General Method for the Synthesis of 2-Methylthio-3-substituted Pyrroles using Keten Dithioacetals

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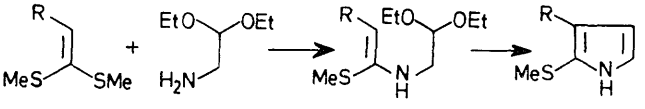
Summary The 2,3-substituted pyrroles (**4**) have been prepared by a general method by cyclization in cold ethereal HCl of the methylthio-amino-vinyl compounds (**3**), which were obtained by condensation of the keten dithioacetals (**1**) with 2,2-diethoxyethylamine (**2**).

ALTHOUGH there are several synthetic routes to pyrrole and its derivatives,[1] no method is available for the synthesis of the hitherto unknown class of pyrroles (**4**) functionalised in the 2- and 3-positions. We report here a useful synthetic route to these derivatives (**4**) from (**3**).



(1) (2) (3) (4)

a; R = PhCO
b; R = *p*-MeC_6H_4CO
c; R = *p*-$MeOC_6H_4CO$
d; R = *p*-$EtOC_6H_4CO$
e; R = *p*-ClC_6H_4CO
f; R = *p*-BrC_6H_4CO
g; R = MeCO
h; R = NO_2

In a general procedure, a solution of compound (**3a**)‡§ [prepared by the reaction of equimolar amounts of (**1a**)[2] and (**2**) in refluxing EtOH for 25—40 h] in dry ethereal HCl at 10 °C was stirred at room temperature for 1—2·5 h, to give the pyrrole (**4a**) in 62% yield. The pyrroles (**4b**—**h**)‡ were prepared similarly (Table).

TABLE

Compound	Yield/%	Compound	M.p./°C	Yield[a]/%
(**3a**)	55	(**4a**)	129—130	62
(**3b**)	59	(**4b**)	152—153	56
(**3c**)	61	(**4c**)	156—157	54
(**3d**)	57	(**4d**)	105—106	50
(**3e**)	59	(**4e**)	153—154	52[b]
(**3f**)	58	(**4f**)	160—161	50[b]
(**3g**)	61	(**4g**)	158	58
(**3h**)	62	(**4h**)	193—194	55

[a] Reaction time 1 h unless otherwise noted. [b] Reaction time 2·5 h.

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‡ All compounds were characterised by i.r., n.m.r., and mass spectral data and elemental analysis.

§ Compounds (**3a**—**h**) were oils or low melting solids, purified by passing through a silica gel column.

The method is particularly useful for the synthesis of 3-acyl or -aroyl pyrroles, since none of the known reactions of pyrroles leads to preferential substitution in the 3-position.[3] The method can also be extended to *N*-substituted pyrroles by using the appropriate compound (**2**).

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