) and the "Fonds de la Recherche Fondamentale et Collective" for financial support.

References and Notes

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(6) Structural analyses are based essentially on ^1H NMR which also indicates the presence of E and Z isomers. Stable α-chloroenamines were also characterized by ^{13}C NMR and mass spectroscopy.

(7) Products 5 and 6 were fully characterized by ir, ^1H and ^{13}C NMR and mass spectroscopy. An X-ray diffraction analysis was effected on 5h which confirmed the proposed structure.

(8) Review : T.L. Gilchrist and G.E. Gymer, Adv. Heter. Chem., 16, 33, (1974).

(Received in UK 5 November 1979)