Reactions of *N*-(1,3-Oxathiol-2-ylidene) Tertiary Iminium Salts with Nucleophiles Containing an Amino-group[†]

By KENTARO HIRAI* and TERUYUKI ISHIBA

(*Shionogi Research Laboratory, Shionogi and Co., Ltd., Fukushima-ku, Osaka, Japan*)

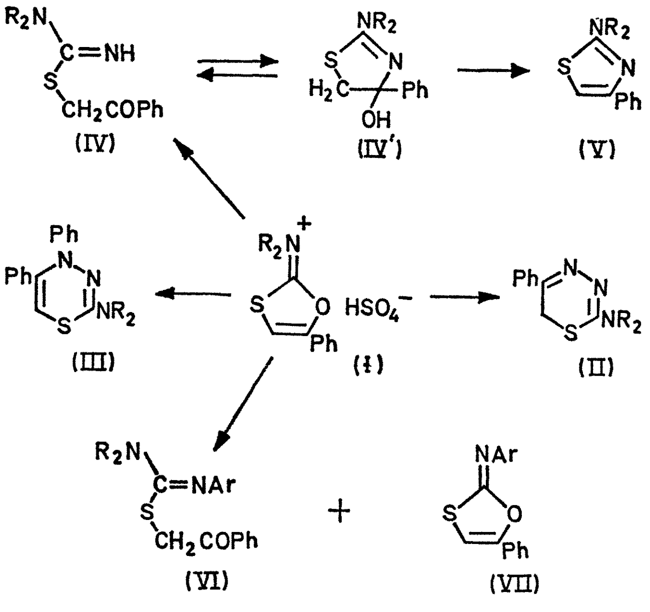
Summary Reactions of 2-immonio-1,3-oxathioles with amino-nucleophiles provide simple access to a variety of heterocyclic compounds.

THE reactions of *N*-(5-aryl-1,3-oxathiol-2-ylidene)tertiary iminium salts (I)[1–3] with active methylene compounds in the presence of base have been shown to give the ring-opened addition products,[1] 1,3-oxathiol-2-ylidenes,[1] or thiophens[4] depending on the nature of the reagents and the reaction conditions.

We now report a convenient method for the synthesis of a variety of heterocyclic compounds from (I) and nucleophiles containing an amino-group.[‡]

Reaction of (Ia) (R_2N = piperidino) with an excess of hydrazine hydrate was carried out in aqueous solution at room temperature to give 2-piperidino-5-phenyl-1,3,4-thiadiazine (II; R_2N = piperidino),[§] yellow prisms, m.p. 92—93° (96%); λ_{max} (EtOH) 226, 260, 286, and 347 nm (log ϵ 4·08, 3·99, 3·90, and 3·96); τ ($CDCl_3$) 6·47 (SCH_2). The structure was confirmed by an unequivocal synthesis from phenacyl bromide and piperidinothiosemicarbazide.[5]

A similar reaction occurred with an excess of phenylhydrazine in CH_2Cl_2 solution, from which diphenyl-1,3,4-thiadiazine (III; R_2N = piperidino), m.p. 120—123° (61%), was obtained. The spectral data of (III) are λ_{max} (EtOH) 241, and 267 nm (log ϵ 4·13, 4·30); τ ($CDCl_3$) 4·40 (SCH=).



When conc. NH_4OH was added to an aqueous solution of (Ia), crystals of (IVa) or (IV'a) (R_2N = piperidino) were obtained in 85% yield. Although analysis indicated that

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[†] A part of this work was presented at the 3rd International Congress of Heterocyclic Chemistry, Sendai, Japan, August 1971, Abstracts of the papers, p. 612.

[‡] After this work was completed, we received a personal communication from Dr. Hartmann, who obtained 2-aryl-4-amino-5-benzoylthiazole or 2-aryl-4-amino(hydroxy, phenyl)-thiophen from the reaction of 2-aryl-1,3-oxathiolium salts[3] with cyanamide or active-methylene compounds in the presence of base. (H. Hartmann, *Z. Chem.*, in the press.)

[§] All new compounds gave satisfactory elemental analyses.

Reactions of (Ia) *and arylamines* (1 : 3 *molar ratio*)

Ar	Solvent	(VI) (%)	M.p.	(VII) (%)	M.p.
Ph	CH_2Cl_2	99·5	oil	—	—
Ph	H_2O	32	—	21·6	131—133°[a]
C_6H_4-Me-*p*	CH_2Cl_2	96	43—44°	—	—
C_6H_4-Me-*p*	H_2O	56·5	—	29·6	129—131°
C_6H_4-Cl-*p*	CH_2Cl_2	88	81—83°	—	—

[a] Ref. 7, m.p. 137—138°.

these contained one H_2O more than 2-piperidino-5-phenylthiazole (Va; R_2N = piperidino), on attempted recrystallization from AcOEt the substance was readily converted into (Va), colourless prisms, m.p. 74—75°. The spectral data of (Va) are λ_{max} (EtOH) 239 and 287 nm (log ϵ 4·41 and 3·87); τ ($CDCl_3$) 3·28 (SCH=). Similarly, thiazoles (Vb) (R_2N = morpholino), m.p. 79—80°, and (Vc) (R_2N = dimethylamino) HCl salt, m.p. 182—186°, were obtained in 83—91% yield from (Ib) (R_2N = morpholino)[2] and (Ic) (R_2N = dimethylamino),[2,3] respectively. The intermediates (IVb,c or IV′b,c; R_2N = morpholino, dimethylamino) were isolated by careful treatment and converted quite readily into thiazoles (Vb,c).[6]

Reaction of (Ia) with arylamine was found to occur in two different ways, giving 2-arylimino-1,3-oxathiole (VII)[7] and ring-opened addition products (VI). In CH_2Cl_2 solution, the reaction afforded (VI) exclusively. In aqueous solution, however, (VII) was obtained accompanied by (VI).

These reactions proceed smoothly and are general in scope for heterocyclic synthesis. Initial reaction takes place between the nitrogen of the nucleophiles and the C-2 position in the 1,3-oxathiole ring to give an adduct. Loss of a proton results in C–O bond cleavage to give the imino-ketone derivative, which is immediately trapped by intramolecular addition of the amino-group to the carbonyl; the compound then suffers dehydration to afford the 1,3,4-thiadiazine or the thiazole. In the case of the weak basic arylamine, however, proton transfer to the piperidino nitrogen followed by extrusion of the piperidine molecule gave the 2-arylimino-1,3-oxathiole.

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