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FORMATION OF PYRROLES FROM β-CHLOROAZOALKENES AND 1,3-DICARBONYL COMPOUNDS

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The azoalkenes (1) have been prepared from the corresponding hydrazones of dichloroacetaldehyde; they react with 1,3-dicarbonyl compounds to give first the addition–elimination products (4) and then pyrroles (6).

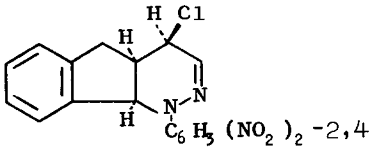
Conjugated azoalkenes are known to be susceptible to nucleophilic attack at the β-carbon atom.[1] If a potential leaving group is present at this position, an addition–elimination reaction should take place with nucleophiles (as is known with β-chloroenones, for example[2]). We have prepared several azoalkenes bearing β-chloro substituents in order to investigate the scope of this reaction, and describe here the properties of two such compounds derived from dichloroacetaldehyde.

Dichloroacetaldehyde 2,4-dinitrophenylhydrazone[3] was stirred with anhydrous sodium carbonate in dichloromethane at room temperature for 24 h. This gave the azoalkene (1a)(71%) as an orange–red crystalline solid, m.p. 73–74° C, which is stable for several months in the absence of moisture. The methoxycarbonylhydrazone[4] of dichloroacetaldehyde similarly gave the azoalkene (1b). This compound was isolated as an orange crystalline solid but the solid decomposed rapidly and it was not fully characterised. The azoalkene was, however, stable in solution for several days: its solution in carbon tetrachloride showed ν_{max} 1770 cm^{-1} (C=O), λ_{max} 412 nm, and δ 3.97 (3H), 7.46 (1H, d), and 7.78 (1H, d, *J* 12 Hz). In subsequent investigations the azoalkene (1b) was generated *in situ* from dichloroacetaldehyde methoxycarbonylhydrazone.

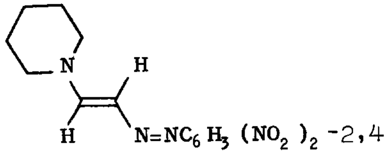
$$Cl_2CHCH{=}NNHX \xrightarrow{Na_2CO_3} ClCH{=}CHN{=}NX$$

(1) a; X = $C_6H_3(NO_2)_2$-2,4
b; X = CO_2Me

In common with several other azoalkenes,[5] these compounds give cycloadducts with olefins. For example, (1a) reacted with an excess of indene in dichloromethane (6 days, 20° C) to give the tetrahydropyridazine (2)(94%), m.p. 152—154° C.[6] They also react readily with nucleophiles by an addition—elimination sequence, an example being the rapid formation of the azoalkene (3), m.p. 153—154° C, when (1a) was treated with an excess of piperidine at room temperature.



(2)



(3)

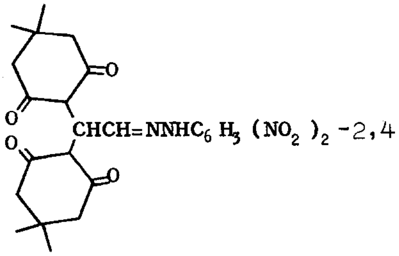
Both azoalkenes reacted readily with 1,3-dicarbonyl compounds in the presence of sodium carbonate. Adducts could be isolated in moderate yields after 6—24 h at room temperature: these were characterised as the addition—elimination products (4). Analogous reactions of dichloroacetaldehyde oxime with activated methylene compounds have recently been described by Severin and his co-workers.[7]

$$\begin{matrix}YCO\\ZCO\end{matrix}\!\!>C{=}CHCH{=}NNHX$$

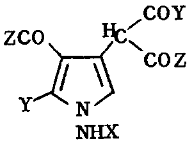
(4)

X	Y	Z	Isolated yield, %	M.p. °C
$C_6H_3(NO_2)_2$-2,4	Me	Me	65	170
CO_2Me	Me	Me	57	149—150
CO_2Me	Ph	Ph	50	125—127
CO_2Me	OEt	OEt	25	90—93

The moderate yields were in part due to the presence of a second product in each of the reaction mixtures. When the reactions were continued for several days in the presence of an excess of the 1,3-dicarbonyl compounds, these second products became the major components. They proved to be 2:1 adducts, formed by conjugate addition of a second mole of the 1,3-dicarbonyl compounds to the activated double bonds of the intermediates (4). Thus, dimedone (2 moles) gave the adduct (5)(74%), m.p. 176° C, when reacted with the azoalkene (1a)(1 mole) and sodium carbonate in dichloromethane for 4 days. This compound was cyclised to the pyrrole (6a) when warmed with ethanolic hydrochloric acid. By a similar sequence of reactions the pyrrole (6b) was formed from (1a) and ethyl acetoacetate. Acetylacetone gave the pyrroles (6c) and (6d) directly without the need for acid catalysis of the cyclisation. The structures of the pyrroles were assigned on the basis of analytical and spectroscopic data.



(5)



(6)

		X	Y	Z	Isolated yield, %	M.p. °C
(6)	a;	$C_6H_3(NO_2)_2$-2,4	$-CH_2CMe_2CH_2-$		55	235
	b;	$C_6H_3(NO_2)_2$-2,4	Me	OEt	53	111–114
	c;	$C_6H_3(NO_2)_2$-2,4	Me	Me	86	190–191
	d;	CO_2Me	Me	Me	40	151–153

The formation of 2:1 adducts is not limited to 1,3-dicarbonyl compounds as nucleophiles: products analogous to (5) were also isolated from the reactions of indole and of thiols with the azoalkene (1a). The reactions with 1,3-dicarbonyl compounds do, however, provide a simple route to pyrroles which are not readily accessible by other means. The route complements others to 1-aminopyrroles which have recently been described, and which involve either azoalkenes[9] or dialkylhydrazones of glyoxal[10] as starting materials.

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[2] A. E. Pohland and W. R. Benson, Chem. Rev., 66, 161 (1966).

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[4] This compound, m.p. 180–181° C, was prepared (66%) from dichloroacetaldehyde and methoxycarbonylhydrazine in propionic acid, the method being that used previously to prepare the tosylhydrazone [K. Bott, *Chem. Ber.*, **108**, 402 (1975)].

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[6] The isomer (2), with the stereochemistry shown, is the product expected from *endo* addition to the *E*-azoalkene. The structure is consistent with the coupling constants observed for the hydrogen atoms attached to the heterocyclic ring: $J_{3,4}$ = 3.0, $J_{4,4a}$ = 6.9, and $J_{4a,9b}$ = 7.0 Hz.

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[8] All showed signals in the ^1H n.m.r. spectra for the hydrogen atoms at the 5-positions of the pyrroles as singlets in the range 6.5–7.0 δ. e.g., (6d): δ 1.90 (6H), 2.20 (3H), 2.41 (3H), 3.78 (3H), 6.68 (1H), and 9.68 (1H).

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