MOLECULAR COMPOUNDS OF OXAZOLES WITH ACETYLENEDICARBOXYLIC ACID

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Oxazoles form with acetylendicarboxylic acid molecular compounds in the ratio 2 : 1 or 4 : 1.

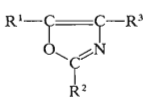
In connection with investigations on reactions of 5-benzyloxazoles with acetylenic carboxylic acids and their esters[1], the oxazoles were observed to afford individual crystalline substances when simply mixed at room temperature with acetylenedicarboxylic acid. These substances are soluble in ether, acetonitrile, and also (in contrast to acetylenedicarboxylic acid) in chloroform and tetrachloromethane, but are insoluble in water. The original idea that Diels–Alder adducts are involved (analogous to those resulting from the reaction of oxazoles with esters of acetylenedicarboxylic acid[2]) was at variance with the oxazole–acid ratio 2 : 1 (4 : 1 in the case of 4,5-diphenyloxazole) determined by elemental analysis. When dried in a high vacuum, the addition compounds of low-boiling oxazoles were observed to release gradually oxazoles. The adducts derived from oxazoles unsubstituted at position 2 were less stable than the parent oxazoles and decomposed in the course of several days to weeks with the formation of undefined tars from which only the ammonium salt of acetylenedicarboxylic acid was isolated. From the solution of adducts, acetylenedicarboxylic acid could be quantitatively extracted with aqueous sodium hydrogen carbonate while the unchanged oxazole remained in the organic solvent.

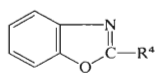
The existence of salts is excluded on the basis of IR spectra lacking bands attributable to the ionic bond; the spectra of addition compounds represent superposition of those of the two starting components. Also the UV and mass spectra were identical with those of the starting oxazoles. It may thus be inferred that the adducts are molecular compounds. This conclusion is not at variance with ^{1}H-NMR spectra despite some deviations from those of the starting components. Signals of the proton at position 2 or protons of the methyl group at position 2 were shifted downfield by about 0·05 – 0·2 ppm in the ^{1}H-NMR spectra of addition products. A similar but weaker shift was exhibited by signals of protons at positions 4 and 5 of the oxazole ring (Table I and II). In the case of 4-phenyloxazole, one singlet is formed

TABLE I
The ^{1}H-NMR and UV Spectra of Some Oxazoles

Oxazoles	^{1}H-NMR	UV
I	2·04 (s, 3 H, CH_3), 2·19 (s, 3 H, CH_3), 2·36 (s, 3 H, 2-CH_3)	λ_{max} 220 nm (ε 2 900)
II	7·38 (m, 3 H, arom), 7·75 (m, 2 H, arom), 7·95 (s, 2 H, $H_{(2)}H_{(5)}$)	λ_{max} 211 nm (ε 2 700) λ_{max} 245 nm (ε 11 000)
III	7·42 (m, 6 H, arom), 7·70 (m, 2 H, arom), 8·02 (m, 2 H, arom), 7·59 (s, H, $H_{(4)}$) (ref.[3])	λ_{min} 212 nm (ε 25 000) λ_{max} 220 nm (ε 27 000) λ_{max} 310 nm (ε 42 000)
IV	7·34 (m, 6 H, arom), 7·61 (m, 4 H, arom), 7·94 (s, H, $H_{(2)}$)	λ_{min} 212 nm (ε 13 000) λ_{max} 222 nm (ε 20 000) λ_{max} 280 nm (ε 14 000)
V	2·55 (s, 3 H, 2-CH_3), 7·34 (m, 6 H, arom), 7·60 (m, 4 H, arom)	—
VIII	1·84 (m, 4 H, CH_2), 2·55 (m, 4 H, allyl), 7·71 (s, H, $H_{(2)}$)	λ_{max} 224 nm (ε 5 200)
X	2·61 (s, 3 H, 2-CH_3), 7·18—7·50 (m, 3 H, $H_{(5,6,7)}$), 7·64 (m, H, $H_{(4)}$) (ref.[4])	ref.[5]
XI	7·20—7·60 (m, 6 H, arom), 7·75 (m, H, arom), 8·23 (m, 2 H, arom)	ref.[5]
XII	2·73 (s, 3 H, 2-CH_3), 7·23—7·95 (m, 5 H, arom), 8·45 (dd, H, arom)	—

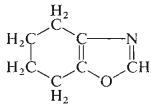
by signals of protons at positions 2 and 5 whereas two singlets may be observed in the spectrum of the corresponding addition compound. It may thus be concluded that the adducts are stable under measurement conditions ($CDCl_3$, 20°C) and do not



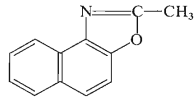


I, $R^1 = R^2 = R^3 = CH_3$
II, $R^1 = R^2 = H$, $R^3 = C_6H_5$
III, $R^1 = R^2 = C_6H_5$, $R^3 = H$
IV, $R^1 = R^3 = C_6H_5$, $R^2 = H$
V, $R^1 = R^3 = C_6H_5$, $R^2 = CH_3$
VI, $R^1 = C_6H_5$, $R^2 = H$, $R^3 = CH_2C_6H_5$
VII, $R^1 = CH_2C_6H_5$, $R^2 = H$, $R^3 = C_6H_5$

IX, $R^4 = H$
X, $R^4 = CH_3$
XI, $R^4 = C_6H_5$



VIII



XII

TABLE II

Molecular Compounds of Oxazoles and Acetylenedicarboxylic Acid

Oxazoles (ref.)	M.p., °C	^{1}H-NMR[a]		Formula (m. w.)	Calculated/Found		
					% C	% H	% N
$I_{(6)}$	96–98	2·42	(s, 3 H, 2-CH_3)	$C_{16}H_{20}N_2O_6$	57·14	5·99	8·33
				(336·3)	56·88	5·87	8·17
$II_{(7)}$	83–86	7·98	(s, H, $H_{(5)}$)	$C_{22}H_{16}N_2O_6$	65·34	3·99	6·93
		8·01	(s, H, $H_{(2)}$)	(404·4)	65·40	4·15	7·06
$III_{(8)}$	117–119	7·66	(s, H, $H_{(4)}$)	$C_{34}H_{24}N_2O_6$	73·37	4·35	5·03
				(556·6)	72·99	4·31	5·22
$IV_{(7)}$	90–91	8·09	(s, H, $H_{(2)}$)	$C_{64}H_{46}N_4O_8$[b]	76·94	4·64	5·61
				(999·0)	76·87	4·74	5·82
$V_{(9)}$	85–87	2·62	(s, 3 H, 2-CH_3)	$C_{36}H_{28}N_2O_6$	73·96	4·83	4·79
				(584·6)	73·83	4·94	5·01
$VI_{(1)}$	96–98	—		$C_{36}H_{28}N_2O_6$	73·96	4·83	4·79
				(584·6)	74·01	4·78	4·85
$VII_{(1)}$	88–91	—		$C_{36}H_{28}N_2O_6$	73·96	4·83	4·79
				(584·6)	73,93	4·88	4·95
$VIII_{(10)}$	66–68	7·93	(s, H, $H_{(2)}$)	$C_{18}H_{20}N_2O_6$	59·99	5·59	7·77
				(360·4)	59·34	5·36	7·48
$IX_{(11)}$	63–68	—		[c]		[c]	
$X_{(12)}$	64–65	2·70	(s, 3 H, 2-CH_3)	$C_{20}H_{16}N_2O_6$	63·15	4·24	7·37
				(380·3)	62·81	4·33	7·57
$XI_{(12)}$	115–117	[d]		$C_{30}H_{20}N_2O_6$	71·42	4·00	5·55
				(504·5)	70·72	4·05	5·86
$XII_{(13)}$	135–136	2·76	(s, 3 H, 2-CH_3)	$C_{28}H_{20}N_2O_6$	69·99	4·20	5·83
				(480·5)	70·01	4·42	6·21

[a] Only significant differences with respect to the ^{1}H-NMR of oxazoles are shown; [b] COOH calculated: 9·01%; found: 8·91%; [c] the analysis was not performed because of a rapid decomposition; [d] the differences are not significant.

decompose with the formation of components. Similar signal shifts of protons on aromatic substituents are more difficult to interprete because of the complexity of multiplets.

The addition compounds were prepared from several oxazoles substituted at positions 2, 4, and 5 by various combinations of alkyl and aryl groups, from benzoxazoles, and from naphthoxazole. None of the substituents used affected the formation of adducts in a negative manner. Only two oxazoles were found to be resistant towards the formation of molecular compounds, namely, 5-benzyl-4-methyloxazole (in contrast to 5-benzyl-4-phenyloxazole) and 2,4,5-triphenyloxazole.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). The UV spectra were taken on a Specord UV-VIS apparatus (Zeiss, Jena). The ^{1}H-NMR spectra were recorded in deuteriochloroform (hexamethyldisiloxane as internal standard) on a Varian HA-100 apparatus. The oxazoles and benzoxazoles were prepared by reported procedures (Table II).

4,5,6,7-Tetrahydrobenzoxazole

A solution of conc. sulfuric acid (10 g) in formamide (20 g) was added dropwise with stirring and ice-cooling into a mixture of 2-chlorocyclohexanone (22 g; 0·17 mol) in formamide (50 g). The whole mixture was gradually heated until a vigorous reaction set in (at about 60°C). The reaction was mitigated by external ice-cooling (the mixture began to deposit a crystalline slurry). The mixture was made alkaline with 20% aqueous sodium hydroxide and extracted with ether. The ethereal solution was washed with water, dried over anhydrous magnesium sulfate, evaporated, and the residue[7,10] distilled (b.p. 80—85°C/12 Torr); yield, 40%.

Preparation of Molecular Compounds

A. A mixture of the appropriate oxazole (2 mmol) and acetylenedicarboxylic acid (0·114 g; 1 mmol) was triturated on an agate dish. The initial liquefaction was followed by solidification. The yield of a crystalline powder was quantitative.

B. The appropriate oxazole (2 mmol) was added into 1M ethereal acetylenedicarboxylic acid (1 ml). The mixture was stirred (and moderately heated, if necessary) to obtain a solution which was subjected to crystallisation at −75°C.

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