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THERMAL REARRANGEMENT OF 3*H*-PYRROLES BY COMPETITIVE [1,5]-SIGMATROPIC SHIFTS, AND THE REVERSIBILITY OF THE 3*H*- TO 2*H*-PYRROLE INTERCONVERSION

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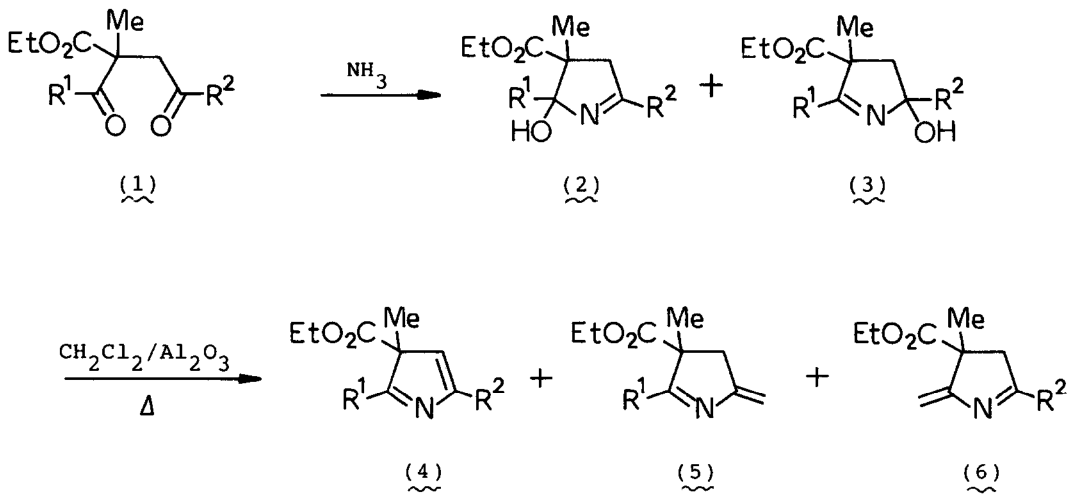
Summary: *3-Ethoxycarbonyl-3*H*-pyrroles are converted* via *thermal [1,5]-ester shifts to the isomeric 1*H*-pyrrole-4- and* N*-esters. Isolable intermediate 2*H*-pyrroles are converted into the same products, and also into the 3*H*-pyrroles, demonstrating conclusively the reversibility of the 3*H*- to 2*H*-pyrrole interconversion.*

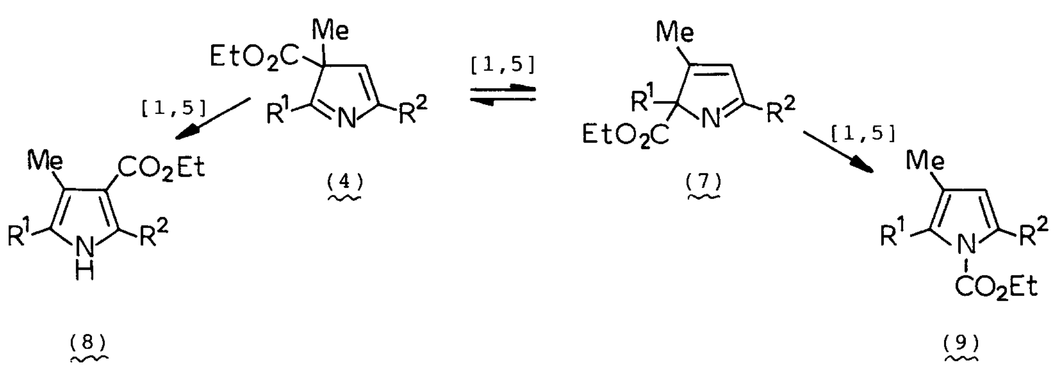
Although thermal [1,5]-sigmatropic rearrangements of 2*H*-pyrroles, to give ultimately 1*H*-pyrroles, are well documented,[1] similar rearrangements starting from 3*H*-pyrroles do not appear to have been described. While 3*H*-pyrroles are clearly unobserved intermediates in some reported rearrangements of 2*H*-pyrroles,[1a,b] and appear to be in equilibrium with the 2*H*-isomers, although at undetectably low concentrations, during Diels Alder cyclo-additions,[2] rearrangements starting from these molecules have all been reported to proceed by ionic mechanisms. Thus, McEwen and co-workers rationalised the observed products from the rearrangement of 2,3,3,5-tetra-aryl 3*H*-pyrroles in strong acid, or on fusion with potassium hydroxide, in terms respectively of cationic and anionic intermediates.[3] Further, Wong and co-workers showed by kinetics studies that the conversion of 2,3,3,4,5-penta-alkyl 3*H*-pyrroles to the 2*H*-isomers was irreversible, proceeding *via* a Wagner-Meerwein type mechanism which was catalysed by acids.[4] We have now prepared the first examples of 3*H*-pyrroles having an ester group at C-3, and report the migration of this group by competitive [1,5]-sigmatropic shifts to C-2, C-4, and N, as well as the thermal interconversion of the 3*H*- and 2*H*-pyrrole isomers.

3*H*-Pyrroles (4)[5] were prepared by dehydration of the mixture of isomeric hydroxy-pyrrolines (2) and (3), formed in turn by treatment of the diketo-esters (1) with liquid ammonia.[6] As with our earlier reported preparation of 3*H*-pyrroles by this approach,[7] isomeric methylene-pyrrolines (5) and (6) were also found when respectively R^2 and R^1 were methyl groups, and could sometimes be separated by sequential treatment by hydrochloric acid and sodium hydroxide,[7] or by rapid passage through a short alumina column, eluting with ether-light petroleum (1:2).



a; $R^1 = R^2 = Me$
b; $R^1 = Me$; $R^2 = Ph$
c; $R^1 = Ph$; $R^2 = Me$
d; $R^1 = R^2 = Ph$
e; $R^1 = Me$
f; $R^2 = Me$
g; $R^1 = Ph$
h; $R^2 = Ph$

Thermolysis of the mixed isomers (4a), (5e) and (6f)[8] in boiling dry *p*-xylene under N_2 gave after 48 h only the 1*H*-pyrroles (8a) and (9a)[9], cleanly, in high yield, and in a ratio of 8:5. In boiling toluene, the same two products were formed in the same ratio after 120 h, while after only 60 h, a mixture of (4a), (5e), (6f), (8a), (9a), and the 2*H*-pyrrole (7a) were all present by ^1H n.m.r. spectroscopy. Isolation of (7a)[10] by column chromatography (neutral Al_2O_3/benzene) and subsequent thermolysis in *p*-xylene gave a mixture of (8a) and (9a), this time in a ratio of 2:1. These results are consistent with the interconversion of (4a) and (7a) by a reversible [1,5]-ester shift, and the non reversible conversion of these respectively to (8a) and (9a).



Further corroboration comes from the thermolyses of (4b-d), and of the 2*H*-pyrrole (7b); the results are summarised in Table 1.

Table 1. Thermolyses of 3*H*-pyrroles (**4**) and 2*H*-pyrroles (**7**)

Compounds	Solvent^a	Time	(**8**):(**9**) ratio^b
(**4a**)+(**5e**)+(**6f**)	*p*-xylene	48 h	8:5
	Toluene	120 h	8:5
(**4b**)+(**6h**)	*p*-xylene	70 h	4:1
	Toluene	144 h	4:1
(**4c**)	*p*-xylene	26 h	9:1
	Toluene	144 h	9:1
(**4d**)	*p*-xylene	4 h	24:1
	Toluene	72 h	24:1
(**7a**)	*p*-xylene	48 h	2:1
(**7b**)	*p*-xylene	72 h	2:1

a) Reflux under dry N_2. b) From integrals of 90 MHz ^{1}H n.m.r. spectra.

When the thermolysis of (**7b**) was interrupted after 36 h, ^{1}H n.m.r. spectroscopy revealed the presence of the 3*H*-pyrrole (**4b**)[11] in addition to the products (**8b**) and (**9b**), establishing conclusively the reversible interconversion of the 3*H*- and 2*H*-pyrrole isomers.

The universal predominance of the 4-ester (**8**) over the *N*-ester (**9**), even from 2*H*-pyrroles (**7**), demonstrates the precedence of C → C over C → N [1,5]-sigmatropic shifts in this series, and suggests that the aromaticity in the products (**9**) must develop very late in the rearrangement.

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5. Characterised fully by i.r., ^{1}H, and ^{13}C n.m.r. spectroscopy. *E.g.* (4a) $\nu_{max.}$ (film) 1 741, 1 633, 1 588, 1 230, and 1 090 cm^{-1}, δ_H(CDCl$_3$) 1.22 (3 H, t), 1.40 (3 H, s), 2.13 (3 H, d, *J* 1.3 Hz), 2.22 (3 H, s), 4.11 (1 H, q), 4.12 (1 H, q), and 5.75 (1 H, q, *J* 1.3 Hz); δ_C(CDCl$_3$), 14.1q, 16.1q, 18.5q, 61.4t, 66.8s, 122.9d, 153.7s, 170.5s, and 182.3s.
6. All compounds were fully characterised spectroscopically, and new compounds by microanalysis, where they could be obtained pure.
7. P. K. Chiu, K. H. Lui, P. N. Maini, and M. P. Sammes, *J. Chem. Soc., Chem. Commun.*, 1987, 109.
8. Analogous mixed isomers had earlier been shown to exist in thermal equilibrium (Ref. 7).
9. δ_H(CDCl$_3$) (8a) 1.33 (3 H, t), 2.09 (3 H, s), 2.14 (3 H, s), 2.44 (3 H, s), 4.25 (2 H, q), and 8.29 (1 H, br); (9a) 1.38 (3 H, t), 1.92 (3 H, s), 2.29 (3 H, s), 2.36 (2H, s), 4.36 (2 H, s), and 5.72 (1 H, s).
10. δ_H(CDCl$_3$) 1.23 (3 H, t), 1.49 (3 H, s), 2.04 (2 H, d, *J* 1.3 Hz), 2.24 (3 H, s), 4.13 (2 H, q), and 6.03 (1 H, q, *J* 1.3 Hz).
11. δ_H(CDCl$_3$) 1.21 (3 H, t), 1.51 (3 H, s), 2.33 (3 H, s), 4.12 (1 H, q), 4.14 (1 H, q), 6.41 (1 H, s), and 7.3-7.9 (5 H, m).

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