Heterodiene Synthesis. Part XVII.[1] Reactions of 2-Oxoindolin-3-ylidene Derivatives with Enamines: a Michael Pathway as an Alternative to 1,2- and 1,4-Cycloadditions

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The reactions of enamines with 2-oxoindolin-3-ylidene-acetates and -acetophenones have been studied. With enamines derived from aldehydes the former gave either 1,2- or 1,4-cycloaddition products, as previously described for the latter. However, both substrates gave only Michael-type adducts with enamines derived from cyclopentanone. The mechanism is discussed in terms of both frontier orbital interaction and stabilized dipolar intermediates.

We have previously [2] examined the reaction of *N*-substituted 2-oxoindolin-3-ylideneacetophenones with aldehyde-derived enamines, which gave 1,4- or 1,2-cycloadducts depending on the nature of the *N*-substituent. In polar solvents, these cycloadducts undergo ready ring opening with formation of Michael-type enamines.[3] Since these results do not agree with the reported regioselectivity of attack of ethyl 1-benzyl-2-oxoindolin-3-ylideneacetate on 1-pyrrolidinocyclopentene,[4] we have investigated the reaction of 2-oxoindolin-3-ylideneacetates and -acetophenones (1a—g) with enamines derived from aldehydes and from ketones (E1)—(E3).

Reaction of 2-Oxoindolin-3-ylideneacetates with Aldehyde-derived Enamines.—The *E*-configuration of the methyl 2-oxoindolin-3-ylideneacetates (1a—c) was assigned by comparison of their n.m.r. spectra (signals of the vinylic proton and H-4; Table 5) with previously reported values for ethyl ester (1d) [5] and acetophenone derivatives.[2]

Colourless cycloadducts were isolated under conditions similar to those used previously for oxoindolinylideneacetophenones.[2] Both i.r. (Table 1) and n.m.r. spectra (see Experimental section) support the occurrence of 1,4- and 1,2-cycloaddition for *N*-acyl and *N*-alkyl derivatives, respectively (Scheme 1).

TABLE 1

I.r. data (cm^{-1})

Compound	ν(C=C exocyclic)	ν(C=C dihydropyran)	ν(C=O lactam)	ν(C=O ester)	ν(C=O acetyl)
(1a)	1 640m		1 765s	1 705—1 716s	
(2a)	Absent		1 745s [a]		1 718s
(3a)	Absent	1 638s	Absent	1 743s	1 709s
(4a)	Absent	1 638s	Absent	1 741s	1 710s
(1b)	1 651m		1 715s [a]		
(2b)	Absent		1 690s	1 740s	
(3b)	Absent	Absent	1 715s	1 740s	
(4b)	Absent	Absent	1 705s	1 738s	
(1c)	1 648m		1 720s [a]		
(2c)	Absent		1 720s	1 746s	
(3c)	Absent	Absent	1 720s	1 748s	
(4c)	Absent	Absent	1 712s	1 732s	
(1d)	1 650m [a]		1 710s [a]		
(2d) [b]	Absent		1 705—1 735s [a]		
(3d)	Absent	Absent	1 700s	1 726s	
(4d)	Absent	Absent	1 710s	1 731s	
(4d*)	Absent	1 625m	Absent	1 727s	

[a] Broad band. [b] Film.

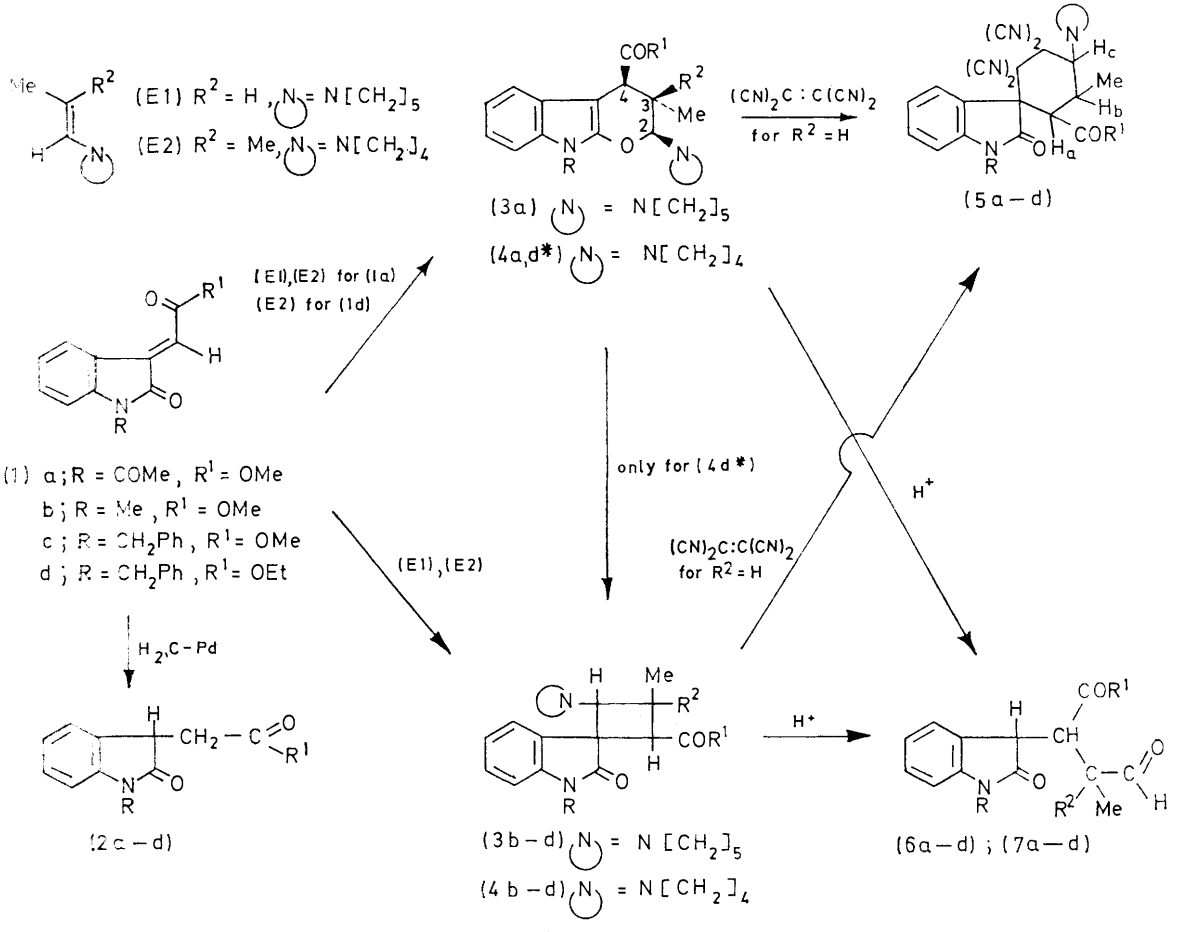
The alternative Michael structure for the adduct from

[1] Part XVI, G. Tacconi, P. P. Righetti, E. Selva, A. Coda Corsico, and G. Desimoni, *J.C.S. Perkin I*, 1976, 1248.
[2] G. Tacconi, A. Gamba, F. Marinone, and G. Desimoni, *Tetrahedron*, 1971, **27**, 561.
[3] G. Tacconi, F. Marinone, A. Gamba, and G. Desimoni, *Tetrahedron*, 1972, **28**, 1517.
[4] R. L. Autrey and F. C. Tahk, *Tetrahedron*, 1968, **24**, 3337.
[5] R. L. Autrey and F. C. Tahk, *Tetrahedron*, 1967, **23**, 901.

the β-monomethyl-substituted enamine (E1) was excluded since treatment of the adducts with tetracyanoethylene gave spiro[cyclohexaneindole]s (5), whose configurations were assigned by n.m.r. (Table 2).

Each cycloadduct gave an open-chain aldehyde on acted with 1-pyrrolidinocyclopentene (E3). Under mild conditions, colourless adducts were obtained which could sometimes be isolated in the solid state and sometimes handled in solution only (1c, d, and g).

Whereas *N*-substituents had different and sometimes



SCHEME 1

TABLE 2

N.m.r. data of the tetracyanoethylene adducts (5)

Compd.	Chemical shifts (δ) H_a	H_b	H_c	H_d	R	R^1	Aromatics	Coupling constants (Hz) J_{ab}	J_{bc}	J_{bd}
(5a)	3.3(d) [a]	3.6(m) [a]	3.17(d)	1.10(d)	COMe 2.73(s)	Me 3.38(s)	7.25—8.5(m)	10.6	11.7	5.4
(5b)	3.2(d) [b]	3.6(m) [a]	3.1(d) [b]	1.04(d)	Me 3.26(s)	Me 3.32(s)	6.8—7.8(m)	10.6	10.6	5.5
(5c)	3.24(d)	3.6(m)	3.2(d) [a]	1.08(d)	CH_2Ph δ_A 5.00, δ_B 4.89 (J_{AB} — 17.3)	Me 3.27(s)	6.7—7.8(m)	10.0	10.6	5.6
(5d)	3.25(d)	3.7(m) [c]	3.16(d)	1.08(d)	CH_2Ph δ_A 5.02, δ_B 4.88 (J_{AB} — 15.3)	Et 0.73(t), 3.79 (q) (J 6.8)	6.7—7.8(m)	10.6	11.7	6.5

[a] Partially overlapped by CO_2Me signal. [b] Partially overlapped by CO_2Me and NMe signals. [c] Overlapped by $MeCH_2{\cdot}O_2C$ signal.

hydrolytic cleavage. The close analogy of the above described behaviour with that of previously reported oxoindolinylideneacetophenones [2,3] was also exemplified in the adduct isomerization (4d*) ⟶ (4d).

Reaction with 1-*Pyrrolidinocyclopentene.*—Both oxoindolinylidene-acetates and -acetophenones (1a—g) reopposite effects on the type of heterodiene reaction with aldehyde-derived enamines, the i.r. spectra of the new adducts (Table 3) show the reaction to be independent of the *N*-substituent. Since the lactam carbonyl band is always present, a 1,4-cycloaddition can be excluded. Analogously, the presence of a new band in the enamine

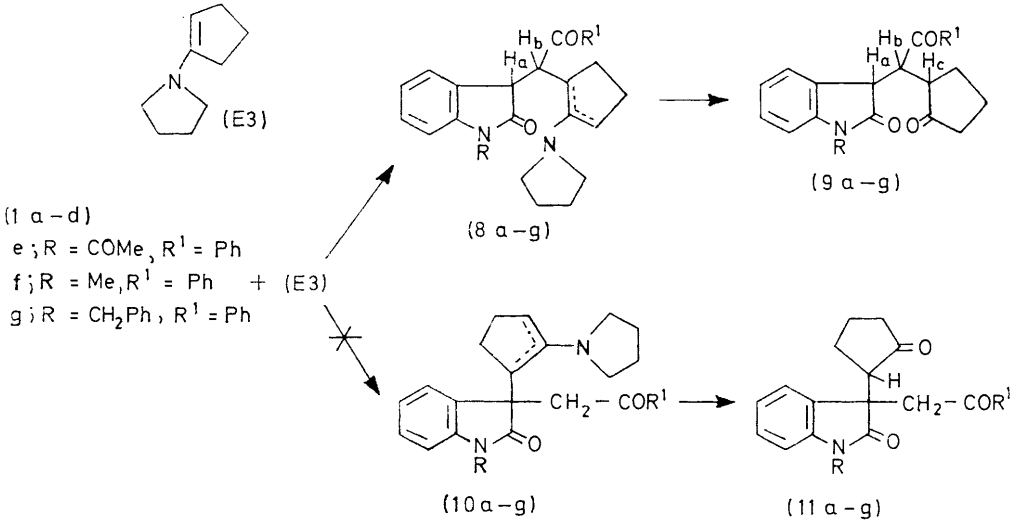
TABLE 3

I.r. spectra (cm^{-1}) of the adducts (8a—g)

Compd.	ν(C=C enamine)	ν(C=O lactam)	ν(C=O ester)	ν(C=O acetyl)
(8a)	1 633s	1 755s	1 734s	1 710s
(8b)	1 630m	1 710s	1 725s	
(8c) [a]	1 630m	1 720s	1 740s	
(8d) [a]	1 630s	1 710—1 735s [b] (ketone)		
(8e)	1 630s	1 745s	1 680s	1 704s
(8f)	1 628s	1 710s	1 675s	
(8g) [a]	1 630w	1 715s	1 679m	

[a] In spectroscopic grade benzene; NaCl cell, path length 0.10 mm, concn. 0.032M. [b] Broad band.

double bond region supports the occurrence of a Michael-type reaction, in contrast with formation of a spirocyclobutane by 1,2-cycloaddition (Scheme 2).



SCHEME 2

TABLE 4

N.m.r. data of the enamine hydrolysis products (9)

Compound	Chemical shifts (δ) H_a	H_b	H_c [a]	R	R^1	$[CH_2]_3$	Aromatic	Coupling constants (Hz) J_{ab}	J_{bc}
(9a)	4.33(d)	3.69(dd)	2.50(m)	COMe 2.64(s)	OMe 3.57(s)	1.5—2.5(m)	7.05—8.3(m)	3.9	2.7
(9b)	4.15(d)	3.85(dd)	2.52(m)	Me 3.20(s)	OMe 3.64(s)	1.2—2.7(m)	6.7—7.5(m)	4.0	4.6
(9c)	4.27(d)	3.89(dd)	2.53(m)	CH_2Ph δ_A 4.97, δ_B 4.82 (J_{AB} — 15.3)	OMe 3.62(s)	1.2—2.75(m)	6.65—7.5(m)	4.0	4.6
(9d)	4.29(d)	3.86(dd)	2.50(m)	CH_2Ph δ_A 4.93, δ_B 4.82 (J_{AB} — 14.6)	OEt 1.11(t), 4.09(q) (J 7.0)	1.2—2.8(m)	6.55—7.55(m)	4.0	4.6
(9e) Isomer (A) (66%)	4.15(d)	4.52(dd)	*b*	COMe 2.73(s)	Ph	1.1—2.6(m)	6.9—8.35(m)	2.8	8.3
(9e) Isomer (B) (34%)	3.76(d)	4.21(dd)	*b*	COMe 2.68(s)	Ph	1.1—2.6(m)	6.9—8.35(m)	2.6	8.0
(9f) Isomer (A) (63%)	3.94(d)	4.65(dd)	2.78(m)	Me 3.22(s)	Ph	1.15—2.8(m)	6.8—8.3(m)	3.3	7.1
(9f) Isomer (B) (37%)	3.55(d)	4.33(dd)	3.04(m)	Me 3.17(s)	Ph	1.15—2.8(m)	6.8—8.3(m)	2.0	10.0
(9g) Isomer (A) (74%)	4.13(d)	4.73(dd)	*b*	CH_2Ph 4.96(s)	Ph	1.15—2.8(m)	6.55—8.3(m)	3.4	6.7
(9g) Isomer (B) (26%)	3.68(d)	4.37(dd)	*b*	CH_2Ph 4.90(s)	Ph	1.15—2.8(m)	6.55—8.3(m)	2.4	10.0

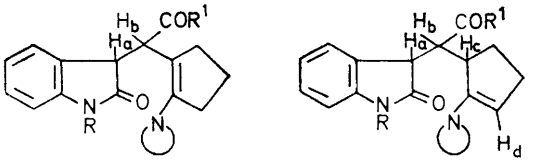
[a] Confirmed by decoupling. [b] Not determined.

Hydrolytic cleavage of all these adducts gave cyclopentanone derivatives (9a—g) in *ca.* 90% yield. N.m.r. data (Table 4) elucidated the regioselectivity of attack and made possible a decision between the regioisomeric structures (8) and (10). Owing to the presence of chiral centres a second diastereoisomer is sometimes present, but the signals for H_a, H_b, and H_c (confirmed by decoupling experiments) are only consistent with structure (9), originating from (8). Structures (10) and (11), suggested [4] for *N*-benzyl derivatives, are excluded by the double doublet nature of the H_b signal.

The n.m.r. spectra of the adducts (8) are not particularly informative even at low temperature since the ester derivatives show overlap of H_a and H_b signals. Furthermore several isomers are present owing to the presence of easily equilibrating chiral centres. Nevertheless, the spectra of a few adducts, particularly (8f,)† show the presence of at least two isomers (A and B) differing in the position of the enamine double bond. The more easily detectable isomer (A) shows H_a and H_b signals as

† A copy of the n.m.r. spectrum is available on request.

two clear doublets at δ 4.81 and 4.45. In the spectrum of isomer (B) the signal H_a seems to be partly overlapped by the signal of the same proton of the other isomer. Furthermore H_b seems to resonate at about the same chemical shift as H_d (δ 4.2), not far from the vinylic



(A) (B)

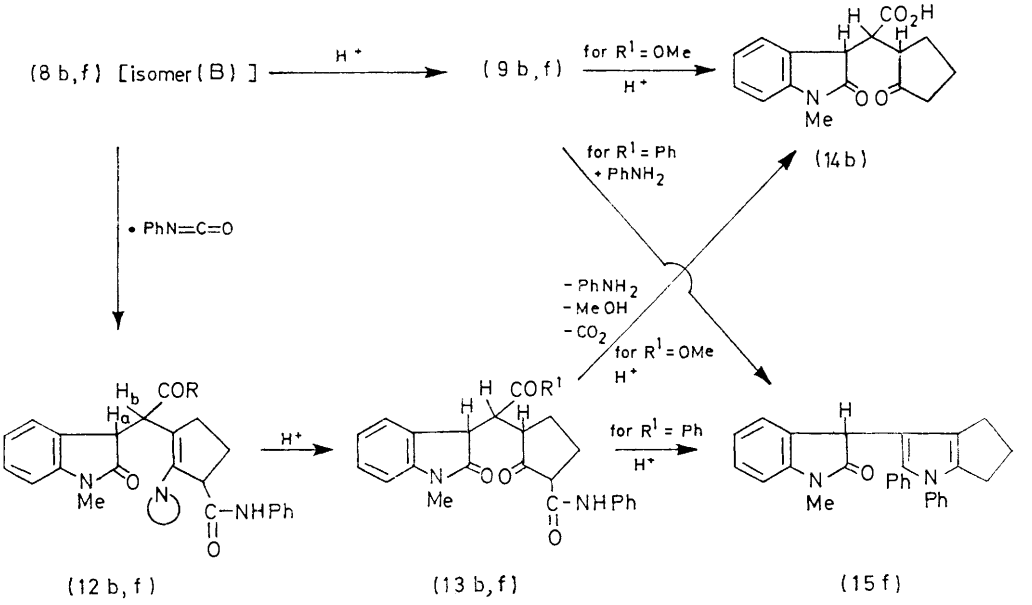
proton signal of the starting enamine.[6] Unfortunately the close proximity of H_a and H_{b-d} signals prevents unambiguous decoupling experiments. The (A) : (B) isomer distribution is roughly estimated as 3 : 2.

with the iminium function.[9] Reaction for *ca.* 24 h in the cold gives yields of 50%, but further crops, giving a total of up to 70—75%, are obtained if the mixtures are set aside for 1 week. A slow equilibration between (A) and the less highly substituted isomer (B) is invoked; this is not usual in this field,[8,10] but has been found under more severe conditions.[10]

Mild hydrolysis of compounds (12b and f) gave the ketones (13b and f), which could be related to (9b and f) through compounds (14b) and (15f) as shown in Scheme 3.

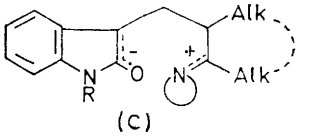
DISCUSSION

The differences in behaviour of the same substrates with aldehyde- and cyclopentanone-derived enamines can be rationalized in terms of the electronic character of the enamines. An LCAO MO calculation [11] has shown



SCHEME 3

In order to demonstrate the presence of the isomer (B) in the reaction mixture, the adducts (8b and f) were treated with phenyl isocyanate, which is known to be a useful reagent for characterizing the less highly substituted enamines.[7,8] Scheme 3 illustrates the reactions performed. Electrophilic attack of the isocyanate on isomer (B) gave the carbamoyl derivatives (12b and f). The position of the double bond in these new enamine derivatives was demonstrated by n.m.r.: the H_a and H_b signals were clear doublets at δ 4.34 and 4.71. The absence of a vinylic proton signal at about δ 4.2 excludes the possibility that the phenyl isocyanate had reacted with the more highly substituted isomer (A). The preferred elimination of H_c from isomer (B) can be rationalized in terms of better overlap of the leaving C–H bond that α-alkyl substituents increase electron density at the β-carbon atom. Therefore a cyclic enamine can act as a strong nucleophile in the overall reaction. This gives rise to a zwitterionic intermediate (C), with the positive



(C)

charge largely stabilized by the alkyl residue adjacent to the amino-group. In this case proton loss occurs more easily than ring closure, independent of the nature of the indole *N*-substituent. If the alkyl group is not present,

[6] A. G. Cook, ' Enamines,' M. Dekker, New York, 1969, p. 46.
[7] D. Pocar, R. Stradi, and B. Gioia, *Gazzetta*, 1968, **98**, 958.
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[10] F. P. Colonna, M. Forchiassin, G. Pitacco, A. Risaliti, and E. Valentin, *Tetrahedron*, 1970, **26**, 5289.
[11] M. Holik, J. Janak, and M. Ferles, *Coll. Czech. Chem. Comm.*, 1967, **32**, 3546.

a Michael reaction occurs only in polar solvents,[3] which can stabilize the zwitterion.

Another, and probably better, explanation of the difference in behaviour can be given in terms of frontier orbitals. If the αβ-unsaturated carbonyl system of the oxoindolinylidene derivative behaves as an acceptor and the enamine as a donor,[12] the dominant interaction occurs between the LUMO of the former and the HOMO of the latter. If we consider the effect of substituents on the frontier orbitals, the electron-attracting carbonyl group (CO_2R or COPh) causes a lowering of the LUMO of the oxoindolinylidene derivative. On the other hand, if the energy of the HOMO corresponds to the negative magnitude of the ionization potential (i.p.) [1-pyrrolidinocyclopentene (E3) has its first i.p. at 7.33 eV [13,14]] one can predict a lower energy value for 1-piperidinopropene (E1) from a simple substituent effect. The ββ-dimethyl-substituted 1-pyrrolidinoisobutene (E2) should have a lower i.p. than the monomethyl-substituted parent, but its value is unexpectedly high (7.66 eV [15]) owing to allylic strain between the *cis*-methyl group and the pyrrolidine α-CH_2, which hinders mesomerism.

Thus the asymmetry of the enamine coefficients [11] parallels the strong electron transfer due to orbital proximity [16] and both strongly favour a zwitterionic pathway giving rise to the intermediate (C).[17]

The dramatic effect of the electron-attracting carbonyl group on the oxoindole is conveniently shown by comparison with the reaction of 1-acetyl-3-benzylideneindolin-2-one with 1-pyrrolidinocyclohexene (i.p. 7.28 eV [18]); its absence causes the formation of the 1,4-cycloadduct only.[19]

EXPERIMENTAL

I.r. spectra were determined for Nujol mulls unless otherwise stated with a Perkin-Elmer 257 spectrophotometer. N.m.r. spectra were obtained with a Perkin-Elmer R 12A spectrophotometer ($CDCl_3$ as solvent). Microanalyses were performed by Dr. L. D. Maggi.

TABLE 5

2-Oxoindolin-3-ylideneacetates (1a—d)

Compd.	Physical aspect [yield (%)]	M.p. (°C)	Elemental analysis (%)	N.m.r.[a] :CH	N.m.r.[a] H-4
(1a)	Soft yellow needles [80]	138—140 [b]	Found: C, 63.6; H, 4.65; N, 6.9 $C_{13}H_{11}NO_4$: C, 63.65; H, 4.5; N, 5.7	6.90	8.66
(1b)	Orange needles [86]	140—141 [b]	Found: C, 66.15; H, 5.15; N, 6.45 $C_{12}H_{11}NO_3$: C, 66.35; H, 5.1; N, 6.45	6.90	8.55
(1c)	Yellow-orange needles [93]	123—124 [b]	Found: C, 73.35; H, 5.2; N, 5.0 $C_{18}H_{15}NO_3$: C, 73.7; H, 5.15; N, 4.8	7.01	8.58
(1d) [c]	Yellow-orange needles [80]	79—80 [b]		6.98 [d]	8.59 [d]

[a] Vinylic proton as sharp singlet, H-4 as less sharp doublet. [b] From ethanol. [c] Lit.,[5] m.p. 79.5—80.5° (from 75% EtOH). [d] Lit.,[5] 6.98, 8.59.

TABLE 6

2-Oxoindolin-3-ylacetates (2a—d)

Compd.	Physical aspect	M.p. (°C) or T_{subl} (°C) [p/mmHg]	Elemental analysis (%)
(2a)	White crystals	58—59 [a,b] (soft. 53)	Found: C, 62.9; H, 5.4; N, 5.75 $C_{13}H_{13}NO_4$: C, 63.15; H, 5.3; N, 5.65
(2b)	White needles	70—71 [a]	Found: C, 65.45; H, 6.1; N, 6.65 $C_{12}H_{13}NO_3$: C, 65.75; H, 6.0; N, 6.4
(2c)	Soft white needles	108—109 [c]	Found: C, 73.45; H, 5.75; N, 4.75 $C_{18}H_{17}NO_3$: C, 73.2; H, 5.8; N, 4.75
(2d)	Pale yellow oil	155—160 [0.01]	Found: C, 73.85; H, 6.35; N, 4.6 $C_{19}H_{19}NO_3$: C, 73.75; H, 6.2; N, 4.55

[a] From ethanol. [b] Dried 4 h at 80°, 0.4 mm pressure. [c] From ligroine.

2-Oxoindolin-3-ylideneacetates (1a—d).—These were prepared by the reported method [20] from the appropriate isatins [21] and methoxycarbonyl- or ethoxycarbonyl-methylenetriphenylphosphorane.[22] The products obtained are summarized in Table 5.

2-Oxoindolin-3-ylideneacetophenones (1e—g).—1-Acetyl-,[23] 1-methyl-,[24] and 1-benzyl-[2] 2-oxoindolin-3-ylideneacetophenones (1e—g) were prepared by the reported methods.

2-Oxoindolin-3-ylacetates (2a—d).—These were prepared in nearly quantitative yield by hydrogenation at room temperature and pressure of the corresponding oxoindolinyl-

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[13] R. Sustmann and H. Trill, *Angew. Chem. Internat. Edn.*, 1972, **11**, 838.
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ideneacetates (1a—d) over palladium–charcoal in ethanol (Table 6).

Reactions of the Indolinylideneacetates (1a—d) *with the Enamines* (E1) *and* (E2).—Freshly distilled 1-piperidinopropene (E1) [25] was added to a stirred suspension of the acetate (1a—d) (1 mmol) in light petroleum (b.p. 60—80 °C; 5.0 ml). Stirring at room temperature was continued until the coloured starting material had disappeared. The white precipitate was filtered off and washed with cold light petroleum. For (1b) the solvent had to be partially evaporated off before filtration.

Freshly distilled 1-pyrrolidinoisobutene (E2) [26] and the powdered acetate (1a—d) were mixed and stirred at room temperature until a cream coloured mass had formed. This was ground with cold light petroleum and the white solid was filtered off and washed with cold light petroleum. In the case of the acetate (1d), the starting material had completely dissolved in a few minutes; the light red solution was kept at −10 °C overnight, and the product (4d) was separated by grinding the resulting white solid with cold light petroleum. When the reaction mixture was stirred at room temperature the product (4d*) separated as a white crystalline solid. A sample of (4d*) stored at −10 °C had undergone complete isomerization to (4d) after a few weeks, as shown from the i.r. spectrum.

By these methods the *spiro*[*cyclobutaneindolin*]*ones* (1,2-cycloadducts) and the *tetrahydropyrano*[2,3-b]*indoles* (1,4-cycloadducts) reported in Table 7 were obtained. Satisfactory elemental analyses were obtained from crude samples dried for 2 h at room temperature and 0.1 mmHg. The n.m.r. spectrum of (3a) at −20 °C showed δ 4.48 (1 H, d, $J_{2,3}$ 9.6 Hz, 2-H), 3.44 (1 H, d, $J_{3,4}$ 10.6 Hz, 4-H), 1.05 (3 H, d, J 6.5 Hz, 3-Me), 3.72 (3 H, s, CO_2Me), 2.55 (3 H, s, NAc), and 6.9—8.5 (4 H, m, ArH) (3-H signal overlapped by signals of piperidine).

Reactions of the Cycloadducts (3a—d) *with Tetracyanoethylene.*—To a cooled and stirred solution of tetracyanoethylene (0.128 g, 1 mmol) in ethyl acetate (4.0 ml), the adduct (3a—d) (1 mmol) was added rapidly, and after a few minutes white crystalline products began to precipitate. The suspension was stirred for 10—30 min and the solid was filtered off and washed with ethyl acetate. For (3a), a small amount of cold light petroleum was added after 30 min and the solid was filtered off and washed with light petroleum. Correct elemental analyses were obtained from crude samples dried for 5 h at room temperature and 0.1 mmHg. Yields, m.p.s, reaction times, elemental analyses, and i.r. spectra of the isolated *adducts* (5a—d) are summarized in Table 8.

Hydrolytic Cleavage of the Cycloadducts (3a—d) *and* (4a—d).—The adduct (3a—d) or (4a—d) (2 mmol) was added to cooled, stirred, dilute acetic acid. Cooling and stirring were continued for the time reported in Table 9, a large amount

TABLE 7

Cycloadducts from compounds (1a—d) with aldehyde-derived enamines

Compd.	Enamine	React. time [ratio (mmol) of (1) to (E1) or (E2)]	Type of cycloaddn.	M.p. (°C) [yield (%)]	Elemental analysis (%)
(3a)	(E1)	20 [a] (1 : 4)	1,4	95—97 [b] [95]	Found: C, 68.0; H, 7.15; N, 7.8 $C_{21}H_{26}N_2O_4$: C, 68.1; H, 7.05; N, 7.55
(4a)	(E2)	15 [a] (1 : 3)	1,4	100—102 [b] [95]	Found: C, 67.9; H, 7.05; N, 7.85 $C_{21}H_{26}N_2O_4$: C, 68.1; H, 7.05; N, 7.55
(3b)	(E1)	2 [c] (1 : 2)	1,2	80—82 [b] [65]	Found: C, 69.9; H, 7.65; N, 8.55 $C_{20}H_{26}N_2O_3$: C, 70.15; H, 7.65; N, 8.2
(4b)	(E2)	30 [a] (1 : 6)	1,2	76 [b] [81]	Found: C, 69.95; H, 7.65; N, 8.2 $C_{20}H_{26}N_2O_3$: C, 70.15; H, 7.65; N, 8.2
(3c)	(E1)	30 [a] (1 : 4)	1,2	88—90 [b] [71]	Found: C, 74.7; H, 7.25; N, 6.55 $C_{26}H_{30}N_2O_3$: C, 74.6; H, 7.25; N, 6.7
(4c)	(E2)	30 [a] (1 : 5)	1,2	120—121 [b] [93]	Found: C, 74.3; H, 7.15; N, 7.1 $C_{26}H_{30}N_2O_3$: C, 74.6; H, 7.25; N, 6.7
(3d)	(E1)	10 [a] (1 : 3)	1,2	102—104 [b] [79]	Found: C, 74.65; H, 7.35; N, 6.25 $C_{27}H_{32}N_2O_3$: C, 74.95; H, 7.45; N, 6.5
(4d)	(E2)	*d* (1 : 5)	1,2	66—68 [b] [65]	Found: C, 74.7; H, 7.5; N, 6.7 $C_{27}H_{32}N_2O_3$: C, 74.95; H, 7.45; N, 6.5
(4d*)	(E2)	*d* (1 : 5)	1,4	75—77 [b] [69]	Found: C, 75.2; H, 7.6; N, 6.5 $C_{27}H_{32}N_2O_3$: C, 74.95; H, 7.45; N, 6.5

[a] Min. [b] Crude sample dried 2 h at room temperature and 0.1 mmHg. [c] Hours. [d] See text.

TABLE 8

Spiro[cyclohexaneindolin]ones from compounds (3—d) with tetracyanoethylene

Compd.	M.p. (°C) [yield (%)]	React. time	Elemental analysis (%)	I.r. ν(C=N)	I.r. ν(C=O lactam)	I.r. ν(C=O ester)	I.r. ν(C=O acetyl)
(5a)	113—115 [a] [80]	30 [b]	Found: C, 65.05; H, 5.25; N, 16.9 $C_{27}H_{26}N_6O_4$: C, 65.05; H, 5.25; N, 16.85	2 250w	1 760s	17 30s [c]	
(5b)	139—140 [a] [83]	10 [b]	Found: C, 66.5; H, 5.8; N, 17.9 $C_{26}H_{26}N_6O_3$: C, 66.35; H, 5.55; N, 17.85	2 250w	1 725s	1 748s	
(5c)	139—140 [a] [92]	10 [b]	Found: C, 69.95; H, 5.6; N, 15.5 $C_{32}H_{30}N_6O_3$: C, 70.3; H, 5.55; N, 15.4	2 250w	1 730s	1 741s	
(5d)	141—142 [a] [90]	10 [b]	Found: C, 70.25; H, 5.8; N, 15.1 $C_{33}H_{32}N_6O_3$: C, 70.7; H, 5.75; N, 15.0	2 255w	1 728s	1 735s	

[a] Crude sample dried 5 h at room temperature and 0.1 mmHg. [b] Min. [c] Broad band.

[25] G. Opitz, M. Hellmann, and H. W. Schubert, *Annalen*, 1959, **623**, 112.

[26] E. Benzing, *Angew. Chem.*, 1959, **71**, 521.

of water was added, and the emulsion was extracted with diethyl ether. The extract was washed with sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. The crystalline or oily residue was purified by crystallization or sublimation. For (3b), (4a), and (4b) the reaction mixture gave a crystalline precipitate which was filtered off after b.p. 30—60° (1 : 1; 9.0 ml)], compound (1a—g) (2 mmol) was added. Cooling and stirring were maintained until the starting material had disappeared and a pale yellow precipitate had formed (30—40 min). The solid was filtered off and washed with cold light petroleum. All adducts could be stored at low temperature; correct elemental analyses

TABLE 9

Hydrolytic cleavage of the adducts (3a—d) and (4a—d)

Compd.	Physical aspect [yield (%)]	AcOH (ml)	H_2O (ml)	React. time	M.p. (°C) or T_{subl} (°C) [p/mmHg]	Elemental analysis (%)
(6a)	White crystals [78]	40	16	30 [a]	112—114 [b]	Found: C, 63.3; H, 5.85; N, 4.8 $C_{16}H_{17}NO_5$: C, 63.35; H, 5.65; N, 4.6
(6b)	White crystals [75]	22	8	30 [a]	89—91 [c]	Found: C, 65.1; H, 6.25; N, 5.25 $C_{15}H_{17}NO_4$: C, 65.45; H, 6.2; N, 5.1
(6c)	Pale yellow oil [60]	25	10	20 [a]	135—140 [0.10]	Found: C, 71.25; H, 6.05; N, 4.4 $C_{21}H_{21}NO_4$: C, 71.8; H, 6.0; N, 4.0
(6d)	Pale yellow oil [55]	12	3	90 [a]	145—150 [0.10]	Found: C, 72.05; H, 6.55; N, 3.75 $C_{22}H_{23}NO_4$: C, 72.3; H, 6.35; N, 3.85
(7a)	White crystals [88]	15	6	25 [a]	113—115 [b]	Found: C, 64.4; H, 6.15; N, 4.5 $C_{17}H_{19}NO_5$: C, 64.35; H, 6.05; N, 4.4
(7b)	White crystals [83]	13.5	5.5	20 [a]	97—99 [c]	Found: C, 66.0; H, 6.6; N, 5.05 $C_{16}H_{19}NO_4$: C, 66.4; H, 6.6; N, 4.85
(7c)	White crystals [90]	42	17	30 [a]	107—109 [b]	Found: C, 72.4; H, 6.4; N, 4.0 $C_{22}H_{23}NO_4$: C, 72.3; H, 6.35; N, 3.85
(7d)	Pale yellow oil [52]	8	2	90 [a]	135—140 [0.10]	Found: C, 72.7; H, 6.55; N, 3.6 $C_{23}H_{25}NO_4$: C, 72.8; H, 6.65; N, 3.7

[a] Min. [b] From ethanol. [c] From di-isopropyl ether.

TABLE 10

Reactions of the oxoindolinylidene derivatives (1) with 1-pyrrolidinocyclopentene

Compd.	Physical aspect [yield (%)]	M.p. (°C)	Elemental analysis (%)
(8a)	White crystals [73]	72—73 [a]	Found: C, 68.85; H, 7.0; N, 7.4 $C_{22}H_{26}N_2O_4$: C, 69.1; H, 6.85; N, 7.35
(8b)	White crystals [68]	66—68 [a]	Found: C, 70.85; H, 7.45; N, 7.7 $C_{21}H_{26}N_2O_3$: C, 71.15; H, 7.4; N, 7.9
(8e)	Pale yellow crystals [75]	89—91 [a]	Found: C, 75.35; H, 6.6; N, 6.5 $C_{27}H_{28}N_2O_3$: C, 75.65; H, 6.6; N, 6.55
(8f)	Pale yellow crystals [74]	81—83 [a]	Found: C, 77.95; H, 7.2; N, 7.05 $C_{26}H_{28}N_2O_2$: C, 77.95; H, 7.05; N, 7.0

[a] Crude sample dried 6 h at room temperature and 0.4 mmHg

TABLE 11

Hydrolytic cleavage of the adducts (8a—g)

Compd.	Physical aspect [yield (%)]	M.p. (°C)	Elemental analysis (%)
(9a)	Small white crystals [88]	162—163 [a] (soft. 158)	Found: C, 65.6; H, 6.05; N, 4.5 $C_{18}H_{19}NO_5$: C, 65.65; H, 5.8; N, 4.25
(9b)	Soft white needles [87]	124—125 [a]	Found: C, 68.0; H, 6.2; N, 4.65 $C_{17}H_{19}NO_4$: C, 67.75; H, 6.35; N, 4.65
(9c)	Prisms [92]	122—123 [a]	Found: C, 73.2; H, 6.3; N, 3.9 $C_{23}H_{23}NO_4$: C, 73.2; H, 6.15; N, 3.7
(9d)	Crystals [90]	153—154 [a]	Found: C, 73.5; H, 6.7; N, 3.75 $C_{24}H_{25}NO_4$: C, 73.65; H, 6.45; N, 3.6
(9e)	White crystals [92]	171—172 [a]	Found: C, 73.7; H, 5.35; N, 3.7 $C_{23}H_{21}NO_4$: C, 73.6; H, 5.65; N, 3.75
(9f)	White crystals [92]	142—143 [a] (soft. 139)	Found: C, 76.35; H, 6.2; N, 4.1 $C_{22}H_{21}NO_3$: C, 76.05; H, 6.1; N, 4.05
(9g)	White crystals [87]	174—175 [a] (soft. 172)	Found: C, 79.6; H, 6.0; N, 3.45 $C_{28}H_{25}NO_3$: C, 79.4; H, 5.95; N, 3.3

[a] From ethanol.

dilution with water. Yields, m.p.s, reaction conditions, and elemental analyses of isolated *adducts* (6) and (7) are summarized in Table 9.

Reaction of the Oxoindolinylidene Derivatives (1a—g) *with the Enamine* (E3).—To a cooled, stirred solution of 1-pyrrolidinocyclopentene (E3) [27] (2 mmol) in anhydrous diethyl ether (9.0 ml) [for (1b), diethyl ether–light petroleum, were obtained from crude samples dried for 6 h at room temperature and 0.4 mmHg. Compounds (1c, d, and g) always gave clear pale yellow solutions which were directly hydrolysed as described below. Properties of the isolated *adducts* (8) are summarized in Table 10.

[27] M. E. Kuehne, *J. Amer. Chem. Soc.*, 1959, **81**, 5400.

Hydrolytic Cleavage of the Adducts (8a—g).—To a cooled and stirred suspension of the adduct (8a, b, e, or f) (1 mmol) in diethyl ether (7.0 ml), a cooled mixture of acetic acid (2.0 ml) and water (5.0 ml) was added. For (8c, d, and g) the above-mentioned reaction solutions were used. The stirred emulsion was cooled for 2 h and then maintained at 0 °C for 48 h. The residual ether was evaporated off at room temperature and solid sodium hydrogen carbonate was cautiously added with stirring until neutralization was achieved. Stirring gradually changed the oily precipitate into a crystalline solid, which was filtered off and washed with water. All the isolated *adducts* (9) were crystallized and Table 11 summarizes their properties.

Reaction of the Adduct (8b) *with Phenyl Isocyanate*.—To a cooled and stirred suspension of (8b) (0.7 g, 2 mmol) in anhydrous diethyl ether (5.0 ml), a cooled solution of phenyl isocyanate (2 mmol) in anhydrous diethyl ether (5.0 ml) was added. Cooling and stirring were continued for 3 days and the precipitate was filtered off and washed with diethyl ether. After 6 h drying at room temperature and 0.4 mmHg pressure white crystals of the *phenylcarbamoyl derivative* (12b) (0.62 g, 65%) were obtained; m.p. 127—129°; $\nu_{max.}$ 3 300, 1 738, 1 710, and 1 633 cm^{-1} (NH, C=O of ester, C=O of lactam, and C=C respectively) (Found: C, 70.6; H, 6.75; N, 8.6. $C_{28}H_{31}N_3O_4$ requires C, 71.0; H, 6.6; N, 8.85%).

Reaction of the Adduct (8f) *with Phenyl Isocyanate*.—A cooled and stirred suspension of (8f) (0.8 g, 2 mmol) in anhydrous diethyl ether (12.0 ml) was treated with phenyl isocyanate (2.2 mmol). Stirring and cooling were maintained for 2 h and the clear yellow solution was kept cold for 7 h. The yellow precipitate was separated (0.2 g), and further crops were obtained from the cooled solution after 24 h (0.25—0.30 g) and 4 days (0.2 g). After a week the solution was evaporated and from the residue, ground with ethyl acetate, a final crop (0.10 g) was obtained (total yield *ca.* 75%) as bright yellow needles (from ethyl acetate), m.p. 143—145°; a sample of the *phenylcarbamoyl derivative* (12f) dried to constant weight (6 h at 100 °C and 0.4 mmHg) had m.p. 146—147°: $\nu_{max.}$ 3 310, 1 695, 1 675, and 1 628 cm^{-1} (NH, C=O of lactam, C=O of ketone, and C=C, respectively) (Found: C, 74.7; H, 6.7; N, 7.65. $C_{33}H_{33}N_3O_3,0.5\text{-}C_4H_8O_2$ requires C, 74.55; H, 6.6; N, 7.45%. Found: C, 75.9; H, 6.45; N, 8.15. $C_{33}H_{33}N_3O_3$ requires C, 76.25; H, 6.4; N, 8.1%).

Mild Hydrolysis of the Enamine (12b).—0.5N-Hydrochloric acid (6.0 ml) was added to a stirred suspension of the enamine (12b) (0.47 g, 1 mmol) in acetone (21.0 ml). Stirring at room temperature was continued for 48 h and the solvent was evaporated off. The aqueous suspension was neutralized with sodium hydrogen carbonate and the white precipitate was filtered off and washed with water (0.34 g, 81%; softens at 55 °C); every attempt to crystallize the white amorphous *ketone* (13b) was unsuccessful but after careful drying at room temperature under vacuum an acceptable elemental analysis was obtained (Found: C, 67.9; H, 6.3; N, 6.75. $C_{24}H_{24}N_2O_5$ requires C, 68.55; H, 5.75; N, 6.65%).

Mild Hydrolysis of the Enamine (12f).—The method used for (13b) was employed. A first crop of the *ketone* (13f) was directly separated from the acetone solution, and a second crop was obtained as described above. The white crystals had m.p. 198—199° with softening at 195° (from ethanol) (Found: C, 74.4; H, 5.65; N, 6.15. $C_{29}H_{26}N_2O_4$ requires C, 74.65; H, 5.6; N, 6.0%); $\nu_{max.}$ 3 330, 1 745, 1 703, and 1 668 cm^{-1} (NH, C=O of cyclanone, C=O of lactam, and PhC=O, respectively.

(1-*Methyl*-2-*oxoindolin*-3-*yl*)-(2-*oxocyclopentyl*)*acetic Acid* (14b).—A mixture of acetic acid (8.0 ml), concentrated hydrochloric acid (4.0 ml), and the ketone (13b) (0.42 g, 1 mmol) was refluxed gently for 2 h, steam distilled, and extracted several times with ether. The extract was evaporated and the oily residue dissolved in a saturated solution of sodium hydrogen carbonate (10—12 ml). After washing with ether, the aqueous layers were acidified with concentrated hydrochloric acid (to pH 2—3) giving the *acid* (14b) as white crystals (0.17 g, 60%), m.p. 184—186° (from ethanol) (Found: C, 66.75; H, 6.1; N, 5.0. $C_{16}H_{17}\text{-}NO_4$ requires C, 66.9; H, 5.95; N, 4.9%). The steam-distilled aqueous solution was basified (pH 8) with potassium hydroxide solution (50%) and extracted with ether. Acetic anhydride (0.27 ml) was added to the ethereal solution, which was then evaporated to dryness. Bright platelets of acetanilide (0.1 g, 77%) were obtained.

(*b*) By the above method but starting from (9b) (1 mmol), (14b) was obtained in 88—90% yield.

1-*Methyl*-3-(1,4,5,6-*tetrahydro*-1,2-*diphenylcyclopenta*[b]-*pyrrol*-3-*yl*)*indolin*-2-*one* (15f).—(*a*) A mixture of acetic acid–concentrated hydrochloric acid (2 : 1; 14.0 ml) and the ketone (13f) (0.46 g, 1 mmol) was gently refluxed for 3 h, and the solution was then steam distilled. The suspension was extracted several times with ether; evaporation of the ethereal solution gave a residue which was chromatographed [kieselgel; cyclohexane–ethyl acetate (7 : 3) as eluant]. Two fractions were obtained: the pyrrole (15f) (first fraction), white platelets (0.13 g, 33%), m.p. 205—206° (from ethanol), $\nu_{max.}$ 1 713 cm^{-1} (C=O of lactam), δ 1.5—3.0 (6 H, m, $[CH_2]_3$), 3.23 (3 H, s, NMe), 4.59 (1 H, s, 3-H), and 6.7—7.65 (14 H, m, ArH); and the ketone (9f) (second fraction), white crystals (56%), identical (m.p. and i.r.) with the sample obtained by hydrolytic clevage of (8f). From the steam-distilled aqueous solution, acetanilide (77%) was obtained as previously described for (13b).

(*b*) A mixture of (9f) (1 mmol), aniline (1 mmol), and acetic acid–concentrated hydrochloric acid (2 : 1; 14.0 ml) was refluxed for 3 h. Compound (15f) (35%) and unchanged (9f) (45%) were isolated as above.

We thank Professor P. Grünanger for discussions and suggestions, and the Consiglio Nazionale delle Ricerche (Rome) for financial support.

[6/197 *Received*, 29*th January*, 1976]