Isomers and Aza-analogues of Indoxyl Containing Nitrogen at a Ring-fusion Position: Coupling Reactions with Electrophiles and Attempted Oxidations

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Derivatives of four series of compounds derived from isomers of indoxyl with the nitrogen at the bridgehead and two further series of aza-analogues are prepared and their absorption properties studied.

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Indigo **1** and its derivatives continue to represent a most important class of dyes, showing high color density combined with excellent stability. The concept of the "merostabilization" of free radicals which was formulated in our laboratory in 1964 [1], proposes that RXYC· in which X = a donor and Y = an electron acceptor group is more stable than *either* $RCX_2^{\cdot}$ or $RCY_2^{\cdot}$; it was later supported by the preparation of several examples of merostabilized radicals [2,3]. The concept had been expressed in early theoretical work by Dewar [4], and was developed independently for nitrogen radicals XYN· by Balaban [5] under the name "push-pull stabilization". More recently, the principle has been much extended (see, *e.g.*, [6,7]); it has been referred to as "captodative" stabilization of radicals by Viehe [6].

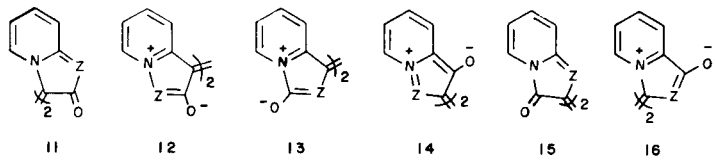
Recently, Klessinger [8] suggested that the intense color of indigo was attributable to merostabilization (captodative stabilization): if the two halves of the molecule are uncoupled, this is seen in **2**. It can be envisaged that the *excited state* of indigo is merostabilized. The rule of *Calczy*, that the absorption maximum is at a higher wavelength in **3a** than in **4** (see discussion in ref [9]) can be rationalized by merostabilization in the two 'halves' in **3b** which can be derived from **3a** but not from **4**. Other compounds of these types are highly coloured, *e.g.*, the microbial pigment violacein **5** forms violet-black microcrystals (λ max 585 nm), and the simpler analog **6** resembles violacein spectroscopically (λ max 490) [10]. In fact the essential chromophore of indigo is the six atom fragment **7**, as demonstrated convincingly by Luettke and his co-workers [11].

Similar considerations should apply to isomers of indigo. The six of these which comprise the other possibilities of combining two of the fragments **8**, **9**, and/or **10** are all known [11a]: isoindigo represents the symmetrical dimer of **9**, *beta*-isoindigo that of **10**, while indirubin combines **8** with **9**. They are all dyes (for a summary see [12]).

Six further symmetrical isomers of indigo can be envisaged **11a-16a** in which the nitrogen atom is present at the bridge-position. It is with analogues of these compounds and their monoaza derivatives **11b-16b** that the present paper is concerned.

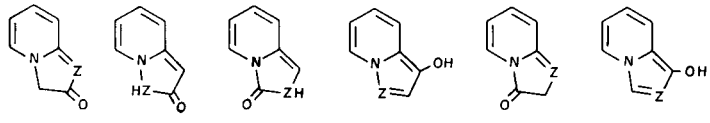
We consider first the corresponding parent systems. Compounds **11-16** can be considered as derived from **17-22** by oxidative dimerization (loss of 4H from two molecules of precursor), just as indigo is derived from indoxyl. Systems **11** and **15** show a simple correspondence of this type with systems **17** and **21**, respectively. However, because of the zwitterionic nature of systems **12**, **13**, **14**, and **16**, the corresponding neutral precursors (**18**, **19**, **20**, and **22**, respectively) show either an OH or ZH group.

Block 3



11 12 13 14 15 16

Series a: Z = CH, Series b: Z = N

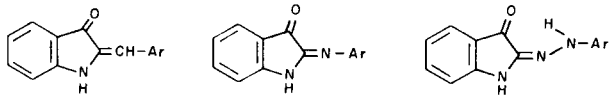


17 18 19 20 21 22

Series a: Z = CH, Series b: Z = N, Series c: Z = CR

Parent systems *17*-**22** are of interest not only as precursors to indigo isomers but also because they are expected to behave as interesting coupling components yielding condensation products with, *e.g.*, arenealdehydes, aryl nitroso compounds, and arenediazonium salts, comparable to compounds **23**, **24**, and **25** which are formed in such reactions by indoxyl. Some such products of coupling reactions are known, as mentioned later.

Block 4



23 24 25

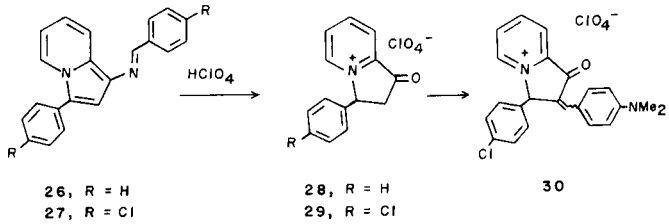
In series **a**, where Z = CH, only three parent compounds exist, because **17** = **18**, **19** = **21**, and **20** = **22**. To avoid ambiguity in determining the position of oxidation or the position of coupling, we have worked with four systems of series **c** in which R is a suitable blocking substituent: we discuss successively systems **20c**, **22c**, **17c**, and **18c**. As is discussed for the individual systems, scattered literature work is available on several of them, but no systematic investigation of the field has previously been undertaken. We have now studied system **19** = **21** and its substituted derivatives.

In series **b**, where Z = N, considerably more literature work is available, particularly for **17b** [13a] and **21b** [13b]. These are the systems that we have subjected to further study among the aza derivatives.

3-(4-Chlorophenyl)-2,3-dihydro-1-oxoindolizinium Perchlorate (**29**).

Indolizinium salt **28** was prepared previously in unstated yield [14] from 2-acetylpyridine, benzaldehyde, and ammonium acetate, *via* an intermediate imine **26** which was then hydrolysed by perchloric acid (Scheme 1). We find that, in place of column chromatography, imine **26** may be obtained (*ca.* 20%) by filtering the crude product in dichloromethane through neutral alumina to remove most of the dark impurities. The crude product was then absorbed on neutral alumina and Soxhlet extracted with hexane to give imine **26** of fair purity. Hydrolysis to give indolizinium **28** was then performed as reported [14] by Kroehnke. This preparation was inconvenient, however, for the large scale preparation of derivatives due to the low yield of formation and to the length of time necessary for isolation of the product. Instead, we prepared *p*-chloro derivative **27** by the reported [14] procedure in fair to good yields over several preparations (15-29%). Hydrolysis, as before, gave **29**.

Scheme I



26, R = H
27, R = Cl

28, R = H
29, R = Cl

30

Reaction of **29** with *p*-dimethylaminobenzaldehyde under basic conditions gave the purple benzylidene derivative **30** (72%) with a carbonyl stretching band at 1668 cm^{-1}. Expected ^1H nmr features included the NMe_2 singlet at δ 3.04 and ^{13}C nmr signals for carbonyl (180.2 ppm), methine (70.0 ppm), and NMe_2 (39.6 ppm) carbons. A hypsochromic shift and a decrease in extinction coefficient were observed for **30** in going from neutral to acid or to basic solution (Table 1).

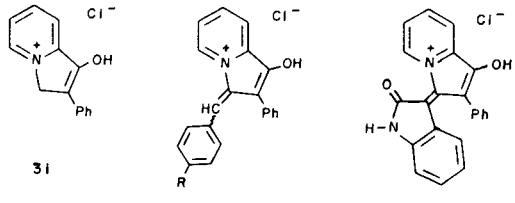
An apparent dimer of undetermined structure was produced during recrystallisation of **29** from methanol, or by warming an aqueous solution of **29** on a steam bath.

1-Hydroxy-2-phenyl-3*H*-indolizinium Chloride **31**.

Compound **31** is readily prepared [15] by cyclisation of the pyridinium salt formed from 2-hydroxymethylpyridine and phenacyl bromide (62% overall). In solution, ^{1}H nmr shows the C-3 methylene protons as a 2H singlet (δ 5.57) with no vicinal splitting, thus, the cation exits in solution in its enolic form. The ir spectrum shows hydroxy stretching at 3510 cm^{-1}, but no carbonyl absorption.

Aldol condensations of **31** with 4-dimethylaminobenzaldehyde, with 4-nitrobenzaldehyde, and with isatin gave the expected reaction products **32**, **33**, and **34**, respectively, (54-94%). The structures were confirmed spectrally: compounds **32**, **33**, and **34** all exist in the hydroxy tautomer shown as evidenced by broad hydroxy absorption at 3400 cm^{-1} and by the lack of carbonyl absorption in the ir spectra. In the ^{1}H nmr, the NMe_2 signal at δ 3.36 (in **32**) and the A_2B_2 patterns for the *p*-disubstituted benzene rings (in **32** and **33**) were found as expected. The configuration about the C-3 olefin double bond has not been determined for **32** and **33**.

Block 5



31 **32**, R = NMe_2; **33**, R = NO_2 **34**

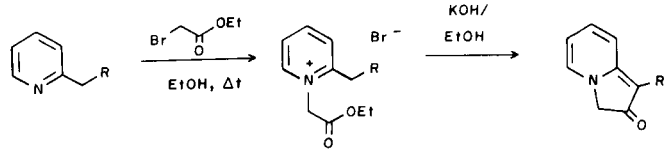
In the ^{1}H spectrum of **34**, a 5H broad singlet (δ 7.21) is seen for the phenyl protons and a 1H doublet (δ 9.74, J = 6 Hz) for the α-pyridinium proton (H-5). The presence of an upfield 2H multiplet centered at δ 6.46 suggests anisotropic shielding of the indole C-4 and C-5 protons by the phenyl group and hence that **34** exists as the *Z*- rather than the *E*-isomer. In the ^{13}C nmr spectrum, the lactam carbonyl appears at 176 ppm, while the enolic nature of the indolizine carbonyl is supported by the lack of an upfield signal for C-2 of the indolizine ring.

In going from neutral to acidic or basic media, both **32** and **33** showed hypsochromic shifts. Compound **34** displayed multiple absorptions in the visible region; an increase in the molar absorptivity was observed in going to basic media (Table 1).

Synthesis and Reactions of 1-Methyl- and 1-Phenyl-2,3-dihydroindolizin-2-one **37**, **38**.

Ethyl bromoacetate with 2-ethylpyridine and with 2-benzylpyridine gave the pyridinium salts **35** and **36**, respectively. Treatment with potassium hydroxide in ethanol afforded the indolizine derivatives **37** and **38**, respectively (Scheme 2) [16]. Although column chromatography and subsequent recrystallisation were reported as essential to obtain pure **38**, we found that simply washing the crude material with water gave **38** suitable for use in further reactions, in almost quantitative yield (*c.f.* 73% reported [16]. Alternatively, **38** was prepared (47%) by treatment with aqueous sodium bicarbonate at room temperature for 20 hours followed by recrystallisation of the resulting solid. The methyl analogue **37** could, however, only be obtained as a solid after column chromatography, and was therefore usually generated *in situ* for further reaction.

Scheme 2



35, R = CH_3; **36**, R = Ph **37**, R = CH_3; **38**, R = Ph

Table 1

UV-Visible Spectra [a] of Indolizinium Derivatives

Compound	Solvent	Neutral Medium [b]		Acidic Medium [c]		Basic Medium [d]	
		λ max	ε	λ max	ε	λ max	ε
30	MeOH	545	22000	540	870	--	--
32	MeOH	610	2200	530	900	480	3400
33	MeOH	580	5000	455	4800	--	--
34	MeOH	475	2000	--	--	460	7400
		670	1500	670	1400	--	--
54	MeOH	500	54000	--	--	495	7500
58	MeOH	460	6600	532	47000	435	9900

[a] λ max in the range 400-850 nm. [b] In methanol/water (80:20). [c] In methane methanol/hydrogen chloride, 2*N* in hydrochloric acid. [d] In methanol/sodium hydroxide, 2*N* in sodium hydroxide.

Condensation of 1-methylindolizin-2-one **37** and *p*-nitrosodimethylaniline gave the imine **39** (25%) as a violet oil after column chromatography (Scheme 3). The ^{1}H nmr spectrum showed two singlets at δ 1.75 (CH_3) and 3.00 ($CN(CH_3)_2$), an A_2B_2 system at δ 6.80 and δ 8.25. (1,4-disubstituted aromatic ring), and a multiplet at δ 6.10 (H-6).

Treatment of **37** with benzenediazonium chloride gave the azo dye **41** (35%) as a green oil after chromatography. Its ^{1}H nmr displayed only the characteristic multiplet at delta 6.25 (H-5) and signals in the aromatic region.

Heating 2,3-dihydro-1-phenylindolizin-2-one **38** with *p*-nitrosodimethylaniline in ethanol in the presence of piperidine afforded, without further purification, the pure dyestuff **40** (90%) as violet crystals (Scheme 3). The ^{1}H nmr showed an A_2B_2 system at delta 6.70 and delta 8.32, due to the 1,4-disubstituted aromatic ring, and a multiplet at delta 5.90-6.15, assigned to H-6 of the indolizine moiety. Conveniently, **40** can be prepared by heating **36** with *p*-nitrosodimethylaniline in the presence of piperidine, generating **38** *in situ*. The uv visible spectrum of **40** (Table 2) showed a bathochromic shift upon addition of 2 *M* hydrochloric acid accompanied by an increase of the extinction coefficient.

Coupling **38** with benzenediazonium chloride gave an intense green dye **42** (57%) as a green crystaline solid. The ^{13}C nmr (75 MHz) showed 6 singlets and 10 doublets, as expected for both oxo and hydroxy tautomeric structures; however singlets at 168.9 ppm (vinylogous amide carbon C-2) and 151.8 ppm, (amidine carbon C-3), demonstrate that the coupling product exists largely in the oxo form. The uv-visible absorption maximum of **42** is dependent on the acid strength: although no change (λ max 436 nm) was observed in going from neutral media to 2 *M* hydrochloric acid, in 12 *M* hydrochloric acid there was a bathochromic shift to 521 nm.

In a similar manner, **38** with 4-nitrophenyldiazonium chloride gave **43** as a green solid. Its ^{1}H nmr (deuteriochloroform-trifluoroacetic acid) showed: a doublet at δ 9.25, due to H-5 (α-pyridinium proton), and an A_2B_2 pattern at δ 8.30-8.50 for the 1,4-disubstituted aromatic ring. Whether the product exists in non-acidic solution as the oxo or hydroxy form is uncertain as its low solubility in non-acidic media precluded obtaining its ^{13}C nmr.

With *p*-nitrobenzaldehyde, **38** gave at least 5 components (tlc). Treatment of **38** with electron donor substituted aldehydes and with acetone afforded the orange-red

Table 2

UV-Visible Spectra of 2,3-Dihydro-1-phenylindolizin-2-ones

Compound	Solvent	Neutral Medium		Acidic Medium	
		λ max (nm)	ϵ	λ max (nm)	ϵ
40	Ethanol	530	21600	621	25300
42	Ethanol	436	28200	435	25900 [a]
42	Chloroform	440	17900	521	13900 [b]

[a] In 2*M* hydrochloric acid. [b] In 12*M* hydrochloric acid.

Scheme 3

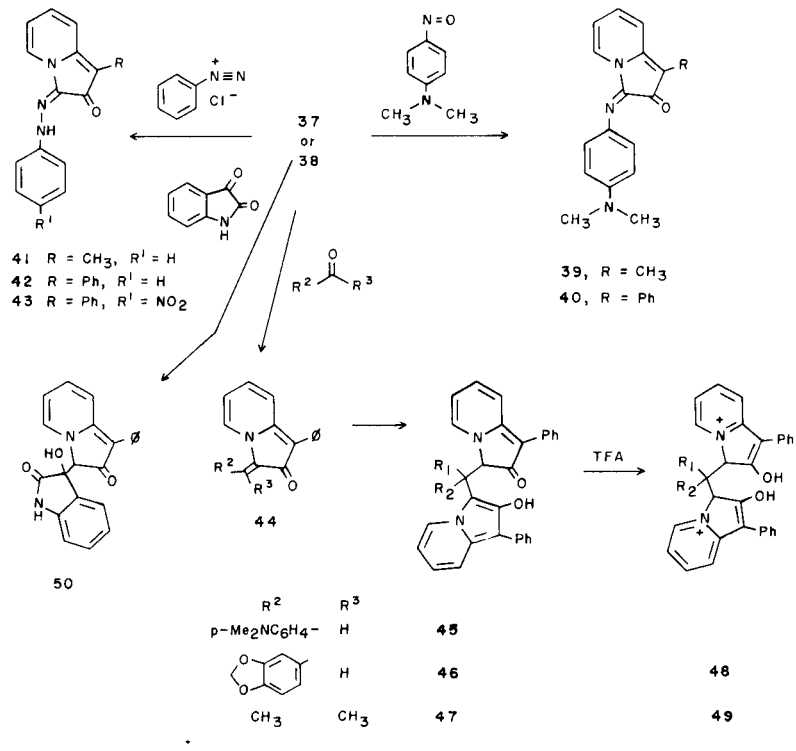


Table 3

UV-Visible Spectra of Imidazo[1,2-*a*]pyridines

Compound	Solvent	Basic Medium (+ sodium hydroxide)		Acidic Medium (hydrogen bromide)	
		λ max (nm)	ε	λ max (nm)	ε
11b	Acetic acid	--	--	502 [a]	14100
61	Ethanol	520	2000	512	630
				346	4500
62	Ethanol	329	7200	340	6300
				280	5900
63	Water	500	25700	529 [b]	3300
65	Dichloromethane	534	11000	--	--
		502	10000		
65	Ethanol	--	--	384	18700
				292	21300
				--	--
				290	22500

[a] I. Mosby, "Heterocyclic Systems with Bridged Nitrogen", 1961, 480: λ max = 480-540 nm. [b] *Ibid* [7]: λ max (water) = 514 nm, ε = 31600, also reported λ max = 520 nm.

2:1 adducts **45**, **46**, and **47**, respectively, in fair yields (Scheme 3). The formation of these compounds can be explained by Michael addition of **38** to the *in situ* formed alkylidene derivatives **44**. Two doublets at δ 4.40 and δ 5.60, in the ^{1}H nmr (deuteriochloroform): of **45**, corresponded to two aliphatic carbon signals (doublets at 47.8 ppm and 69.6 ppm in the ^{13}C nmr), indicating that one of the indolizin-2-one moieties exists in the enolic form.

Compounds **46** and **47** were soluble only in trifluoroacetic acid, forming their bispyridinium salts **48** and **49**, respectively. The ^{1}H nmr spectrum of **48** displayed a characteristic double doublet at δ 4.05 (J_1 = 6 Hz, J_2 = 10 Hz), assigned to the benzylic methine proton. The ^{13}C spectra of **48** and **49** exhibited the benzylic methine [**48**: 52.6 ppm (d)] and *gem*-dimethyl [**49**: 68.8 ppm (s)] carbons. In addition, C-3 and C-3′ carbons are displayed at 68.2 and 68.8 ppm in **48** and at 68.2 ppm in **49**. The ir spectra of **46** and **47** show a carbonyl band at 1580 cm^{-1} together with weak hydroxy stretching at 3400 (br) cm^{-1} again indicating that one of the indolizin-2-one moities exists in the enolic form.

The 2:1 structure of the adducts is consistent with the mass spectra of **45-47**. Although molecular ions of these products were not seen, alkylidene derivatives of **44** arising from retro-Michael reactions were observed: thus, **47** gave **44** with m/z = 249.11 (Calcd. for $C_{17}H_{15}NO$, m/z = 249.11) and **38** with m/z = 209.08 (Calcd. for $C_{14}H_{11}NO$, m/z = 209.08).

Reaction of **38** with isatin led to the ketol **50** as shown by ^{1}H and ^{13}C nmr spectroscopy and by elemental analysis. Attempted dehydration of **50** failed: acetic anhydride gave the enol acetate as shown by ^{1}H nmr spectroscopy.

Oxidative dimerisation of **38**, following reported procedures with potassium ferricyanide [17,18] and 2-chloro-2-nitropropane [19] gave only brown intractable material. In a similar manner as reported [19] for the preparation of indigo from indoxyl acetate, **38** was converted to its acetate **59** and oxidative dimerisation was attempted. Although reported [16] to form in low yield, we found that **59** could be produced in 69% yield simply by refluxing **38** in benzene with a slight excess of acetic anhydride for 1 hour and chromatographing the crude material on basic alumina. Attempted oxidation [19] of **59** with 2-chloronitropropane gave black uncharacteriseable materials. Oxidation with potassium ferricyanide [18] gave two main products after separation by column chromatography. However, these were not found to be the desired dimer **11a** and were not considered further.

2,3-Dihydro-1-methyl-2-oxo-5,7-diphenylindolizinium Chloride **53**.

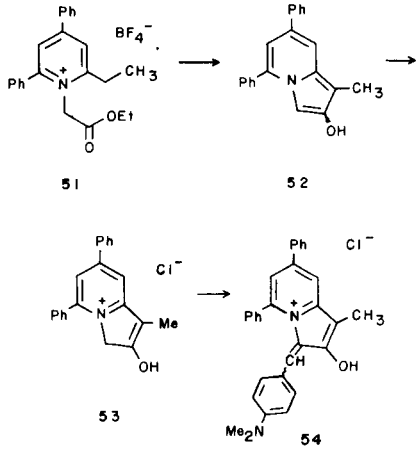
As discussed earlier, attempts to prepare benzylidene derivatives of **38** with electron-donor-substituted benzaldehydes gave instead 2:1 Michael adducts: we hoped to reduce Michael addition to the β-enone carbon by sterically hindering this position with a 5-phenyl substituent. We prepared pyridinium salt **51** (68%) through a pyrylium to pyridinium conversion [20] with glycine ethyl ester hydrochloride. Cyclisation readily occurred using aqueous sodium bicarbonate at 100° for 20-30 minutes to give the red indolizine **52** (43%) which was purified by absorption on silica gel. The free base slowly darkened on exposure to air and was therefore stored as the hydrochloride **53**.

The structure of **53** is clearly demonstrated by the ^{1}H nmr singlets for the 1-methyl (δ 2.13) and for the 3-methylene (δ 5.25) protons. The ir spectrum reveals broad absorption at 3000-2600 cm^{-1}, typical for enolic

systems, and shows no carbonyl absorption. The ^{13}C nmr and elemental analysis provided further evidence for its structure.

Reaction of **53** with *p*-dimethylaminobenzaldehyde gave the benzylidene derivative **54** (30%) as a dark green solid while none of the desired product was realized with *p*-nitro benzaldehyde. The ^1H nmr of **54** showed: singlets at δ 3.38, 2.24, and 7.23 for the NMe_2, the methyl, and the vinyl protons, respectively, and a broad singlet for the aromatic protons at δ 7.4-8.2. The ir showed broad hydroxy stretching at 2500 cm^{-1}. Readily assignable peaks from the ^{13}C nmr were the methyl group (6.7 ppm), the dimethylamino group (47.2 ppm), and C-1 (109.6 ppm). The stereochemistry at C-3 was not assignable from spectroscopic methods. It is likely *E* around the olefinic system since the *Z*-isomer would suffer severe steric interactions between the phenyl on the olefin and the phenyl group at C-5 of the indolizine ring. A significant decrease in extinction coefficient was seen in basic solution as compared to neutral media (Table 1).

Scheme 4

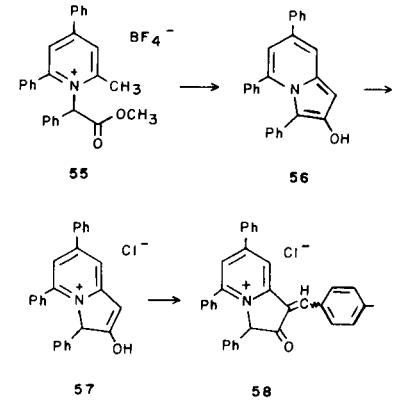


51 52 53 54

2-Hydroxy-3,5,7-triphenyl-3*H*-indolizinium Chloride **57**.

Attempts to condense ethyl 2-bromo-2-phenylacetate with 2-picoline or with 2-benzylpyridine failed to give any of the pyridinium salt needed for cyclisation to the desired indolizine. However, a 3-substituted indolizine could be prepared by a pyrylium to pyridinium transformation as described above. In this case, 2-methyl-4,6-diphenylpyryl ium tetrafluoroborate [21] and phenylglycine methyl ester hydrochloride gave pyridinium **55** (34%): the ^1H nmr spectrum showed singlets for the OMe at δ 4.07 and for C-CH_3 at δ 2.61. The ^{13}C spectrum was in agreement with its assigned structure displaying signals for the α-methyl (23.6 ppm), methoxy (71.1 ppm), methine (55.3 ppm), and carbonyl (167.6 ppm) carbons. Cyclisation occurred readily with hot aqueous bicarbonate at reflux to give indolizine **56** as the major product. Although the reaction was not clean (6 products by tlc), the presence of **56** may be inferred from strong hydroxy ir absorption and by the formation of the hydrochloride salt **57** (74%). The ^1H nmr analysis of the crude salt showed it to be suprisingly clean. Signals were observed only in the 6-8 ppm region of the spectrum. The lack of any upfield signals suggested that the compound was enolized in trifluoroacetic acid solution. That the compound existed as the 3H isomer was evident from its off-resonance ^{13}C spectrum which showed two doublets at 73.25 ppm and 96.00 ppm for C-3 and C-1, respectively, and a singlet at 173.75 ppm for C-2. The enolic form is clearly displayed in its ir spectrum (nujol) by weak OH absorption at 3400-3000 cm^{-1}.

Scheme 5



55 56 57 58

Reaction of **57** with *p*-dimethylaminobenzaldehyde provided the benzylidine derivative **58** as a violet solid (58%). The ^1H nmr spectrum disclosed the presence of the NMe_2 group (δ 3.28). The ^{13}C nmr, aided by the use of an INEPT [22] pulse sequence, clearly showed by the observed signals for the methine (72.7 ppm, 3°) and the oxo (189.9 ppm, 4°) carbons that **58** existed in the oxo rather than the hydroxy form. The ir analysis provided further evidence by the strong carbonyl absorption at 1701 cm^{-1}.

A strong bathochromic shift as well as hyperchromic effect is observed for **58** on going from neutral to acidic media (Table 1). Basic media has a slight hyperchromic effect and a hypsochromic shift.

Reactions of 2,3-Dihydro-2-oxoimidazo[1,2-*a*]pyridine Hydrobromide **60**.

2,3-Dihydro-2-oxoimidazo[1,2-*a*]pyridine. HBr **60**, the parent of system **11b**, is easily available from 2-aminopyridine and ethyl bromoacetate [23], although heating for 3 hours at 100° (rather than 5 minutes at 20°) [23] was needed for a satisfactory yield.

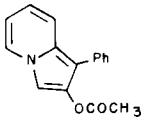
Reaction of **53** with *p*-dimethylaminobenzaldehyde gave the benzylidene derivative **54** (30%) as a dark green solid while none of the desired product was realized with *p*-nitro

benzaldehyde. The ^1H nmr of **54** showed: singlets at δ 3.38, 2.24, and 7.23 for the NMe_2, the methyl, and the vinyl protons, respectively, and a broad singlet for the

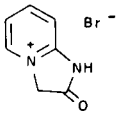
The condensation of hydrobromide **60** with aromatic aldehydes has been reported previously [23,24]. Compounds **62** and **63** had properties in agreement with the published data. The new *p*-nitrobenzylidene derivative **61** was characterized spectroscopically (^1H, ^{13}C nmr: absence of CH_2-signal). The uv-visible spectra of **61-63** are recorded in Table 3. A hypsochromic shift was observed upon addition of base to **62** and **63**, while the *p*-nitroanalogue **61** showed a bathochromic shift.

Oxidative dimerisation of **60** by Chichibabin's method [17] using potassium ferricyanide gave a green solid which produced an intense red solution in either acid or alcohol. Although spectral data (^1H, ^{13}C nmr) confirmed the oxidation process [25], the elemental analysis of dimer **11b** is not satisfactory. The uv-visible spectrum of **11b** in acetic acid is recorded in Table 3.

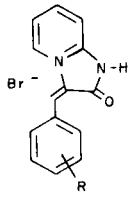
Block 6



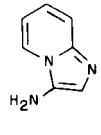
59



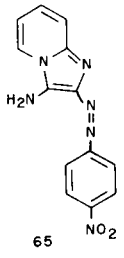
60



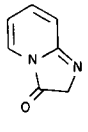
61, R = p-NO_2
62, R = o-NO_2
63, R = p-NMe_2



64



65



66

Reactions of 3-Aminoimidazo[1,2-*a*]pyridine **64**.

2-Aminopyridine with formaldehyde, sodium hydrogen sulfite, and potassium cyanide gives 3-aminoimidazo-[1,2-*a*]pyridine **64**, which is hydrolyzed to *N*-(2-pyridyl)-glycine hydrochloride, and then cyclised with phosphorus oxychloride to compound **66** [26]. Coupling **64** with *p*-nitro-benzenediazonium chloride gave the intensely red **65**. The ^1H nmr spectrum of the product supported coupling at the C-2 position rather than at the amino group (no signal at δ 8.1, absence of H-2). Unambiguous evidence for the structure **65** was provided by the ^{13}C nmr, which showed 5 singlets and 6 doublets: two singlets at 151.2 ppm and 150.1 ppm were assigned to the amidino-carbons C-3 and C-2, respectively. The uv-visible spectra of **65** in ethanol (*acidic medium*) dichloromethane and (*neutral medium*) (Table 3) showed broad absorption in the 500-535 nm region.

Reactions of **66** with aldehydes [*e.g.*: *p*-dimethylaminobenzaldehyde], and carboxyl derivatives (*e.g.*: ethyl orthoformate) have been previously reported [26]. However, the availability of **66** in quantity is limited as it is unstable, decomposing spontaneously on standing at room temperature. Reaction of *N*-(2-pyridyl)glycine hydrochloride with aromatic aldehydes under anhydrous conditions did not lead directly to the corresponding benzylidine derivative of **66**.

Conclusions.

Our attempts to mimic the intense color of indigo by the preparation of isomers and aza-analogs which perserve the merostabilization at each end of an inter-ring double bond have been only partially successful. We found difficulty in the preparation of dimers by oxidative coupling. However, a variety of benzylidine derivations have been successfully prepared, often with intense color. Many of these compounds were isolated as cations: proton removal generated a zwitterionic intermediate, the bathochromic shifts found for these products were less than expected.

EXPERIMENTAL

Melting points were determined using a Kofler hot-stage microscope and are uncorrected. Spectra were recorded on the following instruments: ^1H nmr with either a Varian Model A-60A, a Varian Model EM 360L, a JEOL Model JNM-FX 100 (100 MHz) with TMS as internal standard; ^{13}C nmr with a JEOL Model JNM-FX 100 (25.05 MHz) and a Nicolet NT-300 (75.45 MHz); ir with a Perkin-Elmer Model 283B grating spectrophotometer; uv spectra with a PYE-UNICAM 8-200 or a Perkin-Elmer 330 spectrophotometer; and mass spectra with an AEI MS 30.

The following compounds were prepared by the literature method quoted: 2,3-dihydro-1-oxo-3-phenyl-1*H*-indolizinium perchlorate **28** mp 185° (lit [14] not reported); 1-(4-chlorobenzylidenamino)-3-(4-chlorophenyl)indolizine **27** mp 166-168° (lit [14] 167-168°); 2,3-dihydro-1-oxo-3-(4-chlorophenyl)indolizinium perchlorate **29** mp 217-221° (lit [14] 218-220°); 1-hydroxy-2-phenyl-3*H*-indolizinium chloride **31**, mp >360°; (lit [15] >360°); 2,3-dihydro-1-methylindolizin-2-one **37**, oil, (see discussion in text) (lit [16] 126-128°); 2,3-dihydro-1-phenylindolizin-2-one **38**, mp 130-133° (lit [16] 136-138°); 2-acetyl-1-phenylindolizine **59**, mp 72-74° (lit [16] 74-75°); 2-methyl-4,6-diphenylpyrylium tetrafluoroborate, mp 235-242° (lit [21] 248.5-256.8°); 2-ethyl-4,6-diphenylpyrylium tetrafluoroborate, mp 257-260° (lit [21] 261-262°); methyl α-aminophenylacetate hydrochloride, mp 196-198° (lit [27] 200-202°); 2,3-dihydro-2-oxoimidazo[1,2-*a*]pyridine hydrobromide **60**, mp 245-250° (lit [23] 230-231°); 3-(2-nitrobenzylidene)-imidazo[1,2-*a*]-pyridin-2-one hydrobromide **62**, mp 250-254° (lit [24] 222.5-223.5°); 3-(4-dimethylaminobenzylidene)imidazo[1,2-*a*]pyridin-2-one hydrobromide **63**, mp 270-273° (lit [23] 264-265°); 3-aminoimidazo[1,2-*a*]pyridine **64**, mp 126° (lit [26] 123-124°), 3-oxo-2*H*-imidazo[2,1-*a*]-pyridine **66**, (see discussion in text), (lit [26] *ca.* 190°).

1-Benzylidenamino-3-phenylindolizine **26**.

(Modification of Kroehnke's [14] procedure) 2-Acetylpyridine (24.2 g, 0.199 mole), benzaldehyde were heated at 100° for 30 minutes, cooled and methanol (50 ml) added. After 1 week at 20°, the solvent was

decanted. The green product was washed at 0° with methanol (2 X 20 ml), was taken up in dichloromethane (150 ml) and passed through a short column of neutral alumina (150 g). The alumina was washed with dichloromethane (150 ml) and the combined filtrates concentrated (to *ca.* 200 ml) at 60°/25 mm Hg. Neutral alumina (75 g) was added and the solvent removed at 60°/25 mm Hg. The green powdery product was Soxhlet extracted with hexane for 24 hours. The extract was concentrated to give imine **26** as a red-brown oily solid (9.92 g, 17%), spectroscopically identical with a sample obtained by Kroehnke's [14] method (42%). It was used without further purification.

Alternate Preparation of 2,3-Dihydro-1-phenylindolizin-2-one **38**.

2-Benzyl-1-(ethoxycarbonylmethyl)pyridinium bromide [28] (33.88 g, 0.10 mole) was dissolved in water (130 ml) and sodium bicarbonate (33.89 g, 0.40 mole) was added slowly in small portions over 9 minutes at room temperature. The suspension was diluted with water (20 ml) and stirred for an additional 20 hours at room temperature. The mixture was cooled in an ice-bath, filtered, and was washed with ice-cold water (1 x 15 ml) to give crude **38** as an orange solid which was recrystallized to give indolizin-2-one **38** (9.78 g, 47%) as orange plates, (from water) mp 135-138°; ^{1}H nmr spectrum (deuteriochloroform) identical to that of an authentic sample.

In situ Generation and Trapping of **38**.

2-Benzyl-1-(ethoxycarbonyl)methylpyridinium bromide [28] (0.67 g, 2.0 mmoles) was dissolved in absolute ethanol at room temperature and piperidine (0.29 g, 3.4 mmoles) added. After stirring for 10 minutes at room temperature, *p*-dimethylaminonitrosobenzene (0.33 g, 2.2 mmoles) was added and the mixture refluxed for 10 minutes. The solvent was removed and the product was isolated quantatively as described [16].

1-(Ethoxycarbonyl)methyl-2-ethyl-4,6-diphenylpyridinium Tetrafluoroborate **51**.

2-Ethyl-4,6-diphenylpyrylium tetrafluoroborate [21] (2.0 g, 5.7 mmoles) and glycine ethyl ester hydrochloride (0.80 g, 5.7 mmoles) were mixed in dichloromethane (20 ml) and triethylamine (1.6 ml, 11 mmoles) added. The dark solution was stirred at room temperature for 2 hours and acetic acid (0.69 g, 11 mmoles) was added. After being stirred for 5.5 hours, the solvent was removed (60°/25 mm Hg) to leave a red oil which was triturated with water and ether. The solid was filtered and washed thoroughly with ether and water. Vacuum drying gave pyridinium **51** (1.59 g, 64%), amorphous solid, mp 153-155°; ir (bromoform): 1747, 1623, 1595, 1563 cm^{-1}; ^{1}H nmr (deuteriochloroform): 1.44 (t, 3H, OCH_2CH_3), 1.73 (t, 3H, CH_3), 3.34 (q, 2H, CH_2CH_3), 4.42 (q, 2H, OCH_2CH_3), 5.49 (s, 2H, NCH_2), 7.71 (s, 10H, ArH), 7.88 (d, 1H, J = 2 Hz, Py^+H), 8.19 (d, 1H, J = 2 Hz, Py^+H); ^{13}C nmr (deuteriochloroform): 11.6 (CH_3), 13.7 (OCH_2CH_3), 26.7 (CH_2), 54.2 (NCH_2), 63.1 (OCH_2CH_3), 166.1 (C=O), 123.1-161.0 (Ar-*C*).

Anal. Calcd. for $C_{23}H_{24}BF_4NO_2$: C, 63.8; H, 5.6; N, 3.2. Found: C, 63.8; H, 5.7; N, 3.1.

2,3-Dihydro-1-methyl-2-oxo-5,7-diphenylindolizinium Chloride **53**.

Pyridinium salt **51** (0.5 g, 1.15 mmoles) and sodium bicarbonate (0.5 g, 5.95 mmoles) were added to water (30 ml) and heated for 20-30 minutes at 100° under nitrogen. The solid slowly dissolved yielding a red solution and then a dark oil. The mixture was cooled and extracted with dichloromethane (4 x 20 ml). The combined organic layers were filtered through a pad of silica gel (8 x 6 cm) and then washed with ethyl acetate to remove impurities. The silica gel was washed with methanol and the filtrate concentrated (60°/25 mm Hg) yielding indolizine **52** (0.32 g, 93%) as a red powder which slowly decomposed on exposure to the air; ν max (bromoform): 3400 (br) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.80 (s, 3H, CH_3), 6.4 (s, 1H), 6.89 (s, 1H), 7.33 (s, 1H), 7.5-8.0 (m, 10H, ArH). This was subsequently converted to its hydrochloride salt.

Hydrogen chloride gas was bubbled into a benzene solution of the indolizine until the red color was absent and the precipitated product had dissolved into the solvent. A yellow-green solid slowly precipitated from the benzene layer. A Dean-Stark trap was connected to the apparatus and azetropic distillation was preformed for 12 hours. Upon cooling, the solid was filtered and washed with cold benzene (1 x 30 ml). Vacuum drying gave hydrochloride **53** (60%), needles (from methanol/acetone), mp 230° dec; ir (chloroform): 3000-2600, 1600, 1550, 1372 cm^{-1}; ^{1}H nmr (deuteriochloroform/trifluoroacetic acid): 2.13 (s, 3H, CH_3), 5.25 (s, 2H, NCH_2), 7.3-7.9 (m, 12H, ArH); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 6.3 (CH_3), 57.4 (NCH_2), 104.8 (HOC=C) 112.9-166.0 (Ar-*C*).

Anal. Calcd. for $C_{21}H_{18}ClNO$: C, 75.1; H, 5.4; N, 4.2. Found: C, 75.2; H, 5.5; N, 4.1.

1-[(Methoxycarbonyl)phenylmethyl]-2-methyl-4,6-diphenylpyridinium Tetrafluoroborate **55**.

2-Methyl-4,6-diphenyl-pyrylium tetrafluoroborate [21] (2.0 g, 6.0 mmoles) and methyl α-aminophenylacetate hydrochloride [27] (1.33 g, 6.6 mmoles) were mixed in dichloromethane (15 ml) and triethylamine (1.67 ml, 12 mmoles) was added. The dark solution was stirred at room temperature for 5 hours and acetic acid (1.25 g, 20.8 mmoles) was added. After being stirred for 20 hours, the solvent was removed (40°/25 mm Hg) to give a red oil which was triturated with water and ether. The solid was filtered and thoroughly washed with ether, water, and hot ethyl acetate (2 x 10 ml). Vacuum drying gave pyridinium **55** (0.99 g, 34%), amorphous solid, mp 187° dec; ^{1}H nmr (deuteriochloroform/trifluoroacetic acid): 2.61 (s, 3H, CH_3), 4.07 (s, 3H, OCH_3), 7.0-8.3 (m, 18H, ArH, NCH); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 23.6 (CH_3), 55.3 (NCH), 71.1 (OCH_3), 167.6 (C=O), 126.1-159.2 (Ar-*C*).

Anal. Calcd. for $C_{27}H_{24}BF_4NO_2$: C, 67.4; H, 5.0; N, 2.9. Found: C, 66.9; H, 5.2; N, 3.2.

2-Hydroxy-3,5,7-triphenyl-3*H*-indolizinium Chloride **57**.

Pyridinium salt **55** (1.0 g, 2.1 mmoles) and sodium bicarbonate (1.0 g, 11.9 mmoles) were added to water (50 ml) and heated for 20-30 minutes at 100° under nitrogen. The solid slowly turned gray-blue and then red. The oily mixture was chilled in ice and then extracted with dichloromethane (4 x 20 ml). The combined organic layers were dried over sodium sulfate and rotoevaporated to give an orange solid containing indolizine **56** (0.77 g). Tlc analysis showed six products; ν max (bromoform): 3600-3000 (br), 1600, 1480, 1050, 755 cm^{-1}. This was subsequently converted to its hydrochloride salt.

The crude material was taken up in benzene (150 ml), gravity filtered, and hydrogen chloride gas passed through the orange-red solution for 5 minutes. After standing overnight, the mixture was filtered yielding hydrochloride **57** (0.61 g, 74%) as a yellow solid, microcrystals (from ethyl acetate), mp 178-180° dec; ir (nujol): 3100 br, 1608, 1530, 1410, 1280, 1200, 755, 695 cm^{-1}; ^{1}H nmr (deuteriochloroform/trifluoroacetic acid): 6.25 (s, 1H, H-6), 6.4 (s, 1H), 6.66-6.79 (m, 2H), 7.1-8.0 (m, 15H); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 73.2 (d, C-3), 96.0 (d, C-1), 115.1 (d), 119.3 (d), 127.4 (d), 127.5, 129.4, 129.6, 129.8, 130.0, 131.4, 131.6, 131.9, 132.3 (s), 134.8 (s), 152.3 (s), 156.7 (s), 161.4 (s), 161.8 (s), 173.8 (s, C-2); ms:m/z = 361.1473 (M^+, $C_{26}H_{20}NO$ requires 361.1467), 361 (M^+, 16), 360 (10), 38 (36), 36 (100), 35 (10), 32 (21).

Anal. Calcd. for $C_{26}H_{20}ClNO.1\frac{1}{2}H_2O$: C, 77.4; H, 5.5; N, 3.5. Found: C, 77.9; H, 5.1; N, 3.3.

3,3'-Bi(2,3-dihydro-2-oxoimidazo[1,2-*a*]pyridylidene) **11b**.

To a solution of **60** (2.14 g, 10 mmoles) in water (20 ml) was added dropwise ammonium hydroxide (8 ml, 25%). To the stirred solution was slowly added potassium ferricyanide (3.3 g, 10 mmole). After being stirred for 20 minutes, acetic acid was added and the solid was filtered off and washed with water and acetic acid several times. Drying at 80° gave dimer **11b** (0.8 g, 30%), green amorphous solid, mp 250-255° (lit [17] not reported): ir (bromoform): 1650, 1610, 1545, 1460, 1432, 1300, 1185, 755, 685 cm^{-1}; ^{1}H nmr (deuteriochloroform/trichloroacetic acid): 7.4-9.2 (m, ArH); ^{13}C nmr (deuteriochloroform/trichloroacetic acid): 111.5 (d), 119.3 (d), 123.3 (d), 125.3 (s), 131.9 (d), 133.5 (d), 141.0 (d), 142.4 (s), 147.2 (s), 148.9 (d), 160.3 (s), 164.6 (s).

Anal. Calcd. for $C_{14}H_8N_4O_2.2H_2O$: C, 56.0; H, 4.0; N, 18.7. Found: C,

56.6; H, 3.7; N, 20.0 [29].

General Method for the Condensation of Carbonyl Compounds with Heterocycles.

The heterocyclic starting material (2-4 mmoles), the aldehyde or ketone (2.2-4.4 mmoles), and piperidine (4-5 drops) were refluxed in dry ethanol (10-30 ml) for 90 minutes. After cooling to 0°, the product was filtered off, washed with ice-cold ethanol (*ca.* 10 ml) and purified by recrystallisation, chromatography, or by precipitation with ether from ethanol.

The following were so prepared:

3-(4-Chlorophenyl)-2,3-dihydro-2-[4-(dimethylamino)benzylidene]-1-oxo-1*H*-indolizinium Perchlorate **30**.

Compound **30** was obtained as microcrystals from ethanol in 72% yield, mp 144° dec; ir (bromoform): 1668, 1560, 1520, 1383, 1090 cm^{-1}; ^1H nmr (DMSO-d_6/300 MHz): 3.04 (s, 6H, N*Me*$_2$), 6.68 (d, 2H, J_{AB} = 8 Hz, Ar*H*), 7.47-7.53 (m, 5H, Ar*H*, C*H*), 7.79 (d, 2H, J_{AB} = 8 Hz, Ar*H*), 8.00 (s, 1H, C = C*H*), 8.28 (t, 1H, J = 6 Hz, J = 7 Hz, 6-H), 8.60 (d, 1H, J = 8 Hz, 8-H), 8.80 (t, 1H, J = 8 Hz, 7-H), 9.12 (d, 1H, J = 6 Hz, 5-H); ^{13}C nmr (DMSO-d_6/75 MHz): 39.6 (N*Me*$_2$), 70.0 (*CH*), 111.8 (2-Ar C-3), 118.6 (C-3), 122.0 (2-Ar C-1), 123.1, 129.4 (2-Ar C-2), 131.1, 131.3 (3-Ar C-3), 133.6 (3-Ar C-4), 135.1 (3-Ar C-1), 135.8 (3-Ar C-2), 141.3, 141.4, 145.8 (C-9), 147.3 (C-6), 153.1 (2-Ar C-4), 180.2 (C-1).

Anal. Calcd. for $C_{23}H_{20}Cl_2N_2O_5$: C, 58.1; H, 4.2; N, 5.9. Found: C, 59.8; H, 4.0; N, 5.9 [29].

1-Hydroxy-3-(4-dimethylaminobenzylidene)-2-phenyl-3*H*-indolizinium Chloride **32**.

Compound **32** was obtained as microcrystals after precipitation from ethanol-ether in 54% yield, mp >340°; ir (nujol): 3300 (br), 1580, 1100, 750, 690 cm^{-1}; ^1H nmr (DMSO-d_6): 3.46 (s, 6H, *Me*$_2$), 6.5 (d, 2H, J_{AB} = 9 Hz, Ar*H*), 7.2 (d, 2H, J_{AB} = 9 Hz, Ar*H*), 7.3-7.65 (br s. 5H, Ar*H*), 7.6-8.8 (m, 4H, Py$^+$*H*).

Anal. Calcd. for $C_{23}H_{21}ClN_2O$: C, 73.3; H, 5.6; N, 7.4. Found: C, 73.6; H, 5.3; N, 6.9.

1-Hydroxy-3-(4-nitrobenzylidene)-2-phenyl-3*H*-indolizinium Chloride **33**.

Compound **33** was obtained as microcrystals from ethanol in 94% yield, mp >340°; ir (bromoform): 3440 (br), 1600, 1450 (NO_2), 1390 (NO_2), 1345, cm^{-1}; ^1H nmr (deuteriochloroform/trichloroacetic acid): 7.25 (br s, 5H, Ar*H*), 7.3 (d, 2H, J_{AB} = 8.5 Hz, Ar*H*), 7.9 (d, 2H, J_{AB} = 8.5 Hz, Ar*H*), 8.46 (m, 3H, Py$^+$*H*), 9.53 (d, 1H, J = 6.6 Hz, 5-H); m/z = 343.1079 ($C_{21}H_{15}N_2O_3$ requires 343.1082), m/z 344 (M + 1, 12%), 343 (M$^+$, 10), 342 (M-1, 10), 206 (14), 150 (10), 106 (23), 78 (49), 44 (12), 38 (33), 36 (100), 28 (16).

Anal. Calcd. for $C_{21}H_{15}ClN_2O_3$: C, 66.6; H, 4.0; N, 7.4. Found: C, 67.6; H, 4.2; N, 6.8 [29].

1-Hydroxy-3-(2-oxo-3-indolylidene)-2-phenyl-3*H*-indolizinium Chloride **34**.

Compound **34** was obtained (reflux 30 minutes) as microcrystals after precipitation from ethanol-ether in 77% yield, mp 180°; ir (bromoform): 3400 br (OH), 3180 (NH), 1718 (NC=O) cm^{-1}; ^1H nmr (deuteriochloroform/trichloroacetic acid): 6.53 (m, 2H, 4'-H, 5'-H), 7.21 (br s, 5H, Ar*H*), 7.3-9.0 (m, 6H, Py$^+$*H*, Ar*H*), 9.74 (d, 1H, J = 6 Hz, 5-H); ^{13}C nmr (deuteriochloroform/trichloroacetic acid): 176.6 (*C*=O) 112.2-154.5 (Ar-*C*, C=*C*, Pyr$^+$*C*). Decomposition of **34** was noted during recrystallization.

Anal. Calcd. for $C_{22}H_{15}ClN_2O_2.H_2O$: C, 67.3; H, 4.4; N, 7.1. Found: C, 66.9; H, 4.1; N, 6.4 [29].

(2,3-Dihydro-2-oxo-1-phenylindolizin-3-yl)(2-hydroxy-1-phenylindolizin-3-yl)-[4-(dimethylamino)phenyl]methane **45**.

Compound **45** was obtained as needles from ethanol in 67% yield, mp 210-215°; ir (bromoform): 1580 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): 2.75 (s, 6H, N*Me*$_2$), 4.40 (d, 1H, J = 3 Hz, C*H*), 5.60 (d, 1H, J = 3 Hz, NC*H*), 6.15-6.85 (m, 6H, Ar*H*), 6.90-7.70 (m, 12H, Ar*H*), 7.90-8.10 (m, 4H, Ar*H*); ^{13}C nmr (deuteriochloroform): 40.4 (q, N*Me*$_2$), 47.8 (d, *CH*), 69.6 (d, NCH), 186.7 (s, C=O), 102.8-162.7 (Ar-*C*); m/z 340 (13.4%), 209 (100%).

Anal. Calcd. for $C_{37}H_{31}N_3O_2$: C, 80.8; H, 5.7; N, 7.6. Found: C, 80.3; H, 5.6; N, 7.3.

(2,3-Dihydro-2-oxo-1-phenylindolizin-3-yl)(2-hydroxy-1-phenylindolizin-3-yl)-(piperonyl)methane **46**.

Compound **46** was obtained as (reflux 15 minutes) needles from ethanol in 74% yield, mp 249-251°; ir (bromoform): 3370 (br), 1580 cm^{-1}; ^1H nmr (deuteriochloroform/trifluoroacetic acid): 4.05 (dd, 1H, J_1 = 6 Hz, J_2 = 10 Hz (C*H*), 6.10 (s, 2H, OC*H*$_2$O), 6.2-8.7 (m, 23H, Ar*H*, NC*H*, Py$^+$*H*); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 52.6 (d, *CH*), 68.2 (d, NCH), 68.8 (d, NCH), 102.5 (t, OCH$_2$O); 109.4-167.8 (Ar-*C*, Pyr$^+$*C*, C=*C*).

Anal. Calcd. for $C_{36}H_{26}N_2O_4$: C, 78.5; H, 4.7; N, 5.1. Found: C, 78.7; H, 4.7; N. 4.7.

(2,3-Dihydro-2-oxo-1-phenylindolizin-3-yl)(2-hydroxy-1-phenylindolizin-3-yl)-dimethyl)methane **47**.

Compound **47** was obtained (reflux 3 hours) as plates from ethanol in 50% yield, mp 197-200°; ir (bromoform): 3400, 2960, 1595 cm^{-1}; ^1H nmr (deuteriochloroform/trifluoroacetic acid): 1.50 (br s, 6H, N*Me*$_2$), 6.80 (s, 2H, NC*H*), 7.3-7.9 (m, 15H, Ar*H*), 8.10-8.50 (m, 2H, Ar*H*), 8.85 (d, 1H, J = 5 Hz, 5-H); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 22.2 (q, *CH*$_3$), 40.2 (q, *CH*$_3$), 68.2 (d, NCH), 68.8 (s, *CMe*$_2$); 92.1(HOC=*C*), 111.9-168.7(Ar-*C*, Pyr$^+$*C*); ms: m/z = 249.1145 (*M*$^+$, $C_{17}H_{15}NO$ requires 249.1153). Compound **47** decomposed on attempted recrystallization to give **38** as the major isolated product.

2,3-Dihydro-3-(3-hydroxy-2-oxo-3-indolyl)-1-phenyl-indolizin-2-one **50**.

Compound **50** was obtained (reflux 60 minutes) as microcrystals from ethanol in 70% yield, mp 186-188°; ir (bromoform): 3500 br (OH), 3360 (NH), 1720 (CONH), 1600 (C=O) cm^{-1}; ^1H nmr (DMSO-d_6): 3.35 (s, 1H, O*H*), 4.65 (s, 1H, C*H*), 6.35-7.80 (m, 13H, Ar*H*), 8.35 (d, 1H, J = 6 Hz, 5-H); ^{13}C nmr (DMSO-d_6): 70.4 (d, *CH*), 76.0 (s, *COH*), 175.1 (s, N*C*=O), 183.5 (s, *C*=O), 100.1-161.2 (Ar-*C*, C=*C*).

Anal. Calcd. for $C_{22}H_{16}N_2O_3$: C, 74.1; H, 4.5; N, 7.9. Found: C, 74.0; H, 4.4; N, 7.7.

2-Hydroxy-1-methyl-3-(4-dimethylaminobenzylidene)-5,7-diphenylindolizinium Chloride **54**. (Reflux 90 Minutes).

The solvent was removed from the blue solution by rotoevaporation. The resulting blue solid was Soxhlet extracted with acetone for 62 hours yielding 1.95 g of a mixture of green and black solids in the thimble which were crushed and re-extracted for 45 hours more with acetone. The product from the thimble was dried in a vacuum oven yielding nearly pure benzylidene **54** (1.27 g, 30%). Recrystallisation gave **54** as green cubes (from acetone), mp 240° dec; ir (nujol): 2500 br, 1580, 1540, 1163 cm^{-1}; ^1H nmr (deuteriochloroform/trifluoroacetic acid): 2.24 (s, 3H, C*H*$_3$), 3.38 (s, 6H, N*Me*$_2$), 7.23 (s, 1H, C*H*=C), 7.4-8.2 (m, 16H, Ar-*H*); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 6.7 (q, *CH*$_3$), 47.2 (q, N*Me*$_2$), 109.6 (s, C-1), 150.0 (s, C-6), 154.9 (s, C-5), 156.3 (s, C-9), 156.4 (s, C-2), 113.7 (d), 120.5 (d), 121.4 (d), 127.5 (d), 127.9 (d), 130.2 (d), 131.4 (d), 132.2, 132.6, 133.0, 133.2, 133.4, 133.6, 134.5 (d), 135.5, 143.7; ms: m/z 431 (20%), 430 (70), 429 (82), 428 (19), 413 (18), 311 (10), 310 (33), 299 (25), 298 (17), 215 (18), 147 (11), 134 (70), 43 (19), 38 (30), 36 (100), 28 (20).

Anal. Calcd. for $C_{30}H_{27}ClN_2O$. ½ H_2O: C, 75.7; H, 5.9; N, 5.9. Found: C, 75.5; H, 6.2; N, 5.5.

1-(4-Dimethylaminobenzylidene)-2-oxo-3,5,7-triphenyl-3*H*-indolizinium Chloride **58**.

Compound **58** was obtained (reflux 90 minutes) microcrystals after precipitation from DMSO with ether in (58%) yield mp > 230°; ir (bromoform) 2900, 1701, 1611, 1533, 1505, 1373, 825 cm^{-1}; ^1H nmr (DMSO-d_6): 3.28 (s, 6H, N*Me*$_2$), 6.56 (s, 1H), 6.6-7.9 (m, 16H, Ar*H*), 8.07 (s, 1H), 8.3-9.1 (m, 4H), 9.30 (s, 1H); ^{13}C nmr (DMSO-d_6): 40.0 (N*Me*$_2$, 1°), 72.7 (*CH*, 3°), 108.2 (4°), 112.2 (3°), 113.0 (4°), 113.6 (3°), 120.6 (3°),

122.4 (4°), 126.8 (3°), 128.2 (3°), 128.5 (3°), 129.2 (3°), 130.4 (3°), 131.7 (3°), 131.9 (4°), 133.2 (4°), 134.3 (4°), 138.8 (3°), 149.0 (3°), 151.1 (4°), 154.3 (4°), 155.4 (3°), 159.7 (4°), 189.9 (C-2, 4°); ms: m/z = 493.2260 ($C_{35}H_{29}N_2O$ requires 493.2279), 494 (M^+, 28%), 493 (35), 492 (25), 491 (13), 375 (28), 359 (10), 223 (14), 134 (14), 50 (14), 38 (32), 36 (100), 35 (16), 31 (10), 28 (44).

Anal. Calcd. for $C_{35}H_{29}ClN_2O.H_2O$: C, 76.8; H, 5.7; N, 5.1. Found: C, 76.6; H, 5.4; N, 5.3.

3-(4-Nitrobenzylidene)imidazo[1,2-*a*]pyridin-2-one Hydrobromide **61**.

Compound **61** was obtained (reflux 30 minutes) as microcrystals from ethanol in 55% yield mp 266-272°; ir (bromoform): 3000-2500, 1740, 1650, 1630, 1590, 1570, 1510, 1370, 1350, 1170, 1010, 890, 845, 820, 770, 725 cm^{-1}; ^1H nmr (deuteriochloroform/trifluoroacetic acid): 7.9 (m, 3H), 8.5 (s, 4H), 8.7 (s, 1H), 9.2 (d, 1H, J = 6 Hz, H-5); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 112.5, 120.7, 124.2, 126.2, 131.8, 134.2, 135.1, 137.0, 148.0, 150.2, 159.5.

Anal. Calcd. for $C_{14}H_{10}BrN_3O_3$: C, 48.3; H, 2.9; N, 12.1. Found: C, 47.4; H, 2.8; N, 11.8 [29].

General Method for the Condensation of 4-Dimethylaminonitrosobenzene with Heterocycles.

The heterocyclic starting material (2-4 mmoles), 4-dimethylaminonitrosobenzene (2.2-4.4 mmoles), and piperdine (4-5 drops) were refluxed in anhydrous ethanol (10-30 ml) for 90 minutes. After cooling to 0°, the product was filtered off and washed with a small portion of ice-cold ethanol. Purification was performed either by recrystallisation or by precipitation from an alcohol solution. Alternatively, oily products were purified by column chromatography.

The following compounds were so prepared:

2,3-Dihydro-3-[4-(dimethylamino)phenylimino]-1-methyl-indolizin-2-one **39**.

Preparation from **37** and *p*-dimethylaminonitrosobenzene by the general procedure (reflux 15 minutes) gave an oil on concentration of the solvent. This was purified by column chromatrography on neutral alumina [toluene:ethyl acetate (6:4)] to give imine **39** (25%) as an violet oil which was characterized by its ^1H nmr (deuteriochloroform): 1.75 (s, 3H, C*H*$_3$), 3.00 (s, 6H, N*Me*$_2$), 6.00-6.15 (m, 1H, H-6), 6.30-6.80 (m, 1H, H-7), 6.80 (d, 2H, J_{AB} = 9 Hz), 6.95-7.25 (m, 1H, H-8), 7.90-8.00 (m, 1H, H-5), 8.25 (d, 2H, J_{AB} = 9 Hz).

2,3-Dihydro-3-[4-(dimethylamino)phenylimino]-1-phenylindolizin-2-one **40**.

Compound **40** was obtained (reflux 15 minutes) as microcrystals from ethanol in 90% yield mp 215-217°; ir (bromoform): 1635, 1595, 1510 cm^{-1}; ^1H nmr (deuteriochloroform): 2.90 (s, 6H, N*Me*$_2$), 5.90-6.15 (m, 1H, 6-H), 6.70 (d, 2H, J_{AB} = 10 Hz, Ar*H*), 6.95-7.60 (m, 7H, Ar*H*), 7.85-8.00 (m, 1H, 5-H), 8.32 (d, 2H, J_{AB} = 10 Hz, Ar*H*); ^{13}C nmr (deuteriochloroform): 48.7 (q, N*Me*$_2$), 151.6 (s, *C*=O), 109.3-139.4 (Ar-*C*).

Anal. Calcd. for $C_{22}H_{19}N_3O$: C, 77.4; H, 5.6; N, 12.2. Found: C, 77.5; H, 5.3; N, 12.2.

General Method for Diazo Coupling with Heterocyclics.

The diazonium salt was prepared from the aniline (5 mmoles), water (1.5 ml), and 12 *N* hydrochloric acid (1.5 ml) at 0-5°, and added dropwise at 0-5° to the heterocyclic starting material (4 mmoles) in ethanol (50 ml) and piperidine (1.5 g). The colored first at 0-5° for 30 minutes, then at 20° for 30 minutes, and after this cooled again to 0° and suction filtered. The product was purified by recrystallisation or by column chromatography.

The following compounds were so prepared:

2,3-Dihydro-1-methyl-3-(phenylhydrazono)indolizin-2-one **41**.

Preparation from **37** and benzenediazonium chloride by the general procedure gave an oil on concentration of the crude mixture. This was purified by column chromatrography on neutral alumina [toluene:ethyl acetate (6:4)] to give hydrazone **41** (35%) as a green oil which was characterized by its ^1H nmr (deuteriochloroform): 1.80 (s, 3H, C*H*$_3$), 6.10-6.40 (m, 1H, 8-H), 6.60-7.65 (m, 8H, Ar-*H*), 7.90 (d, 1H, J = 6 Hz, 5-H).

2,3-Dihydro-3-(phenylhydrazono)-1-phenylindolizin-2-one **42**.

Compound **42** was obtained as microcrystals from ethanol in 57% yield mp 218-219°; ir (bromoform): 1630 (C=N), 1580 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform): 6.30-6.50 (m, 1H, 6-H), 6.95-7.80 (m, 13H, Ar*H*, N*H*), 8.10 (d, 1H, J = 6 Hz, 5-H); ^{13}C nmr (deuteriochloroform/75.45 MHz): 103.5 (s), 110.1 (d), 114.4 (d), 115.5 (d), 123.5 (d), 125.5 (d), 126.7 (d), 126.9 (d), 128.4 (d), 129.4 (d), 130.5 (s), 131.9 (s), 135.9 (d), 142.1 (s), 151.8 (s, *C*=N), 168.9 (s, *C*=O).

Anal. Calcd. for $C_{20}H_{15}N_3O$: C, 76.7; H, 4.8; N, 13.4. Found: C, 76.7; H, 4.9; N, 13.4.

2,3-Dihydro-3-[4-(nitrophenyl)hydrazono]-1-phenylindolizin-2-one **43**.

Compound **43** was obtained as microcrystals from ethanol in 60% yield mp 267-273°; ir (bromoform): 3100, 1620 (C=N), 1585 (C=O) cm^{-1}; ^1H nmr (deuteriochloroform/trifluoroacetic acid): 7.5-8.0 (m, 10H, Ar*H*, N*H*), 8.40 (d, 2H, J_{AB} = 7 Hz), 8.5-8.8 (m, 1H, Py^+H), 9.25 (d, 1H, J = 5 Hz, 5-H); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): 145.2 (C-5), 146.5 (NH*C*), 148.8 (*C*NO$_2$), 152.2 (C-8), 153.5 (C-3), 157.1 (C=*C*-OH), 106.7-132.2 (Ar-*C*); ms: m/z = 385.1068 (M^+, $C_{20}H_{14}N_4O_3$ requires 385.1066).

Anal. Calcd. for $C_{20}H_{14}N_4O_3.\frac{1}{2}H_2O$: C, 65.4; H, 4.1; N, 15.3. Found: C, 65.7; H, 3.8; N, 15.2.

3-Amino-2-(4-nitrophenylazo)imidazo[1,2-*a*]pyridine **65**.

Compound **65** was obtained as microcrystals from ethanol in 25% yield mp 237-239°; ir (bromoform): 3400, 1590, 1560, 1320, 1247 cm^{-1}; ^1H nmr (deuteriochloroform/trifluoroacetic acid): 7.20-7.50 (m, 2H, 6-H, 7-H), 8.05 (d, 1H, 8-H), 8.20 (d, 2H, J_{AB} = 12 Hz, Ar*H*), 8.50 (d, 2H, J_{AB} = 12 Hz, Ar*H*), 8.55 (d, 1H, 5-H); ^{13}C nmr (deuteriochloroform/trifluoroacetic acid): (75.45 MHz): 115.5 (d), 117.7 (s), 119.0 (d), 126.3 (d), 127.0 (d), 128.3 (s), 144.3 (d), 146.0 (s), 146.7 (d), 150.1 (s), 151.2 (s); ms: m/z = 282.0865 (M^+, $C_{13}H_{10}N_6O_2$ requires 282.0850), 283 (M+1, 15), 282 (M^+, 59), 266 (19), 119 (10), 105 (92), 79 (39), 78 (100), 67 (26), 52 (22), 51 (29), 39 (23).

Anal. Calcd for $C_{13}H_{10}N_6O_2.\frac{1}{2}H_2O$: C, 53.6; H, 3.8; N, 28.5. Found: C, 53.9; H, 3.5; N, 27.6 [29].

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