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The facile synthesis of 1,2,3-trisubstituted pyrroles from the reaction of chlorocarbenes with 1-azabuta-1,3-dienes

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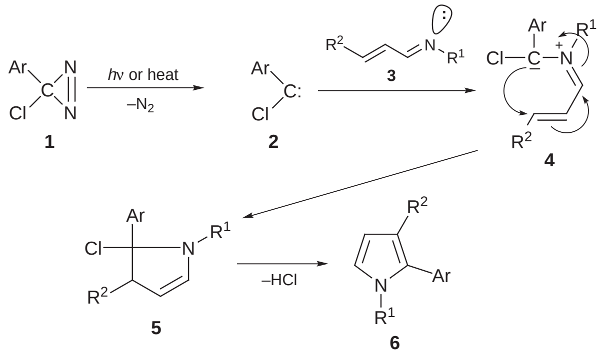
1,2,3-Trisubstituted pyrroles have been synthesized in good yield from the reaction of chlorocarbenes with 1-azabuta-1,3-dienes.

Carbenes and metal carbenoids are useful intermediates in the synthesis of nitrogen-containing heterocyclic compounds of biological importance. Most of the work has been devoted to the reactions of carbenes and metal carbenoids with azomethines that result in aziridines, pyrrolidines, oxazolidines and β-lactams.[1,2] The literature has only two examples where pyrroles appeared as the end product.[3,4] Introducing dimethyl acetylenedicarboxylate to a reaction mixture of *N*-benzylideneaniline and dichlorocarbene, generated by alkaline hydrolysis of $CHCl_3$, results in the formation of a pyrrole derivative in low yield.[3] Thermolysis of chromium carbene complexes with 1-azabuta-1,3-dienes leads to the formation of 1,2,3-trisubstituted pyrroles in good yield.[4] However, no pyrroles could be detected in the reaction of dichlorocarbene with 1-azabuta-1,3-dienes, where dichloroaziridines were isolated in high yield.[3,5] Pyrroles represent an important major class of heterocycles. Their prominence encourages the continuing evolution of new synthetic methods.[6] Our experiments produced a facile one-step synthesis of 1,2,3-trisubstituted pyrroles based on the reaction of arylchlorocarbenes with a variety of 1-azabuta-1,3-dienes under photolytic or thermal conditions.

We propose that the reaction of singlet carbene such as arylchlorocarbene with 1-azabuta-1,3-dienes goes through an azomethine ylide[3] **4** *via* a reaction between the vacant 2p-orbital of the carbene and the nitrogen non-bonding electron pair (Scheme 1). The formed ylide then undergoes intramolecular ring-closure to form a dihydropyrrole **5**, followed by HCl elimination to produce pyrroles.

The arylchlorocarbenes **2** were generated from arylchlorodiazirines **1**[7] by photolysis or thermolysis. We prepared the 1-azabuta-1,3-dienes **3** (R^1 = Me, Bn; R^2 = Me, Ph) from cinnamaldehyde or crotonaldehyde and methyl or benzyl amines. We purified them by distillation under reduced pressure. The chlorocarbenes **2** react rapidly with 1-azabuta-1,3-dienes **3** to presumably yield dihydropyrroles **5**. In all cases, the elimination of HCl from **5** to give pyrroles **6** is instantaneous since no trace of **5** could be found. Yields and melting points of pyrroles **6** are presented in Table 1 and their spectral data[8] compare well with those previously reported for **6a**,**d**.[2,6,9] The yields of pyrroles **6** obtained from photolysis (30–55%) and thermolysis (40–65%) are comparable.†



a Ar = Ph, R^1 = Me, R^2 = Ph
b Ar = *p*-MeC_6H_4, R^1 = Me, R^2 = Ph
c Ar = *p*-ClC_6H_4, R^1 = Me, R^2 = Ph
d Ar = Ph, R^1 = Bn, R^2 = Ph
e Ar = *p*-MeC_6H_4, R^1 = Bn, R^2 = Ph
f Ar = *p*-ClC_6H_4, R^1 = Bn, R^2 = Ph
g Ar = *p*-MeC_6H_4, R^1 = Bn, R^2 = Me

Scheme 1

Table 1 Isolated yields for 1,2,3-trisubstituted pyrroles **6**

					Yield (%)	
Product **6**	Ar	R^1	R^2	Mp/°C	*hν*	Heat
a	Ph	Me	Ph	96–96.5	50	54
b	*p*-MeC_6H_4	Me	Ph	95–96	51	65
c	*p*-ClC_6H_4	Me	Ph	112–113	48	52
d	Ph	Bn	Ph	116–117[a]	40	50
e	*p*-MeC_6H_4	Bn	Ph	132–133	55	58
f	*p*-ClC_6H_4	Bn	Ph	147–148	50	56
g	*p*-MeC_6H_4	Bn	Me	viscous oil	30	40

[a] Only the mp for **6d** has been reported: lit., 117–118 °C (ref. 6).

Photolyses were carried out by irradiation (350 nm) of solutions of the chlorodiazirines **1** (1 mmol) and 1-azabuta-1,3-dienes **3** (2.5 mmol) in hexane (50 ml) at 25 °C for 24 h. For the thermolysis reactions solutions of chlorodiazirines **1** (1 mmol) and the 1-azabuta-1,3-dienes **3** (2.5 mmol) were refluxed in absolute benzene (10 ml) for 3 h. After workup, the pyrroles **6** were purified by column chromatography on silica gel with hexane–Et_2O (10 : 1) as eluent, followed by crystallization from Pr^iOH–hexane (1 : 3).

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Notes and references

† All compounds reported herein gave satisfactory microanalysis data.

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8 *Selected data* for **6a**: δ_H(60 MHz, $CDCl_3$) 3.53 (3H, s), 6.46 (1H, d, *J* 3), 6.76 (1H, d, *J* 3), 7.1–7.5 (10H, m). For **6b**: δ_H (60 MHz, $CDCl_3$) 2.33 (3H, s), 3.47 (3H, s), 6.38 (1H, d, *J* 3), 6.72 (1H, d, *J* 3), 7.1–7.4 (9H, m). For **6c**: δ_H(60 MHz, $CDCl_3$) 3.48 (3H, s), 6.43 (1H, d, *J* 3), 6.76 (1H, d,

J 3), 7.1–7.5 (9H, m); m/z 267 [M^+]. For **6d**: δ_H(300 MHz, $CDCl_3$) 5.00 (2H, s), 6.50 (1H, d, J 3), 6.80 (1H, d, J 3), 7.1–7.4 (15H, m). For **6e**: δ_H(300 MHz, $CDCl_3$) 2.34 (3H, s), 5.00 (2H, s), 6.52 (1H, d, J 3), 6.78 (1H, d, J 3), 7.1–7.4 (14H, m). For **6f**: δ_H(300 MHz, $CDCl_3$) 5.00 (2H, s), 6.52 (1H, d, J 3), 6.82 (1H, d, J 3), 7.1–7.4 (14H, m). For **6g**: δ_H(300 MHz, $CDCl_3$) 2.07 (3H, s), 2.37 (3H, s), 5.00 (2H, s), 6.17 (1H, d, J 3), 6.67 (1H, d, J 3), 7.1–7.4 (9H, m).

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