Novel Dehydrative Ring Transformation of 1-Alkyl-3-aroylpyrrolidines into 1-Alkyl-2-aryl-3-methylpyrrole Derivatives

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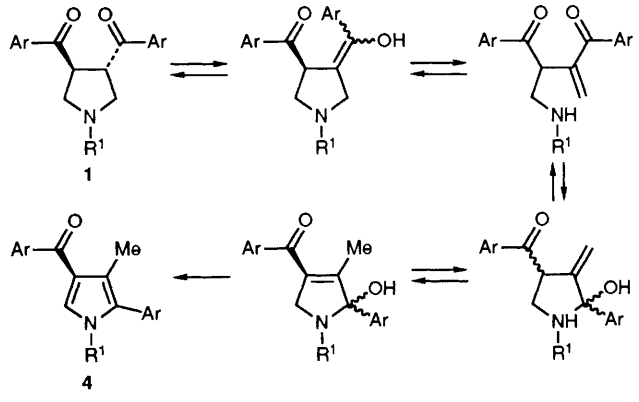
Poly-functionalized pyrroles **4**, **5** and **6** were prepared in a good to high yield by a dehydrative ring transformation of 3-aroylpyrrolidine derivatives **1**, **2** and **3** in ethylene glycol at 130 °C.

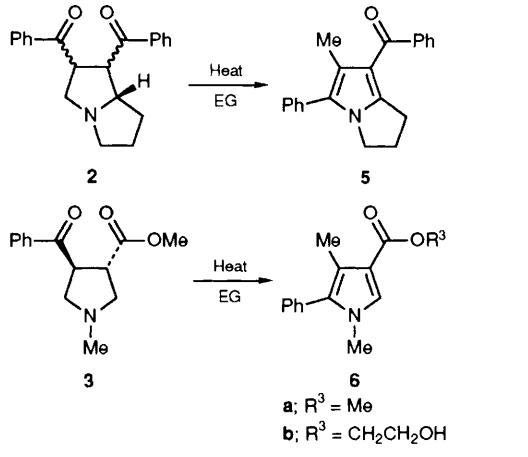
Pyrroles are an important class of heterocycle and many preparative methods have been developed.[1,2] Here we report a novel preparation of 1-alkyl-2-aryl-3-methylpyrroles by a new ring transformation of 1-alkyl-3-aroylpyrrolidines.

trans-1-Alkyl-3,4-diaroylpyrrolidines **1**† were prepared in 31–85% yields from 1,2-diaroylethylenes, paraformaldehyde and amino acids according to a method reported previously.[3] By employing cyclic amino acids, the bicyclic pyrrolidine **2** was obtained in 80% yield as a mixture (1 : 1) of two stereoisomers.‡ The *trans*-aroylpyrrolidine-4-carboxylate **3** was similarly prepared from methyl *trans*-β-benzoylacrylate in 70% yield.

When a solution of *trans*-3,4-dibenzoyl-1-methylpyrrolidine **1a** was heated under the conditions shown in Table 1, 4-benzoyl-1,3-dimethyl-2-phenylpyrrole **4a** was obtained. To our surprise, upon heating **1a** above its melting point (at 130 °C) for 30 min without any solvent, no reaction occurred, and compound **1a** was recovered quantitatively. The transformation of **1a–h** into **4a–h** proceeded smoothly in alcoholic solvents, especially in ethylene glycol as shown in Table 1.



Scheme 1 Ar = *p*-$R^2C_6H_4$



† Compounds **1–6**, which are unknown to the best of our knowledge, were characterized by elemental analysis and IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopy.

‡ The two isomers of **2** were separated by column chromatography on silica gel (Wako gel, C-300), but their stereochemistry has not yet been established. The isomer ratio was determined by ^{1}H NMR spectroscopy.

Table 1 Transformation of **1** and **4**

Compound **1**							Product **4**	
	R^1	R^2	Solvent[a]	Base[b]	Time/h	Temp./°C		Yield (%)
1a	Me	H	EG	—	0.5	130	**4a**	96
			EG	DBU	0.5	130		96
			BuOH	DBU	6	Reflux		93
			Toluene	DBU	32	Reflux		41
1b	Me	Br	EG	—	0.5	130	**4b**	73
1c	Me	Ph	EG	—	0.75	130	**4c**	76
1d	Me	Me	EG	—	0.75	130	**4d**	79
1e	Me	OBu	EG	—	1.5	130	**4e**	63
1f	$PhCH_2$	H	EG	—	2	130	**4f**	75
1g	$PhCH_2$	Br	EG	—	1.75	130	**4g**	77
1h	$PhCH_2$	Me	EG	—	3.75	130	**4h**	75

[a] EG = ethylene glycol. [b] DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

Compound **2** as a mixture of stereoisomers was heated in ethylene glycol at 130 °C for 1.5 h, producing 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]pyrrole **5** in 66% yield. Under similar conditions, **3** afforded two pyrrole esters, **6a** and **6b**, in 28 and 62% yields, respectively.

A tentative route for the conversion of **1** into **4** is shown in Scheme 1.

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