TETRACYANOETHYLATION AND FISCHER REARRANGEMENT

OF SOME 4-OXO-4,5,6,7-TETRAHYDROINDOLES

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The reaction of the 1,2-diaryl-4-oxo-4,5,6,7-tetrahydroindoles, and 3-methyl-4oxo-4,5,6,7-tetrahydroindole with tetracyanoethylene occurred at the 5 position of the tetrahydroindole ring. A Fischer rearrangement of the phenylhydrazones of these 4-oxotetrahydroindoles gave pyrrolo[2,3-c]carbazoles.

Pyrroles and indoles react readily with tetracyanoethylene (TCE) with electrophilic attack by the latter at position 3 of the pyrrole ring [1-3]. However, it is known that TCE, like acrylonitrile [4], can react with alicyclic ketones by the Michael reaction to give α tetracyanoethyl derivatives [5], while tetracyanoethane reacts with carbonyl compounds to form furan derivatives [7].

In a continuation of work on the reactions of the 1,2-diary1-4-oxo-4,5,6,7-tetrahydroin-doles, which have both a pyrrole ring and an alicyclic ketone fragment [8, 9], we have studied the reaction of the indoles Ia-f with TCE.



g: $R^1 = R^3 = H$, $R^2 = C_6 H_5$

It was found that by mild heating (40-60°C) in ethyl acetate solution, the reaction was complete in two to four minutes and gave 62-88% of the tetracyanoethyl-substituted indoles IIa-f, as white or light-colored crystals, which quickly darkened in air (Table 1). When heated to 100-150°C they decomposed, so that satisfactory elemental analysis data could not be obtained.

Even on ionization by electron bombardment in the mass spectrometer, the molecular ion (M^+) of compounds IIa-f* could not always be recorded, and only the use of field desorption (FD) enabled their molecular weight to be established. Primary decay of the M⁺ ion of com-*A peak corresponding to [M-HCN]⁺ is observed in the region of greatest m/z values.

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Compound	Ri*	Decomp. temp., °C	UV spectrum (methanol),	IR spec- trum, cm ⁻¹		Mass spectrum, t m/z	*
			[^] max, nm (1g ε)	vC≔N	vC=0	(relative intensity, %)	Yield
∐a	C_6H_5	150	248 (4,44), 278 (4,23), 474 (4,02)	2240	1635	FD 415 (23), 389 (32), 388 (100)	82
11 Þ	2-CH ₃ C ₆ H ₄	120	245 (4,32), 282 (4,35), 474 (4,44)	2245	1640	429 (78), 402 (38), 375 (20), 365 (33), 364 (100), 301 (100), 245 (55), 244 (60), 230 (44), 149 (84), 91 (25)	88
Πc	3-CH₃C6H₄	120	250 (4,60), 278 (4,38), 475 (4,52)	2240	1650	429 (25), 402 (100), 400 (50), 375 (85), 364 (100), 301 (50), 273 (37), 245 (40), 244 (42), 230 (37), 115 (37)	64
Πq	4-CH₃C ₆ H₄	130	217 (4,60), 250 (4,60), 472 (4,50)	2230	1640	402 [‡] (5), 375 (9), 299 (16), 149 (18), 145 (12), 135 (19), 131 (18), 115 (20), 107 (30), 105 (50), 91 (100)	62
lle	4-BrC₀H₄	140	248 (4,41), 286 (4,19), 468 (4,45)	2220	1650	$460^{324}(27), 439(21), 365(60), 363(53), 244(26), 165(67), 149(73), 121(100), 119(87), 105(80)$	62
ΠĘ	H	110	202 (4,22), 234 (4,30), 440 (4,38)	2260 [vn -11 3400], 2225	1650	277 (23), 250 (15), 168 (10), 150 (10), 149 (20), 129 (14), 128 (100), 111 (20), 109 (15), 105 (13), 103 (100)	85

TABLE 1. Properties of 5-Tetracyanoethy1-4-oxo-4,5,6,7-tetrahydroindoles IIa-f

*IIa-e $R^2 = C_6H_5$, $R^3 = H$; IIf $R^2 = H$, $R^3 = CH_3$. +The M⁺ peak and the 10 most intense peaks are given. Ion peaks for ⁷⁹Br are given in italics. +FD: 430 [M + 1]⁺ (15), 429 M⁺ (19), 404 (10), 403 (16), 402 (100), 400 (21). **FD: 493 (100), 467 (28), 466 (25), 429 (59).

pounds IIa-f occurs primarily by the successive elimination of two molecules of HCN, or with the loss of a molecule of TCE or tetracyanoethane by a McLafferty rearrangement. This type of decay indicates the presence of a tetracyanoethyl residue at position 5 of the heterocyclic nucleus (ring system). This conclusion is supported by the fact that the 3-methyl-4-oxo-4,5, 6,7-tetrahydroindole If also reacts with TCE to give the tetracyanoethyl derivative of IIf, whereas when TCE is mixed with the previously reported 6,6-dimethyl substituted derivative of these ketones [10], the reaction does not take place, possibly because of steric hindrance, and only starting compounds are isolated from the reaction mixtures.

In the UV spectra of compounds IIa-f were observed two short-wave bands at 250 and 280 nm, characteristic of aryl pyrroles [1, 11], and one long-wave band at 468-475 nm, which is probably due to the partially ionized particle formed by strong hydrogen bonding between the acidic proton of the terminal dicyanomethyl group and the carbonyl oxygen atom. Consequently, the C=0 group stretching vibrations absorb at lower frequencies (1640-1645 cm⁻¹) than those of the ketones Ia-f (1660-1650 cm⁻¹) [10].

Conclusive proof of the position of the tetracyanoethyl group was obtained from an analysis of the NMR spectra of compounds IId and e. In addition to a multiplet from the five protons of the 2-C₆H₅ group at 7.1-7.3 ppm and, partly superimposed on this, two 2-proton doublets from the para-substituted 1-phenyl residue at 7.2-7.7 ppm in the upfield region, there was a singlet from the 3-H proton at 6.71-6.72 ppm, a three proton multiplet from the two protons of the methyl group (C(τ)) and one equatorial proton on the C(ϵ) atom at 2.7-2.9 ppm and a multiplet from one proton (6-H_a), centered at 3.30 ppm. Furthermore, in both PMR spectra there was a sharp single-proton doublet of doublets from the 5-H_a proton, since the coupling constants are 5 (axial-equatorial) and 15 Hz (axial-axial). These data confirm that the tetracyanoethyl residue in these compounds in on the 5-C atom and in the equatorial position.

It was found that the presence of methyl groups at position 6 of the 4-oxo-4,5,6,7-tetrahydroindole ring had a significant effect on reactivity, not only at position 5, but also at

Compound	mp,°C	UV spectrum (methano1), λ_{max} , nm (lg E)	IR spec- trum, V _{N-H} , cm ¹	Mass-spectrum,* m/z (rela- tive intensity, %)	Yield, † %				
III.c	175-177	200 (4,22), 228 sh (4,12), 248 (4,28), 253 (4,28), 290 (4,19), 350 sh (3,33), 432 (4,06)	3420	372 (100), 371 (17), 356 (17), 254 (20), 186 (17), 179 (20), 178 (37), 149 (33), 111 (33), 109 (30), 105 (20)	34				
1114	220—223	210 (4,33), 228 sh (4,19), 256 (4,40), 290 (4,28), 351 sh (3,37), 440 (3,08)	3415	372 (100), 371 (12), 357 (5), 356 (13), 254 (17), 253 (9), 186 (12), 149 (9), 105 (5), 91 (100),77 (3)	34				
III£	240—242	202 (4,22), 229 (4,07), 255 (4,28), 295 (4,36), 328 (4,38)	3505 3420	220 (100), 219 (82), 218 (36),205 (17), 191 (27), 190 (16), 179 (11), 178 (12), 165 (9), 164 (10), 152 (9)	21				
III8 ‡.	285—287	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	3460 3420	282 (100), 281 (23), 280 (13), 254 (9), 253 (6), 179 (6), 178 (8), 151 (7), 141 (20), 140 (12)	55				

TABLE 2. Properties of the Pyrrolocarbazoles IIIc, d, f, and g

*The M⁺ peak and the 10 most intense peaks are given. +For the reacting ketone I. +Found: C 84.9; H 5.0%. C₂₀H₁₄N₂. Calculated: C 85.1; H 5.0%.

the carbonyl group. Thus, compounds Ic, d, f, and g, which have no substituent at position 6, when heated with phenylhydrazine hydrochloride, gave, apparently, normal hydrazones (confirmed by the Fischer rearrangement to give the corresponding 1,2-dihydropyrrolo[2,3-c]carbazoles), which are readily oxidized by atmospheric oxygen to the aromatic compounds IIIc, d, f, g, isolated in yields of 21-55% (Table 2). However, the reaction mixture always contains the starting ketones, and the use of excess phenylhydrazone, or an increased reaction time does not increase the yield of the final heterocyclic compounds III. Their UV spectra were very similar to one another; in the IR spectra, there is an N-H stretching band at 3420-3415 cm⁻¹, and in the IR spectra of compounds IIIf and g, an additional band at 3460-3505 cm⁻¹. In the mass spectra of the pyrrolocarbazoles III, there are strong peaks corresponding to M⁺ and [M - H]⁺ ions, which are typical for aryl- and methylindoles [11].



Thus, 4-oxo-4,5,6,7-tetrahydroindoles can serve as suitable starting compounds for the preparative single-stage synthesis of a number of pyrrolo[2,3-c]carbazoles. However, our attempts to carry out an analogous Fischer rearrangement starting from 6,6-dimethyl-substituted 4-oxo-4,5,6,7-tetrahydroindoles were not successful. On prolonged heating in glacial acetic acid, a mixture of phenylhydrazine hydrochloride and 6,6-dimethyl-1,2-diphenyl-4-oxo-4,5,6,7-tetrahydroindole (Ig) gave an 88% yield (based on reacting ketone), of a yellow crystalline material; in the UV, this material absorbed at 402 nm, and in the IR, there was a strong conjugated C=C stretching band, and a band at 1420 cm⁻¹ which we attributed to the azo group. In the mass spectrum of this compound was observed an M⁺ peak with m/z 403; further decay of this ion corresponds well with an enazo structure for IV (see reaction scheme), and leads to the formation of [M-CH₃]⁺, [M-CH₃-C_6H₅N₂]⁺, and [M-CH₃-C_6H₅N₂-H]⁺. The formation of the enazo compound IV, instead of the usual Fischer rearrangement, is also apparently due to steric factors, caused by the geminal methyl groups at the 6 position.

EXPERIMENTAL

UV spectra were obtained on a Varian Cary (in methanol), IR spectra on a UR-20 (in mineral oil), PMR spectra on a Varian XL-100 (in deuterochloroform), using TMS as a standard. Mass spectra were run on a Varian MAT-112 at an ionization energy of 70 eV with direct introduction of the compound into the ion source. Field desorption mass spectra were obtained on a Varian MAT-212, voltage of emitter 6 kV. Preparative chromatographic separation of the compounds was carried out on Silufol UV-254 plates in ethyl acetate-hexane, 3:7; compounds were visualized in UV light.

Characteristics of compounds IIa-f and IIIc, d, f, g are given in Tables 1 and 2.

5-Tetracyanoethyl-4-oxo-4,5,6,7-tetrahydroindoles (IIa-f). To a solution of 0.7 mmoles of the ketone I and 90 mg (0.7 mmole) of TCE in 15 ml of dry ethyl acetate was added 1 drop of concentrated HCl, and the mixture stirred and heated on a water bath (40-45°C) for 2-4 min. The resulting solution was concentrated to 3-4 ml and the precipitate of II filtered off.

Pyrrolo[2,3-c]carbazoles (IIIc, d, f, g). A solution of 0.3 mmole of ketone I and 0.3 mmole of phenylhydrazine hydrochloride in 4 ml of glacial acetic acid was refluxed for 8 h, poured onto 40 g of ice, and the precipitated material separated and washed with water followed by 5% sodium hydroxide solution. After again washing with water, the produce was dried and chromatographed, the bands with R_f 0.45-0.5 yielded the starting ketone, and bands with R_f 0.8-0.9, the pyrrolocarbazole III. The latter was recrystallized from a mixture of ether and hexane (1:1).

6,6-Dimethyl-1,2-diphenyl-4-phenylazo-6,7-dihydroindole (IV) was obtained analogously from 100 mg (0.32 mmole) of ketone Ih and 46 g (0.32 mmole) of phenylhydrazine hydrochloride by refluxing for 10 h. Bands with R_f 0.9 yielded 56 mg (88%, based on the ketone) of the azo compound IV, with mp 230-232° (from a mixture of ether and hexane, 1:1). UV spectrum, λ_{max} (log ε): 250 (3.97); 296 (4.04), 402 nm (4.03). IR spectrum (CC14): 1420 ($\nu_{N=N}$), 1620 cm⁻¹ ($\nu_{C=C}$). Mass spectrum, m/z (%): 403 (33) M⁺, 402 (8), 388 (20), 298 (6), 283 (18), 180 (5), 165 (8), 149 (11), 105 (38), 91 (70), 77 (100).

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