Dimerization of 2-Alkyl-6-methyl-4*H*-1,3-thiazin-4-ones

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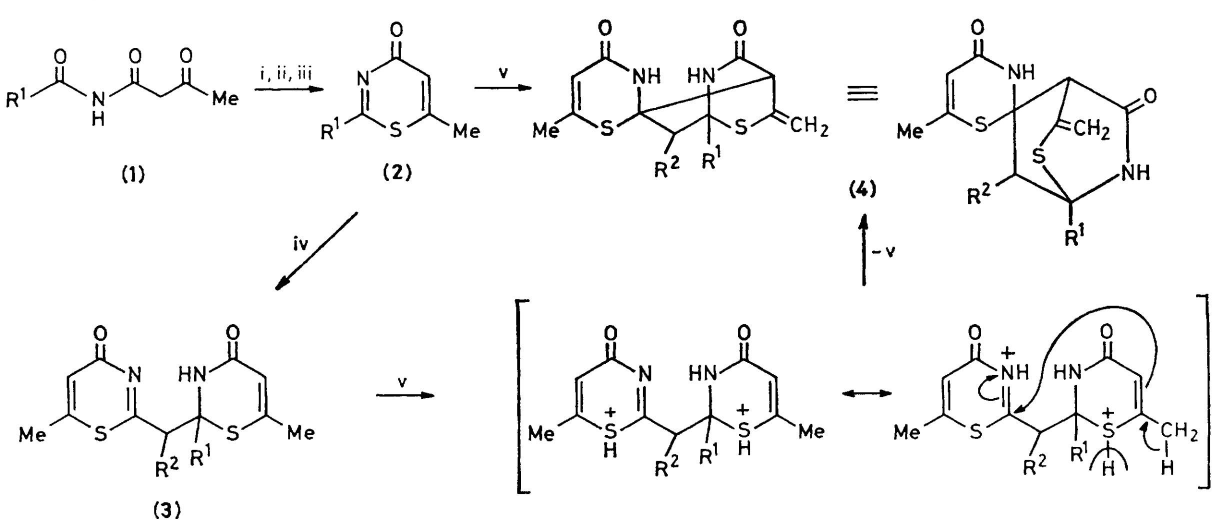
Two unusual modes of dimerization of 2-alkyl-6-methyl-4*H*-1,3-thiazin-4-ones were observed; one gave the linearly combined dimers (**3**) and the other led to the novel spiro-compound (**4**); the structure of one of the spiro-compounds (**4a**) was confirmed by *X*-ray crystallography.

During our studies on 1,3-thiazine chemistry, it was found that 2-alkyl-6-methyl-4*H*-1,3-thiazin-4-ones underwent unexpected dimerizations very readily. Here we report the unusual nature of these dimerizations and structures of the dimers obtained.

The 2-alkyl-6-methyl-4*H*-1,3-thiazin-4-ones (**2a**—**c**, R =



Scheme 1. *Reagents:* i, 70% $HClO_4$, Ac_2O, $CHCl_3$; ii, H_2S; iii, Na_2CO_3; iv, room temp. overnight; v, H^+ (CF_3CO_2H or $ClSO_3H$).

Table 1. Preparation of 2-alkyl-6-methyl-4*H*-1,3-thiazin-4-ones (**2a**—**c**).

Compound	R^1	Yield (%)	B.p., t/°C (p/Torr)
(**2a**)	Me	63	68—70 (0.04)
(**2b**)	Et	67	100—102 (0.02)
(**2c**)	Pr^n	60	100—105 (0.05)

Me, Et, Pr^n) used were prepared from the corresponding *N*-acetoacetylcarboxamides[1] and hydrogen sulphide by a previously reported method[2] (Table 1).

Dimerization of (**2**) took place spontaneously. For example, when the dimethyl compound (**2a**) was left at ambient temperature overnight, it was converted into the dimer (**3a**). Similarly, (**2b**) and (**2c**) were transformed into (**3b**) and (**3c**), respectively. The results are summarized in Table 2. The ^1H and ^{13}C n.m.r., i.r., and mass spectra are all in accordance with their formulations indicated in Scheme 1.

Conversely, treatment of (**2a**—**c**) with acids such as trifluoroacetic or chlorosulphonic acid gave rise to another type of dimer (**4a**—**c**), possessing the spiro-structure. A typical procedure was as follows: the 1,3-thiazin-4-one (**2a**) was dissolved in excess of trifluoroacetic acid, and after a few minutes at room temperature, the solution was evaporated under reduced pressure to afford (**4a**). The structure of (**4a**) was confirmed on the basis of ^1H and ^{13}C n.m.r., i.r., and mass spectra, and an *X*-ray crystallographic analysis (Figure 1).† The results are summarized in Table 2.

In addition, the dimers (**4a**—**c**) were obtained quantitatively by heating a solution of the respective dimers (**3a**—**c**) in *N*,*N*-dimethylformamide at 100 °C for 3 h in the presence of a catalytic amount of trifluoroacetic acid. The dimerization into

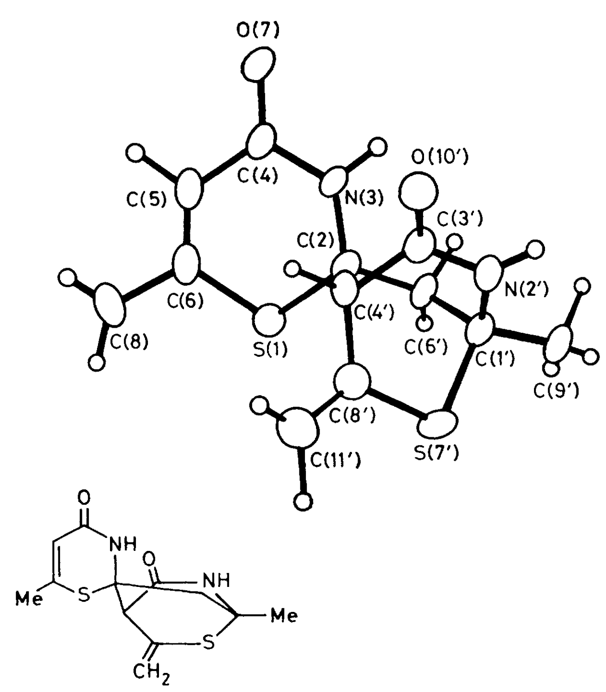


Figure 1. Molecular structure of (**4a**).

Table 2. Dimerization of 2-alkyl-6-methyl-4*H*-1,3-thiazin-4-ones (**2a**—**c**).

Compound	R^1	R^2	Yield (%)[a]	M.p., t/°C (solvent)
(**3a**)	Me	H	60	169—170 (decomp.) (C_6H_6)
(**3b**)	Et	Me	64	163—164 (decomp.) (Me_2CO)
(**3c**)	Pr^n	Et	73	179—180 (decomp.) (Me_2CO)
(**4a**)	Me	H	74	249—252 (decomp.) (EtOH)
(**4b**)	Et	Me	72	251—255 (decomp.) (EtOH)
(**4c**)	Pr^n	Et	80	248—250 (decomp.) (EtOH)

[a] All new compounds gave satisfactory microanalyses: C $\pm$ 0.28; H $\pm$ 0.16; N $\pm$ 0.30.

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† *Crystal data* for (**4a**): $C_{12}H_{14}N_2O_2S_2$, $M = 282.37$, triclinic, $a = 9.7967(3)$, $b = 9.3638(2)$, $c = 8.6754(3)$ Å, $\alpha = 115.191(4)$, $\beta = 69.548(3)$, $\gamma = 109.989(3)°$, $U = 657.01$ Å^3, space group $P\bar{1}$, $Z = 2$, $R = 0.0656$ for 2521 independent reflections (measured on a Philips PW four-circle auto-diffractometer using Cu-K_α radiation). The structure of (**4a**) was solved by direct methods using MULTAN.[3] Atomic parameters were refined by block-diagonal least-squares. Thermal parameters were refined anisotropically for all the non-hydrogen atoms and isotropically for the hydrogen atoms. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

(**4**) thus seems to involve the sequential steps shown in Scheme 1.

These dimerizations were not observed in the cases of 2-phenyl-, 2-isopropyl-, and 2-t-butyl-6-methyl-4*H*-1,3-thiazin-4-ones.

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References

1 Y. Yamamoto, S. Ohnishi, and Y. Azuma, *Synthesis*, 1981, 122.
2 Y. Yamamoto, Y. Azuma, and S. Ohnishi, *Heterocycles*, 1981, **15**, 851.
3 G. Germain, P. Main, and M. M. Woolfson, *Acta. Crystallogr., Sect. A*, 1971, **27**, 368.