Mesoionic 1,2,5-Thiadiazolium-4-olates

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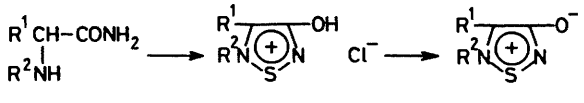
Summary α-Alkylaminophenylacetamide derivatives (**1**) reacted with sulphur monochloride followed by treatment with base to give a new mesoionic heterocyclic system, 1,2,5-thiadiazolium-4-olates (**3**).

THE synthesis of monocyclic 1,2,5-thiadiazoles is well known,[1] but mesoionic compounds belonging to this heterocyclic system have not yet been described.[2] We now report the synthesis and properties of the novel mesoionic 1,2,5-thiadiazolium-4-olates (**3**). 4-Hydroxy-3-substituted-1,2,5-thiadiazoles were readily obtained by ring closure of α-amino acid amides with thionyl chloride,[3] *N*-sulphinylaniline,[3] or more favourably sulphur monochloride.[4] When α-methylamino-α-phenylacetamide (**1a**) was treated with sulphur monochloride in dimethylformamide at 60 °C, 4-hydroxy-2-methyl-3-phenyl-1,2,5-thiadiazolium chloride (**2a**) was obtained in high yield. Treatment of the salt (**2a**) with aqueous sodium hydrogen carbonate gave the mesoionic 1,2,5-thiadiazolium-4-olate (**3a**) as yellow crystals. Since compound (**3a**) was moderately soluble in water, triethylamine was used as base instead of aqueous $NaHCO_3$. Mass spectral and elemental analysis confirmed the structure of (**3a**). Its i.r. spectrum showed carbonyl stretching at 1550 cm^{-1}, and in its ^1H n.m.r. spectrum (**3a**) exhibited a methyl singlet at δ 4·2. Treatment of (**3a**) with dilute sodium hydroxide gave α-methylimino-α-phenylacetamide, which gave the original amino acid amide (**1a**) when reduced with sodium borohydride. Similarly, the action of sodium borohydride on (**3a**) afforded directly the amide



(1) (2) (3)

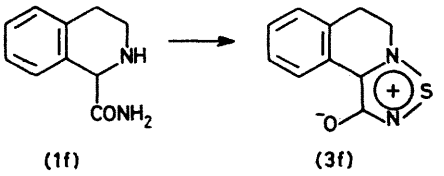
(**1a**). However, compound (**3a**) was stable to hydrochloric acid, producing its hydrochloride (**2a**). Meerwein alkylation of (**3a**) with triethyloxonium tetrafluoroborate[5] in dichloromethane gave the salt of the corresponding *O*-ethyl derivative. The new mesoionic compound (**3a**) was inactive to dipolarophiles such as dimethyl acetylenedicarboxylate.

TABLE. Preparation of mesoionic 1,2,5-thiadiazoles (**3**).

	R^1	R^2	M.p./°C	Yield[a] /%	ν_{CO}/cm^{-1} (KBr)
a	Ph	Me	174—176	58	1550
b	*p*-$MeOC_6H_4$	Me	187—189	50	1560
c	*p*-ClC_6H_4	Me	187—188	48	1580
d	Ph	C_6H_{11}	198—200	58	1570
e	*p*-ClC_6H_4	C_6H_{11}	177—178	45	1570
f	*o*-$CH_2CH_2C_6H_4$		227—228	65	1570

[a] Based on the amide (**1**).

Similarly, other α-amino acid amides (**1b**—**e**) yielded the corresponding mesoionic compounds (**3b**—**e**) as yellow crystals on reaction with sulphur monochloride and subsequent treatment with sodium hydrogen carbonate or triethylamine (Table). Benzylamino derivatives (**1**, R^2 = $PhCH_2$), however, afforded only 2-unsubstituted 4-hydroxy-1,2,5-thiadiazoles. When R^1 = alkyl in the amides (**1**), all the above reactions were unsuccessful. Furthermore, in the case of cyclic amino acid amides, 1,2,3,4-tetrahydroisoquinoline-1-carboxamide (**1f**) gave compound (**3f**), whereas



(**1f**) (**3f**)

piperidine-2-carboxamide and prolinamide failed to form the corresponding mesoionic compounds. An aromatic group at the 3-position in (**3**) appears to be essential for the stability of the mesoionic ring system.

(*Received*, 29*th December* 1978; *Com.* 1381.)

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[2] For a review see: W. D. Ollis and C. A. Ramsden, 'Advances in Heterocyclic Chemistry,' eds. A. R. Katritzky and A. J. Boulton, Academic Press, New York, vol. 19, 1976, p. 1.
[3] S. A. Mizsak and M. Perelman, *J. Org. Chem.*, 1966, **31**, 1964.
[4] L. M. Weinstock, P. Davis, B. Handelsman, and R. Tull, *Tetrahedron Letters*, 1966 ,1263; *J. Org. Chem.*, 1967, **32**, 2823.
[5] H. Meerwein, *Org. Synth.*, 1966, **46**, 113.