Synthesis of Simple Enamino Thioaldehydes

Motomu Muraoka* and Tatsuo Yamamoto

Department of Chemistry, Faculty of Science, Josai University, 1-1 Keyaki-Dai, Sakado, Saitama 350-02, Japan

Simple enamino thioaldehydes (**1**)—(**5**) are synthesised by the thioformylation of aliphatic and alicyclic enamines.

There have been a number of reports regarding the synthesis of stable thioketones,[1] but those of stable thioaldehydes are scanty. Amongst a variety of thioketones, β-heterosubstituted α,β-unsaturated thioketones are especially stable and have been thoroughly studied synthetically.[2] In contrast, no systematic studies on the synthesis of simple enamino thioaldehydes have been reported.[†] All the stable thioaldehydes which have been reported so far are stabilised through conjugation involving a hetero atom, with the exception of 2,4,6-tri-t-butylthiobenzaldehyde which owes its exceptional stability to the steric protection of the thioformyl group by two bulky $\mathrm{Bu^t}$ groups.[4]

We have briefly reported the synthesis of a series of stable thioaldehydes; β-amino-α-cyano- and β-alkylamino-α-cyano-α,β-unsaturated thioaldehydes[5] whose stability is enhanced by the existence of a cyano group at the α-position. We have now synthesised simpler enamino thioaldehydes (aliphatic and alicyclic), which bear no cyano or any other strongly electron-withdrawing group at the α-position, *via* the thioformylation of enamines. It was found that application of the Vilsmeier–Haack aldehyde synthesis using aqueous or alcoholic sodium hydrogen sulphide[‡] is the best method for this reaction. Thus, each enamine was treated with dimethylformamide and phosphoryl chloride to give the corresponding Vilsmeier salt which, when solvolysed *in situ* with NaHS, produced brilliant orange or red crystalline thioaldehydes (**1**)—(**5**).[§] The isolated yields by column chromatography were moderate.[¶]

The thioaldehydes here obtained have distinct melting points and are stable for over several months even at room temperature. The best yield and stability were acquired in the case of thioaldehyde (**1**) which was obtained by the thioformylation of *cis*-(4-morpholino)-1,2-diphenylethylene.[8] We have not succeeded in obtaining 2-alkylamino-1-phenyl-1-

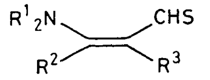
---

[†] In a report concerning the study of enamino thioketones by n.m.r., 3-dimethylaminothioacrolein has been prepared from the corresponding enamino aldehyde and phosphorus pentasulphide but no yield was given, ref. 3.

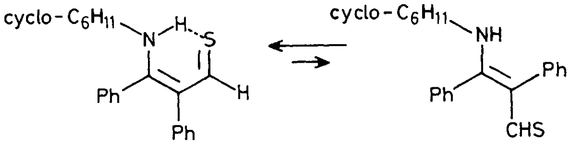
[‡] Reid and his coworkers synthesised several types of heterocyclic thioaldehydes (ref. 6) by a novel application of the Vilsmeier reaction involving aqueous NaHS.

[§] All new thioaldehydes purified by recrystallisation gave satisfactory microanalyses and spectral data in agreement with the proposed structures.

[¶] Isolated yields and melting points of the thioaldehydes are as follows: (**1**) 61%, 170—171 °C; (**2**) 33%, 163.5—164 °C; (**3**) 27%, 139—140 °C; (**4**) 50%, 116—117 °C; (**5**) 23%, 136.5 °C.



(1); R^1_2N = morpholino $R^2 = R^3 = Ph$
(2); R^1_2N = pyrrolidino $R^2 = R^3 = Ph$
(3); R^1_2N = morpholino $R^2 = Ph$, $R^3 = H$
(4); R^1_2N = morpholino $R^2, R^3 = [CH_2]_3$



(5a) (5b)

thioformylethylene owing to the difficulty of the formation of the Vilsmeier salt.||

All the enamino thioaldehydes here described are (*Z*)-isomers because the enamines used, which were prepared by acid-catalysed condensation of the corresponding ketone and amine, display the *cis*-configuration exclusively.[8] The ^1H n.m.r. spectrum of the thioaldehyde (**5**) in $CDCl_3$ suggested the existence of (*E*)-isomer (**5b**) (less than 10%) [hydrogen-bonded imino and thioformyl protons in (*Z*)-isomer (**5a**); δ_{NH} 15.24 and δ_{CHS} 9.82 and those in (*E*)-isomer (**5b**); δ_{NH} 5.41 and δ_{CHS} 9.95 respectively].

Received, 5th June 1985; Com. 775

References

1 See for example; E. Campaigne, *Chem. Rev.*, 1946, **39**, 1; R. Mayer, J. Morgenstern, and J. Fabian, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 277; E. Campaigne, 'The Chemistry of the Carbonyl Group,' ed. S. Patai, Interscience, New York, 1966, p. 917; D. Paquer, *Int. J. Sulfur Chem., Part B*, 1972, **7**, 269; *ibid.*, 1973, **8**, 173; A. Ohno, in 'Organic Chemistry of Sulfur,' ed. S. Oae, Plenum Press, New York, 1977, p. 189.
2 V. A. Usov and M. G. Voronkov, *Sulfur Reports*, 1982, **2**, 39.
3 J. Dabrowski and K. Kamienska-Trela, *Org. Magn. Reson.*, 1972, **4**, 421.
4 R. Okazaki, A. Ishii, N. Fukuda, H. Oyama, and N. Inamoto, *J. Chem. Soc., Chem. Commun.*, 1982, 1187.
5 M. Muraoka, T. Yamamoto, and T. Takeshima, *Chem. Lett.*, 1982, 101.
6 S. McKenzie and D. H. Reid, *J. Chem. Soc., Chem. Commun.*, 1966, 401; J. G. Dingwall, D. H. Reid, and K. Wade, *J. Chem. Soc. (C)*, 1969, 913; S. McKenzie and D. H. Reid, *ibid.*, 1970, 145; R. K. Mackie, S. McKenzie, D. H. Reid, and R. G. Webster, *J. Chem. Soc., Perkin Trans. 1*, 1973, 657.
7 S. C. Tang, G. N. Weinstein, and R. H. Holm, *J. Am. Chem. Soc.*, 1973, **95**, 613.
8 M. E. Munk and Y. K. Kim, *J. Org. Chem.*, 1965, **30**, 3705.

|| Tang and his coworkers (ref. 7) first obtained β-alkylamino-α-phenyl-α,β-unsaturated thioaldehydes by the reaction of 4-phenyl-1,2-dithiolium cation with diamines [ethylenediamine (en) and trimethylenediamine (tn)]; they used the thioaldehydes for the synthesis of tetra-azamacrocycles.