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ADDITION REACTIONS OF HETEROCYCLES—IV
INDOLES AND NITRILIMINES

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Abstract—The reactivity of indole derivatives towards nitrilimines has been studied. Substituents at positions 1, 2 and 3 of the indole ring greatly affect the course of the reaction. 1,3-Dipolar cycloaddition products (3a,8a,dihydropyrazole-[3,4-b]-indole derivatives) and non-cyclic addition products (3-indolyl derivatives) were obtained depending on these substituents. The structures reported were assigned on the basis of satisfactory analytical, spectroscopic and chemical data.

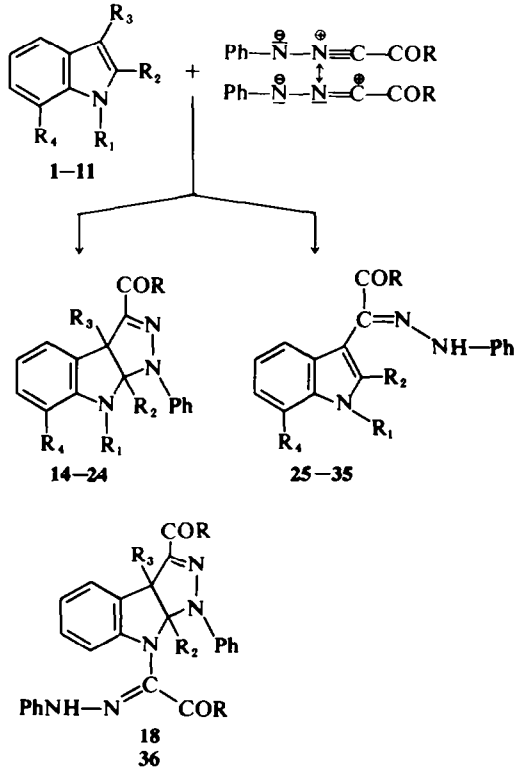
Previously[1,2] we reported that N-methylindole (**1**) reacted with the nitrilimines **12** and **13**, prepared *in situ*, to give the cycloadducts **14** and **15** together with the phenylhydrazone adducts **25** and **26**.

The formation of the phenylhydrazone adducts recalled the well known reactivity of indole derivatives towards other dienophiles;[3] however, the few cycloaddition reactions so far known where the indole nucleus acts as a dipolarophile were performed on 3-substituted indoles[4] and, moreover, were catalysed by acids.

In order to determine if the reaction between N-methylindole and nitrilimines depends on the substituents at positions **1**, **2** and **3** of the indole nucleus, we reacted the indole derivatives **1–11** with the same dipoles **12** and **13**. The results are included in Table 1† and are explained as follows.

The 1-substituted indoles with position 2 and 3 free, e.g. N-methylindole (**1**), 1,7-trimethyleneindole (**2**) and N-indolylpyruvaldehyde phenylhydrazone (**3**), yielded both the cycloadducts **14–18** and the phenylhydrazone adducts **25–29**. The presence of the latter compounds as by-products suggests that dipolar intermediates like **37** form initially and later evolve in different ways. Quantitative data concerning this point is not available at the present, but we suggest that the zwitterions like **37** only account for the formation of the phenylhydrazone adducts while the cycloadducts are formed by a concerted polycentric mechanism.[5]

Proceeding from the mechanism, it seems that a Me group at position 3 affects the reaction because of steric hindrance. In fact, the reaction between 1,3-dimethylindole (**4**) and dipole **13** gave a low yield of the cycloadduct **19**: the primary steric effect



SCHEME 1

of the Me group at position 3 rendering the interaction between the dipole and the indole nucleus less probable and resulting in self-condensation of the dipole,[6] and recovery of the indole. Moreover, the related phenylhydrazone adduct was not obtained, owing to the presence of a Me group instead of a transposable hydrogen atom at position 3.

The substituents at position 2 produced both steric and electronic effects. We observed that in-

†The reactivity of indole derivatives towards nitrilimines has been summarized only on the basis of the main products isolated, which account for 70–80% of the reagents used.

Table 1. Results of reactions between indoles and nitrilimines

	Indoles					Nitrilimines	Products of reaction (yield)		
		R_1	R_2	R_3	R_4	R	Cyclo adducts	3-indolyl derivatives	Bis-adducts
1	1	Me	H	H	H	12 OEt	**14** (35)	**25** (8)	
2	1	Me	H	H	H	13 Me	**15** (36)	**26** (13)	
3	2	*	H	H	*	12 OEt	**16** (27)	**27** (7)	
4	2	*	H	H	*	13 Me	**17** (60)	**28** (8)	
5	3	†	H	H	H	13 Me	**18** (7)	**29** (23)	
6	4	Me	H	Me	H	13 Me	**19** (4)	—	
7	5	Me	Me	H	H	12 OEt	—	**30** (63)	
8	5	Me	Me	H	H	13 Me	—	**31** (64)	
9	6	H	Me	H	H	12 OEt	—	**32** (15)	
10	6	H	Me	H	H	13 Me	—	**33** (45)	
11	7	H	C_6H_5	H	H	12 OEt	—	**34** (20)	
12	7	H	C_6H_5	H	H	13 Me	—	**35** (31)	
13	8	Me	COOMe	H	H	13 Me	**20** (35)	**38** (—)	
14	9	Me	COOEt	H	H	13 Me	**21** (45)	**39** (—)	
15	10	*	COOMe	H	*	13 Me	**22** (23)	**40** (—)	
16	11	H	H	H	H	12 OEt	**23**	—	**36** (24)
17	11	H	H	H	H	13 Me	**24**	—	**18** (30)

*R_1–R_4 = $-(CH_2)_3-$.

†R_1 = $MeCO-\overset{|}{C}=NNHC_6H_5$.

dole derivatives with position 3 free, position 1 free or substituted and position 2 carrying a methyl or phenyl group, e.g. 1,2-dimethylindole (**5**), 2-methylindole (**6**) and 2-phenylindole (**7**), gave only the phenylhydrazone adducts **30–35**, clearly indicating that the steric effect of these groups hinders the cycloaddition reaction. On the contrary, indole derivatives with position 3 free, position 1 substituted and position 2 carrying an ester group, e.g. 1-methyl-2-carbomethoxyindole (**8**), 1-methyl-2-carbethoxyindole (**9**) and 1,7-trimethylene-2-carbomethoxyindole (**10**), gave good yields* of the cycloadducts **20–22**. In these substrates, the possible steric hindrance of the ester groups is balanced by their electrondrawing effect which makes C-2 a strong electrophilic centre and therefore favours the cycloaddition reaction.

Indole itself (**11**), unique amongst the investigated substrates, gave the 1:2 adducts **18** and **36**. We believe that the cycloadducts **23** and **24** which were not isolated, are initially formed and then quickly attacked on the indoline NH group by a second molecule of the nitrilimine or by the related chlorophenylhydrazone. We found that indoline (**41**) reacts easily with α-chloro-α-(N-phenylhydrazone)acetone in the presence of triethylamine giving N-indolinylpyruvaldehyde phenylhydrazone (**42**), in full agreement with our hypothesis. We wish to remark that neither we in this work nor other authors in reactions with different dienophiles[3] have succeeded in isolating adducts at the N atom from indole substrates with position 1 free, therefore we can exclude that the 1:2 adducts **18** and **36** are formed through a process involving initial attack on the N atom; such attack in the case of the reaction of indole (**11**) with the dipole **13**, should afford a mixture of the phenylhydrazone **3**, the 1:2 adduct **18** and the non-cyclic bis-phenylhydrazone adduct **19**. Accordingly, the reaction between the dipole **13** and the indole derivative **3**† afforded not only the 1:2 adduct **18**, identical with the product obtained directly from **11**, but also the bis-phenylhydrazone adduct **19**, while some 40% of unchanged **3** was recovered.

As already[1] found for **14** and **15**, in the NMR spectra (Table 3) all the cycloadducts reported in this paper show the signals of the protons of the groups bonded to the N atom at fields substantially higher than those of the related starting indole derivatives,‡ clearly indicating the loss of the ring current of the pentatomic heterocycle. Apart from signals related to aromatic, methyl, alkoxy and acetyl protons, the spectra also exhibit signals consistent with the **3a** proton in **20–22**, with the **8a** proton in **19** and with the two *cis* **3a**, **8a** protons in

*Starting from N-unsubstituted 2-carbalkoxy-indole derivatives, we obtained quite different products which we shall refer to in a forthcoming paper.

†Prepared by dehydrogenation of N-indolinyl-pyruvaldehyde phenylhydrazone (**42**) on Pd–C, see Experimental.

‡**1**: 3·37 δ, L. A. Cohen, H. Kny and B. Witkop, *J. Am. Chem. Soc.* **82**, 2184 (1960); **2**: 3·97δ; **4**: 3·64 δ; **8**: 3·92 or 4·07 δ; **9**: 3·98 δ; **10**: 4·46 δ, all in $CDCl_3$.

Table 2. Characterization data of 3a,8a-dihydropyrazolo-[3,4-b]-indole derivatives[a] and phenylhydrazones of 3-indolyl derivatives.[a]

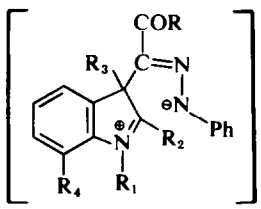
	Recrystd from[b]	M.p. (°C)	Formula	Analysis C	Found H	(Required) N	Ultraviolet[c] λ_{max}, nm (log ε)	Infrared[d] C=O	NH
16	A	143	$C_{21}H_{21}N_3O_2$	72·47 (72·60)	6·07 (6·09)	12·33 (12·10)	245, 303s, 336 (4·23, 3·89, 4·08)	1695	
17	A	181	$C_{20}H_{19}N_3O$	75·75 (75·68)	6·18 (6·03)	13·42 (13·24)	245, 301s, 352 (4·24, 3·75, 4·13)	1653	
18	B	191	$C_{26}H_{23}N_5O_2$	71·36 (71·38)	5·23 (5·30)	15·96 (16·01)	234, 294s, 350 (4·48, 3·96, 4·52)	1658	3205
19	A	206	$C_{19}H_{19}N_3O$	74·71 (74·73)	6·11 (6·27)	13·90 (13·73)	244, 298, 354 (4·30, 3·74, 4·10)	1656	
20	B	153	$C_{20}H_{19}N_3O_3$	68·83 (68·75)	5·63 (5·48)	11·96 (12·03)	244, 308, 325 (4·30, 4·04, 4·02)	1663 1739	
21	B	148	$C_{21}H_{21}N_3O_3$	69·55 (69·40)	5·62 (5·83)	11·65 (11·56)	244, 309, 325s (4·26, 3·99, 3·98)	1667 1730	
22	B	147	$C_{22}H_{21}N_3O_3$	70·22 (70·38)	5·16 (5·64)	11·41 (11·19)	249, 313, 334 (4·25, 4·07, 4·04)	1669 1739	
27	A	169	$C_{21}H_{21}N_3O_2$	72·63 (72·60)	6·13 (6·09)	12·26 (12·10)	286, 351 (4·04, 4·27)	1695	3226
28	A	163	$C_{20}H_{19}N_3O$	75·75 (75·68)	6·23 (6·03)	13·45 (13·24)	293, 365 (4·00, 4·20)	1658	3185
29	A	125	$C_{26}H_{23}N_5O_2 H_2O$	68·54 (68·55)	5·64 (5·53)	15·53 (15·38)	232, 281, 351 (4·47, 4·06, 4·60)	1653 1640	
30	A	163	$C_{20}H_{21}N_3O_2$	71·60 (71·62)	6·27 (6·31)	12·45 (12·53)	285, 341 (4·09, 4·21)	1689	3268
31	A	179	$C_{19}H_{19}N_3O$	74·65 (74·73)	6·19 (6·27)	13·67 (13·76)	283, 352 (4·04, 4·22)	1664	3247
32	A	160	$C_{19}H_{19}N_3O_2$	71·15 (71·01)	5·96 (5·96)	13·24 (13·08)	283, 340 (4·01, 4·15)	1684	3268
33	A	203	$C_{18}H_{17}N_3O$	74·23 (74·20)	5·92 (5·88)	14·51 (14·42)	282, 350 (4·01, 4·23)	1642	3226
34	A	175	$C_{24}H_{21}N_3O_2$	75·08 (75·17)	5·50 (5·52)	10·90 (10·96)	306, 340s (4·43, 4·31)	1689	3311
35	A	204	$C_{23}H_{19}N_3O$	78·24 (78·16)	5·55 (5·42)	11·81 (11·89)	306, 346s (4·44, 4·32)	1658	3236
36	A	153	$C_{28}H_{27}N_5O_4$	67·64 (67·59)	5·66 (5·47)	14·45 (14·08)	232, 291s, 336 (4·49, 4·14, 4·52)	1686 1706	3205
38	B	214	$C_{20}H_{19}N_3O_3$	68·71 (68·75)	5·42 (5·48)	12·10 (12·03)	229, 293, 348 (4·56, 4·31, 4·32)	1656 1706	3305
39	A	219	$C_{21}H_{21}N_3O_3$	69·35 (69·40)	5·65 (5·83)	11·51 (11·56)	229, 293, 347 (4·56, 4·26, 4·26)	1656 1684	3215
40	—	173	$C_{22}H_{21}N_3O_3$	70·27 (70·38)	5·55 (5·64)	11·17 (11·19)	234, 294, 347 (4·59, 4·29, 4·33)	1661 1700	3174

[a] Yellow crystals.
[b] A = ethanol, B = methanol.
[c] Ethanol.
[d] Nujol.

16–17: the last protons appear as two doublets of an AB system, this system also being present in the 1:2 adducts **18** and **36**. The chemical shift data confirmed the correctness of the assignments for 3a-H and 8a-H of **14–17**, **18** and **36** quoted in Table 3. Therefore the 3a-H signal is found at 5·13 δ in **15**, at 5·29 δ in **20**, at 5·24 δ in **21**; analogously, 3a-H appears at 5·06 δ in **17** and at 5·25 δ in **22**. On the other hand, 8a-H resounds at 6·14 δ in **15** but at 5·64 δ in **19**. Therefore, the substitution of a proton with an ester group in 8a shifts 3a-H downfield, while the substitution of a proton by a Me group in **3a** shifts 8a-H upfield. These affects on the shift induced by substituents on the neighbouring *cis* proton are also in agreement with the findings of Huisgen[7] on a series of 1,3-diphenyl-A_2-pyrazoline derivatives.

Besides the NMR data, the easy dehydrogenation of the cycloadducts **16** and **17** to **43** and **44** by chloranil in boiling xylene supports their structures.

Further proof is the acid catalysed transformation into the phenylhydrazone adducts **27–28**, identical with the products obtained directly from **2** when treated with **12** and **13**. This behaviour, already



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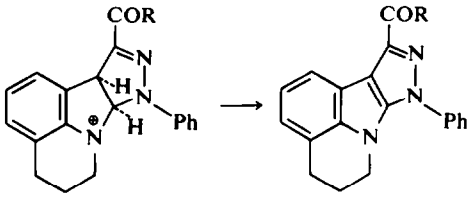

16
17

43
44

observed[1] for **14–15**, is also common to the three cycloadducts **20–22**: we obtained the phenylhydrazone adducts **37–40**, which were not isolated in the direct reaction of **8–10** with **13**. The transformation of cycloadducts into phenylhydrazone adducts is supported by the NMR spectra (Table 3): the protons of the groups bonded to the N atom are shifted downfield by restoring the ring current; moreover, signals related to 3a-H and 8a-H are missing, while a broad signal ascribed to NH appears at 8–9 δ. The shift of the last signal and its dependence on dilution[1,8] are indicative of an *anti* configuration around the phenylhydrazone C=N bond. The IR spectra (Table 2) confirm the occurrence of an NH group; the C=O stretching in the ester **38–40** obviously occurs at lower frequencies (1700 cm^{-1}) than in the related products (**20–22**). The structures of the other phenylhydrazone adducts (**30–35**) are consistent with their IR, UV and NMR spectra (Tables 2 and 3).

Table 3. NMR spectra of 3a,8a-dihydropyrazolo-[3,4-b]-indole derivatives and phenylhydrazones of 3-indolyl derivatives (δ-values, J in Hz)

14 1·34, 4·30 (t, 3H, q, 2H, CH_3—CH_2—, J = 7·1); 2·89 (s, 3H, N—CH_3); 5·04 (d, 1H, 3a-H, J = 10·0); 6·08 (d, 1H, 8a-H, J = 10·0); 6·25–7·60 (m, 9H, Ar-H).

15 2·42 (s, 3H, CH_3CO—); 2·97 (s, 3H, N—CH_3); 5·13 (d, 1H, 3a-H, J = 10·1); 6·14 (d, 1H, 8a-H, J = 10·1); 6·38–7·70 (m, 9H, Ar-H).

16 1·37, 4·32 (t, 3H, q, 2H, CH_3—CH_2—, J = 7·0); 2·57, 1·90, 3·23 (t, 2H, J = 6·0, m, 2H, t, 2H, J = 5·8, 7-CH_2—CH_2—CH_2—N); 5·02 (d, 1H, 3a-H, J = 9·7); 6·25 (d, 1H, 8a-H, J = 9·7); 6·40–7·50 (m, 8H, Ar-H).

17 2·43 (s, 3H, CH_3CO—); 2·57, 1·90, 3·30 (t, 2H, J = 6·0, m, 2H, t, 2H, J = 5·9, 7-CH_2—CH_2—CH_2—N); 5·06 (d, 1H, 3a-H, J = 9·7); 6·28 (d, 1H, 8a-H, J = 9·7); 6·40–7·50 (m, 8H, Ar-H).

18 2·46 (s, 6H, 2 × CH_3CO—); 5·40 (d, 1H, 3a-H, J = 10·5); 6·60 (d, 1H, 8a-H, J = 10·5); 6·0–7·80 (m, 14H, Ar-H); 8·60 (s, 1H, NH).

19 1·74 (s, 3H, 3a-CH_3); 2·39 (s, 3H, CH_3CO—); 2·94 (s, 3H, N—CH_3); 5·64 (s, 1H, 8a-H); 6·20–7·60 (m, 9H, Ar-H).

20 2·45 (s, 3H, CH_3CO—); 2·82 (s, 3H, N—CH_3); 3·79 (s, 3H, —$COOCH_3$); 5·29 (s, 1H, 3a-H); 6·20–7·60 (m, 9H, Ar-H).

21 1·22, 4·24 (t, 3H, q, 2H, —$COOCH_2CH_3$, J = 7·0); 2·42 (s, 3H, CH_3CO—); 2·81 (s, 3H, N—CH_3); 5·24 (s, 1H, 3a-H); 6·20–7·60 (m, 9H, Ar-H).

22 2·44 (s, 3H, CH_3CO—); 2·55, 1·84, 2·94 and 3·54 (t broad, 2H, m, 2H, 2 × m, 2H, 7-CH_2—CH_2—CH_2—N); 3·75 (s, 3H, —$COOCH_3$); 5·25 (s, 1H, 3a-H); 6·30–7·40 (m, 8H, Ar-H).

27 1·40, 4·32 (t, 3H, q, 2H, CH_3—CH_2—, J = 7·0); 3·02, 2·25, 4·20 (t, 2H, J = 6·0, m, 2H, t, 2H, J = 6·0, 7-CH_2—CH_2—CH_2—N); 6·60–7·50 (m, 9H, Ar-H); 8·52 (s, 1H, NH).

28 2·60 (s, 3H, CH_3CO—); 2·95, 2·19, 4·11 (t, 2H, J = 6·0, m, 2H, t, 2H, J = 5·6, 7-CH_2—CH_2—CH_2—N); 6·60–7·30 (m, 9H, Ar-H); 8·45 (s, 1H, NH).

29 1·86 (s, 2H, H_2O); 2·72 (s, 6H, 2 × CH_3CO—); 6·90–7·65 (m, 15H, Ar-H); 9·07 and 9·24 (2 × s, 2H, 2 × NH).

30 1·39, 4·35 (t, 3H, q, 2H, CH_3—CH_2—, J = 7·0); 2·35 (s, 3H, 2-CH_3); 3·72 (s, 3H, N—CH_3); 6·70–7·50 (m, 9H, Ar-H); 8·29 (s, 1H, NH).

31 2·24 (s, 3H, 2-CH_3); 2·65 (s, 3H, CH_3CO—); 3·67 (s, 3H, N—CH_3); 6·70–7·40 (m, 9H, Ar-H); 8·28 (s, 1H, NH).

32 1·35, 4·31 (t, 3H, q, 2H, CH_3—CH_2—, J = 7·0); 2·14 (s, 3H, 2-CH_3); 6·65–7·30 (m, 9H, Ar-H); 8·17 (s, 1H, NH); 8·70 (s, 1H, NH).

33 1·92 (s, 3H, 2-CH_3); 2·68 (s, 3H, CH_3CO—); 6·70–7·40 (m, 9H, Ar-H); 8·25 (s, 1H, NH); 8·87 (s, 1H, NH).

34 1·00, 4·05 (t, 3H, q, 2H, CH_3—CH_2—, J = 7·0); 6·65–7·50 (m, 14H, Ar-H); 8·39 (s, 1H, NH); 9·52 (s, 1H, NH).

35 2·68 (s, 3H, CH_3CO—); 6·50–7·30 (m, 14H, Ar-H); 8·27 (s, 1H, NH); 9·47 (s, 1H, NH).

36 1·47, 4·44 (q, 6H, qt, 4H, 2 × CH_3—CH_2—, J = 7·0); 5·53 (d, 1H, 3a-H, J = 10·8); 6·60 (d, 1H, 8a-H, J = 10·8); 6·33–7·85 (m, 14H, Ar-H); 8·71 (s, 1H, NH).

38 2·68 (s, 3H, CH_3CO—); 3·76 (s, 3H, —$COOCH_3$); 4·12 (s, 3H, N—CH_3); 6·75–7·60 (m, 9H, Ar-H); 8·07 (s, 1H, NH).

39 1·22, 4·21 (t, 3H, q, 2H, —$COOCH_2CH_3$, J = 7·5); 2·65 (s, 3H, CH_3CO—); 4·08 (s, 3H, N—CH_3); 6·75–7·55 (m, 9H, Ar-H); 7·98 (s, 1H, NH).

40 2·64 (s, 3H, CH_3CO—); 2·99, 2·26, 4·56 (m, 2H, m, 2H, m, 2H, 7-CH_2—CH_2—CH_2—N); 3·72 (s, 3H, —$COOCH_3$); 6·75–7·40 (m, 8H, Ar-H); 8·04 (s, 1H, NH).

EXPERIMENTAL

M.ps were determined using a Kofler hotplate and are uncorrected. IR spectra (Nujol mull) were determined on a Perkin-Elmer Infracord 137 instrument. UV spectra (95% EtOH) were determined on a Beckman DB spectrophotometer. NMR spectra (60 MHz, $CDCl_3$) were obtained using a Jeol C-60H spectrometer with TMS as internal standard.

Indole derivatives. Compounds **5**, **6**, **7**, **8** and **11** were commercial products. Compounds **2**,[9] **4**[10] and **9**[11] were prepared as described. Compounds **3** and **10**, not previously reported, are briefly described.

N-*Indolinylpyruvaldehyde phenylhydrazone* (**42**). Indoline (**41**) (1 g) and α-chloro-α-(N-phenylhydrazone)acetone (1·65 g), dissolved in dry THF (25 ml), were treated with triethylamine (3·3 ml). After 2 days, triethylamine hydrochloride (1·15 g) was filtered off and the solvent evaporated under vacuum. The residue was taken up with MeOH and **42** (2·13 g) was obtained as yellow crystals, m.p. 123° from MeOH. (Found: C, 73·20; H, 5·95; N, 15·02. $C_{17}H_{17}N_3O$ requires: C, 73·09; H, 6·13; N, 15·04%); IR: 1650 cm^{-1} (C=O), 3155 cm^{-1} (NH); NMR: 2·45 δ (s, 3H, $COCH_3$), 3·12–3·82 δ (AA'BB' system, 4H, CH_2—CH_2—N), 5·90–7·40 δ (m, 9H, Ar–H), 8·60 δ (s, 1H, NH).

N-*Indolylpyruvaldehyde phenylhydrazone* (**3**). A soln of **42** (3 g) in xylene (150 ml) was heated under reflux for 3 hr in the presence of 10% Pd–C. The catalyst was filtered off, the solvent evaporated under vacuum and the residue chromatographed on silica gel (300 g). The light petroleum benzene 1:1 (1000 ml) and benzene (1000 ml) fractions were discarded and the benzene-EtOAc 3:2 fractions yielded **3** (2·12 g) as yellow crystals, m.p. 125° from MeOH. (Found: C, 73·50; H, 5·39; N, 15·15. $C_{17}H_{15}N_3O$ requires: C, 73·63; H, 5·45; N, 15·15%); IR: 1664 cm^{-1} (C=O), 3175 cm^{-1} (NH); UV: λ_{max} 275, 284s, 345 nm (log ε 3·93, 3·84, 4·30); NMR: 2·60 δ (s, 3H, $COCH_3$), 6·66 δ (q, 1H, H-3, $J_{2,3} = 3·4$ Hz, $J_{3,7} = 0·7$ Hz), 6·70–7·80 δ (m, 10H, Ar–H), 8·10 δ (s, 1H, NH).

1,7-*Trimethylene-2-caromethoxy-indole* (**10**). A suspension of 1,7-trimethyleneindole-2-carboxylic acid[9] in ether was treated with ethereal diazomethane. The product was cromatographed on silica gel (eluent benzene) to give **10**, m.p. 56–57°. (Found: C, 72·56; H, 6·05; N, 6·45. $C_{13}H_{13}NO_2$ requires: C, 72·54; H, 6·09; N, 6·51%); IR: 1692 cm^{-1} (C=O); NMR: 2·90, 2·14, 4·45 δ (t, 2H, J = 6·0 Hz; m, 2H; m, 2H; CH_2—CH_2—CH_2—N), 3·81 δ (s, 3H, $COOCH_3$), 7·08 δ (s, 1H, H-3) 6·80–7·55 δ (m, 3H, Ar–H).

Reaction of indole derivatives with nitrilimines, general procedure. All the reactions were performed on 1 g of indole derivative dissolved in 25 ml dry THF. The stoichiometric amount of ethyl α-chloro-α-(N-phenylhydrazone)acetate or α-chloro-α-(N-phenylhydrazone)acetone and a threefold excess of triethylamine were added. The soln was left at room temp under N_2 for 30 days, triethylamine hydrochloride was filtered off and the solvent was evaporated under vacuum. In some cases, the residue was chromatographed directly on 200 g of neutral alumina (Woelm, act. 1); in other cases the residue was taken up with 20 ml of a suitable solvent, the insoluble part underwent fractional crystallization while the soluble part was chromatographed; this last chromatography was omitted when it resulted in supplying poor amounts of phenylhydrazone or cyclic adducts. The eluents were used in the following order: cyclohexane, cyclohexane-benzene, benzene, benzene-EtOAc in increasing ratios. From all the reaction subjected to chromatography, we isolated variable amounts of unreacted indole derivatives, of dimerization products from **12** and **13**,[6] and minor amounts of unidentified products.

Reaction No 3. The residue was taken up in EtOH (20 ml): the insoluble part (0·8 g) yielded **16** (0·6 g) and **27** (0·15 g) by fractional crystallization: the soluble part is a complex mixture which gave small additional amounts of **27** by chromatography (eluent benzene-EtOAc 98:2).

Reaction No 4. EtOH was added to the residue: the insoluble part (1·45 g) yielded **17** (1·22 g) and **28** (0·16 g) by fractional crystallization.

Reaction No 5. The residue was chromatographed directly: benzene-EtOAc 99:1 eluted **18** (0·11 g), then benzene-EtOAc 98:2 gave **29** (0·36 g).

Reaction No 6. Direct chromatography yielded **19** (0·07 g), eluent cyclohexane-benzene 3:2.

Reaction No 7. After addition of EtOH, **30** (1·45 g) was obtained.

Reaction No 8. After addition of EtOH, **31** (1·35 g) was obtained.

Reaction No 9. After addition of EtOH, **32** (0·15 g) was obtained. The EtOH-soluble fraction was chromatographed: benzene-EtOAc 98:2 eluted **32** (0·17 g) and then 2-methyl-2,3'-(methylindolyl)indoxyl[12] (0·1 g).

Reaction No 10. After addition of EtOH, **33** (1 g) was obtained.

Reaction No 11. The residue was chromatographed directly: benzene-EtOAc 98:2 eluted **34** (0·40 g).

Reaction No 12. The addition of EtOH yielded a mixture (1 g) of **7** and **35**, which gave **35** (0·57 g) by chromatography (eluent benzene-EtOAc 98:2).

Reaction No 13. EtOH was added: the mixture obtained (1·1 g) of **8** and **20** gave **20** (0·64 g) by fractional crystallization.

Reaction No 14. After addition of EtOH, **21** (0·81 g) was obtained.

Reaction No 15. The residue was extracted 5 times with light petroleum and the soln evaporated under vacuum. The new residue was crystallized from MeOH giving **22** (0·38 g).

Reaction No 16. After addition of EtOH, **36** (0·36 g) was obtained. The EtOH-soluble fraction yielded another 0·15 g of **36** by chromatography (eluent benzene-EtOAc 99:1).

Reaction No 17. After addition of EtOH, **28** (0·3 g) was obtained. The EtOH-soluble fraction gave an additional 0·26 g of **18** by chromatography (eluent benzene-EtOAc 99:1).

1-*Phenyl-3-carbethoxy-7,8-trimethylenepyrazole-*[3,4b]-*indole* (**43**) and 1-*phenyl-3-acetyl-7,8-trimethylenepyrazolo-*[3,4b]-*indole* (**44**). A soln of **16** or **17** (2 mmoles) and chloranil (2 mmoles) in xylene (20 ml) was refluxed for 1 hr. The cooled soln was filtered and washed many times with 5% KOH and water until the alkaline reaction disappeared. The solvent was evaporated under vacuum and the residue crystallized from EtOH (charcoal).

From **16**, **43** was obtained (yield 80%), m.p. 129–130°. (Found: C, 73·16; H, 5·64; N, 12·20. $C_{21}H_{19}N_3O_2$ requires: C, 73·02; H, 5·55; N, 12·17%); IR: 1701 cm^{-1} (C=O); UV: λ_{max} 261, 303 nm (log ε 4·27, 4·04); NMR: 1·51 and 4·50 δ (t, 3H; q, 2H; J = 7 Hz, CH_3—CH_2—O); 2·93, 2·12, 3·95 δ (t, 2H, J = 6·0 Hz; m, 2H; t, 2H, J = 5·6 Hz; CH_2—CH_2—CH_2—N); 6·80–8·0 δ (m, 8H, Ar–H).

From **17**, **44** was obtained (yield 80%), m.p. 152–153°. (Found: C, 76·28; H, 5·31; N, 13·24. $C_{20}H_{17}N_3O$ requires: C, 76·17; H, 5·43; N, 13·33%); IR: 1664 cm^{-1} (C=O);

UV λ_{max} 264, 319 nm (log ϵ 4·19, 3·99); NMR: 2·64 δ (s, 3H, $COCH_3$); 2·82, 2·02, 3·84 δ (t, 2H, J = 6·0 Hz; m, 2H; t, 2H, J = 5·6 Hz; CH_2—CH_2—CH_2—N); 6·70–8·0 δ (m, 8H, Ar–H).

Transformation of the cyclic adducts **16**, **17**, **20**, **21** *and* **22** *into the phenylhydrazone adducts* **27**, **28**, **38**, **39** *and* **40** *by acid treatment.* The cyclic adduct (0·5 g) was dissolved in the minimum volume of hot EtOH, catalytic amounts of conc HCl were added and the soln left at room temp for 6 hr. After evaporation of the solvent under vacuum, the product obtained (quantitative yield) was crystallized from a suitable solvent (see Table 2). During the crystallization of **40**, variable amounts of new product, whose structure will be reported in a forthcoming paper, were formed. Analytical and spectroscopic data reported for **40** in Tables 2 and 3 are for a sample washed only with EtOH.

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