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Dedicated to Heinrich Nöth, München, on the occasion of his seventieth birthday

The azomethine imine group of isoquinolinium *N*-arylimides **2** is partially incorporated into an aromatic ring. The nucleophilic-electrophilic 1,3-dipoles **2** undergo cycloadditions to ethylene derivatives bearing either electron-withdrawing or electron-releasing substituents. The regiochemistry is *bidirectional*; electron-attracting substituents appear at the 1-position of the tricyclic adducts. Various enamines, however, adopt an orientation such that the amino function appears at the 2-position. The tricyclic adducts undergo an acid-catalyzed hyrazo rearrangement.

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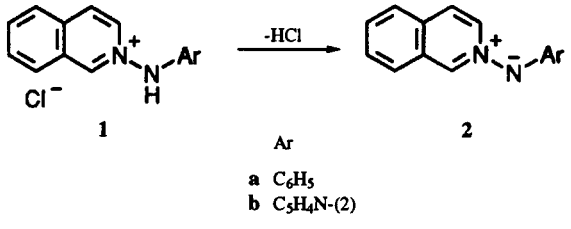
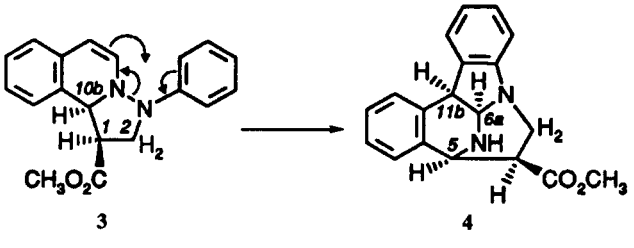
Introduction.

Deprotonation of *N*-arylaminoisoquinolinium salts **1** furnishes the deep-red isoquinolinium *N*-arylimides **2** [2] which undergo 1,3-dipolar cycloadditions. Compounds **2** can be regarded as azomethine imines [3] in which the C=N bond is part of the isoquinoline system. The 1,3-addition to a dipolarophile is accompanied by the loss of aromaticity in the *N*-containing ring, a factor that reduces the 1,3-activity. Cycloadditions of **2** to the C=C bond of twelve α,β-unsaturated carboxylic esters and carbonitriles have been reported to proceed at room temperature with high yields [4]. The structures of the cycloadducts were elucidated by their nmr spectra and X-ray analyses [4,5]. The regiospecific addition of **2a** to methyl acrylate gives rise to **3** as the major diastereoisomer [4], thus suggesting that the imide nitrogen is the nucleophilic center.





Cycloadducts of type **3** are ene-phenylhydrazines which are amenable to an acid-catalyzed hydrazo rearrangement. This reaction can be viewed as a Fischer indole synthesis [6] that stops at the pentacyclic system **4**, *i.e.*, one-step short of the indole [7]. Intramolecular β-elimination with formation of a double bond between C-6a and C-11b of **4** would generate high strain in the incipient 8-membered ring.

The cycloadducts and their rearrangement products are chiral. We arbitrarily chose a representation in which 10b-H of **3** is on the β-side; this hydrogen becomes the 5β-H in the pentacyclic **4**.

Azomethine imines are nucleophilic-electrophilic 1,3-dipoles and belong to type **II** of Sustmann's classification [8,9a]. They combine readily with electron-deficient C=C bonds, slowly (or not at all) with common alkenes and vinyl ethers, but rapidly once more with the electron-rich C=C bonds of enamines.

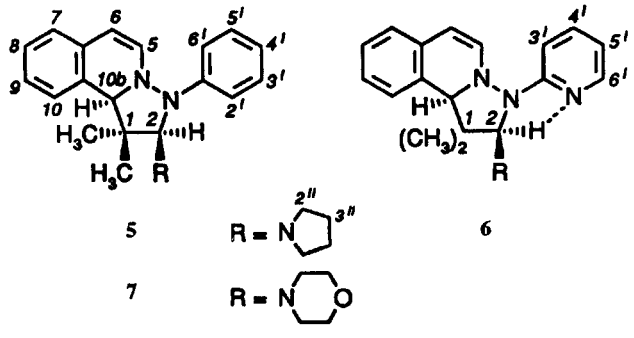
The aromatic azomethine imines **2** do not react with ethylene, for kinetic reasons; the activation barrier is too high. However, the ethylene adducts of **2a** and **2b** are indirectly accessible by cycloadditions to vinyl-triphenylphosphonium bromide and subsequent alkaline hydrolysis [4]. Butyl vinyl ether and 2,3-dihydropyran were also found to be unreactive towards **2**.

We describe here the cycloadditions of **2** to enamines and subsequent reactions of the products.

Enamines of Acetone and 3-Pentanone as Dipolarophiles.

The unstable isoquinolinium *N*-phenylimide (**2a**) was generated from **1a** by the addition of triethylamine in dichloromethane. In the presence of 1 equivalent of 1-pyrrolidinoisobutene, the deep red color of **2a** faded within 5 minutes at room temperature, and the pale-yellow cycloadduct **5** was isolated in 61% yield. The ^{1}H nmr spectra of 1,2-dihydroisoquinoline derivatives show a characteristic AX pattern due to 5-H and 6-H, these signals appearing at δ 6.34 and 5.19 with $J_{5,6}$ = 7.6 Hz in the case of **5**. The electron release by N-4 is responsible for the shielding of the vinylic 6-H. The regiochemistry is deduced from the appearance of two singlets at δ 4.17 and 4.21 for 10b-H and 2-H.

In the ^{13}C nmr spectrum of **5**, the electron donation to the β-carbon atom of the ene-hydrazine is evident from δ(C-6) 99.2, whereas C-5 is strongly deshielded (140.2 ppm). The assignments of all the δ_H and δ_C values (except for those of C-1 to C-4, which fall in the narrow range from 124-128 ppm) are based on comparisons with two-dimensional analyses of related cycloadducts [5].

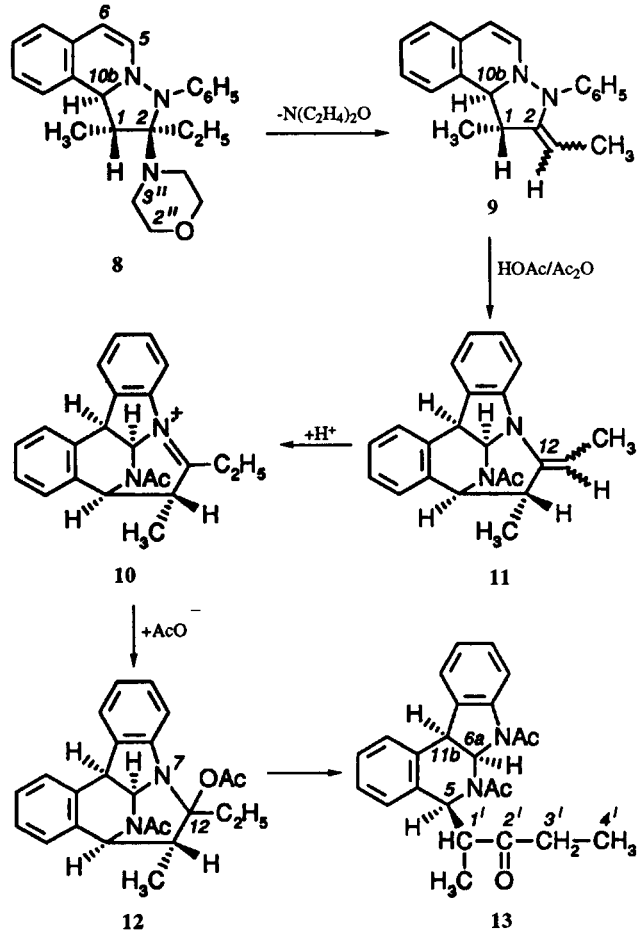


The isoquinolinium *N*-(2-pyridyl)imide (**2b**) is stable in solution, except for a reversible dimerization that makes the crystalline dimer a convenient storage form [2]. In the ^1H nmr spectrum of the analogous orange-yellow adduct **6**, singlets are observed at δ 4.02 for 10b-H and at δ 4.94 for 2-H. The difference of 0.8 ppm in the δ(2-H) of **5** and **6** offers a clue as to the stereochemistry at C-2. In the cycloadducts of **2b** with ethylene or electron-poor C=C bonds, values of δ(2β-H) are found to be 0.6-1.3 ppm higher than those in the adducts of **2a** [4], while the values of δ(2α-H) differ insignificantly. An X-ray analysis of the adduct of **2b** with methyl acrylate confirmed the ^1H nmr evidence for an *intramolecular hydrogen bond* between 2β-H and the pyridine nitrogen [5]. Thus, the 2-H must be on the β side in **5** and **6**.

The free-energy change for the cycloaddition of **2a** and **2b** to 1-pyrrolidinoisobutene is rather small. On warming **5** in organic solvents above 40°, the reversible appearance of the red color of **2a** indicates some dissociation into the reactants. The addition of acrylonitrile induced rapid decolorization as the more stable acrylonitrile adduct was formed. The degree of dissociation of **6** is even greater. According to the uv-vis spectrum, a 0.29 m*M* solution of **6** in chloroform contained 17% of free **2b** after equilibration at 25°, corresponding to $K_{diss} = 10^{-5}\ M^{-1}$. Even the crystals of **5** and **6** smell of pyrrolidinoisobutene when exposed to humid air.

The *in situ* reaction of **2a** with 1-morpholinoisobutene yielded 74% of the colorless crystals of **7**, the ^1H nmr data of which closely resembled those of **5**.

The cycloadducts **5-7** are ene-hydrazines and retain an electron-rich bond C5=C6. A strong infrared stretching vibration is seen at 1620-1635 cm^{-1}. The dipolarophilic activity is insufficient to allow the reaction with a second molecule of **2**. However, more electrophilic 1,3-dipoles such as mesitonitrile *N*-oxide are capable of adding to this type of ene-hydrazine bond [4].



The cycloaddition of **2a** to 3-morpholino-2-pentene is followed by elimination of morpholine from the initially formed **8**. Although the ethylidene compound **9** was not obtained in a pure state, the AB spectrum of 5-H and 6-H is as expected, and the doublet due to 10b-H (δ 3.73) indicates a proton at position 1, *i.e.*, that C-1 is a saturated center. The vinylic 12a-H of the new ene-hydrazine function appears as a multiplet at δ 5.18, and the vinylic methyl signals are suggestive of *cis,trans* isomers. Two pieces of evidence point to the 1β location of the second methyl group. Firstly, the value of 10.0 Hz for $J_{1,10\beta}$ is of the same order as the *trans*-couplings in our tricyclic system [4]. More convincingly, the value of 3.73 for δ(10b-H) is not far from δ 3.59 calculated for the interaction with a

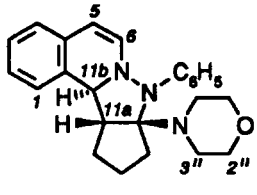
cis-vic methyl group. A statistical analysis of the δ_H values of 40 cycloadducts has provided *substituent increments*, *e.g.*, -0.46 ppm for *cis-vic*-CH_3 and +0.41 ppm for *trans-vic*-CH_3 [4].

Our attempts to characterize the oily **9** from analysis of the product of hydrazo rearrangement led to an unexpected result. In previous examples [10] (see below), treatment with acetic acid and acetic anhydride has proved adequate for inducing the rearrangement. In the case of **9**, instead of the pentacyclic *N*-acetyl derivative **11**, a crystalline compound **13** (25%) was isolated, the molecular formula of which showed that an additional equivalent of acetic acid had been incorporated. The ^{1}H nmr spectrum of **13** featured two methyl signals due to *N*-acetyl groups (δ 2.22, 2.36), one doublet (δ 0.74) due to the 1'-methyl group, and a triplet for the methyl in the 4' position (δ 1.00). The mass spectrum further supports structure **13** by showing the stepwise loss of the side-chain C_5H_9O and of the two acetyl groups.

How is **13** generated? The 12-ethylidene group of the hydrazo rearrangement product **11** is part of a new enamine group, β-protonation of which furnishes **10** in the tentative reaction scheme. Addition of an acetate anion affords the α-aminocarbinol ester **12**. The concluding step, an O → N acetyl migration with concomitant ring-opening at the C12-N7 bond, profits from the release of strain in the condensed tricyclic system of **12**.

Enamines of Cyclic Ketones as Dipolarophiles.

The 1:1 reaction of **2a** with 1-morpholinocyclopentene furnished 43% of the crystalline adduct **14**. The thermochromism of **14** in solution again pointed to a cycloaddition-cycloreversion equilibrium. The doublet at δ_H 4.23 due to 11b-H established the regiochemical course of the addition. The value of 9.7 Hz for $J_{11a,11b}$ suggests a *trans* coupling, although this cannot be concluded unequivocally, since the ranges of *cis* and *trans* coupling constants overlap. The broad multiplet due to 11a-H is centered at δ 3.5.



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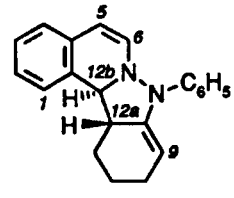

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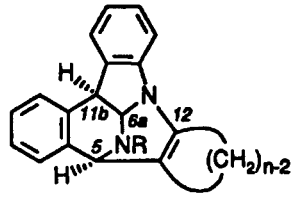
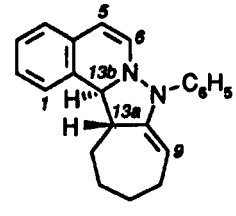


16 n=6, R=H
17 n=6, R=Ac
18 n=7, R=Ac



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The primary cycloadduct of **2a** with 1-morpholinocyclohexene could not be detected. The product of morpholine elimination, **15**, provided an appropriate ^{1}H nmr spectrum, even though an analytically pure specimen was not isolated. The AB spectrum of 5-H and 6-H is as expected, and the doublet due to 12b-H at δ 4.11 (J = 11.0 Hz) indicates that C-1 is not part of the new C=C bond. A side product (12%) crystallized slowly, which turned out to be **16**, the result of a [3.3]-sigmatropic reaction. Its ^{1}H nmr spectrum allowed an unambiguous structural assignment based on comparisons with the spectra of related compounds [7,10]. Besides the appearance of the NH signal, the long-range coupling of 5-H and 6a-H (^{4}J = 1.6 Hz) is typical of a W-shaped bond system.

In a second experiment, the rearrangement of the crude **15** was induced by the addition of acetic acid and acetic anhydride. The ^{1}H nmr spectrum of the *N*-acetyl compound **17** (50%) revealed an equilibrium of *cis,trans* isomers (ratio 70:30) with respect to the rotationally hindered amide group. The adjacent ring protons, 5-H and 6a-H, differ in their δ_H values by 0.7-0.8 ppm in the two amide configurations, whereas the δ_H of the more distant 11b-H changes only marginally.

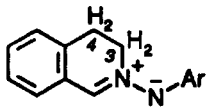
The reaction of 1-morpholinocycloheptene with **2a** was analogous to that of the lower homologue. The product of morpholine elimination was obtained in a crystalline state, and the ^{1}H nmr spectrum confirmed structure **19**; 13b-H gives rise to a doublet at δ 3.82 with $J_{13a,13b}$ = 9.7 Hz. The olefinic 9-H is the X part of an ABCX pattern.

Treatment of **19** with acetic acid and acetic anhydride enacted the hydrazo rearrangement and subsequent *N*-acetylation. The ^{1}H nmr spectrum of **18**, isolated in 60% yield, resembles that of **17**, and the rotamer ratio is similar.

Conclusions.

In cycloadditions of **2** with enamines, the quantitative yields that are observed for the reactions with electrophilic C=C bonds [4] are not attained. The equilibria with the reactants reduce the yield and increase the likelihood of side reactions, *e.g.*, autoxidation. Nevertheless, the ^{1}H nmr examination of the dark mother liquors did not give any indication of the presence of a second regioisomer.

The *N*-imides **2** add to enamines in a direction which is opposite to that observed for the interaction with electrophilic C=C bonds, *e.g.*, **3**. The "bidirectional" behavior is not unexpected; it has also been observed for the 3,4-dihydroisoquinolinium *N*-arylimides **20**, studied by Grashey in our laboratory [11,12].



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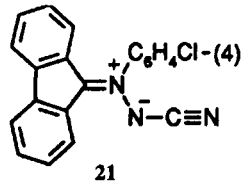

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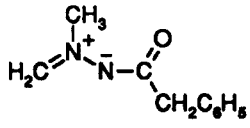

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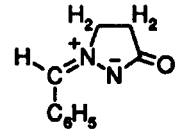

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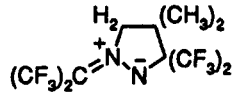

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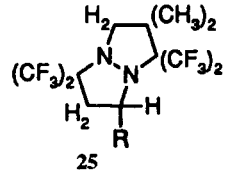

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However, this *bidirectionality* should not be interpreted in terms of fixed nucleophilic and electrophilic centers in azomethine imines. The termini of 1,3-dipoles are ambiphilic [9b]. The point of *orientational switching* is 1,3-dipole-dependent and is different for various azomethine imines. The stable cyanamide derivative **21** was our initial point of reference [13]; there, the switching is slightly shifted to the side of electrophilic C=C bonds as dipolarophiles. Azomethine imine **21** adds to methyl acrylate in the two directions in a 94:6 ratio, whereas the addition to methyl α-ethoxyacrylate is controlled by the electron-releasing ethoxy function and takes place in the same orientation as that established for vinyl ethers and enamines [14].

In the azomethine imines **22** [15] and **23** [16], the basicity and nucleophilicity of the terminal nitrogen is further decreased by *N*-acylation. Regioisomer ratios of 89:11 for **22** [15] and 67:33 for **23** [17] in the reactions with acrylic ester now favor the direction in which the ester group appears in the α-position with respect to the terminal nitrogen function. Finally, the azomethine imine **24**, the intermediate of criss-cross addition, almost attains the unidirectional extreme. According to Burger *et al.*, reaction of **24** with ethyl vinyl ether furnishes only **25**, R = OC_2H_5, and 95% of **25**, R = CO_2CH_3, (*vs.* 5% of the regioisomer), thereby indicating the predominance of the same addition direction for nucleophilic and electrophilic ethylene derivatives [18].

Perturbation MO treatment provides an at least qualitative understanding of regioselectivity phenomena in the framework of the concerted pathway [19,20,9c]. The bidirectionality observed for the cycloadditions of **2** should not lead to the conclusion that a two-step mechanism *via* zwitterionic intermediates is operative. The configuration of *cis,trans* isomeric dipolarophiles is fully retained in the cycloadditions of isoquinolinium *N*-arylimides **2**, as well as in those of the other azomethine imines mentioned.

EXPERIMENTAL

Instruments and Techniques.

The ir spectra (potassium bromide discs, film for oily substances) were recorded with a Perkin-Elmer 125 instrument and subsequently with a Bruker FT model IFS 45. Some of the early nmr spectra, recorded on Bruker WP80 CW (^{1}H 80 MHz) and DS (^{13}C 20 MHz) instruments, were repeated using a Varian XR400S instrument (400 MHz for ^{1}H, 100 MHz for ^{13}C) and are marked; unless otherwise stated, acid-free deuteriochloroform (stored over dry potassium carbonate) was the solvent, with tetramethylsilane as internal standard. The ms is an EI spectrum at 70 eV, recorded on an AET instrument MS 902. Melting points are uncorrected.

(rel-10b-βH)-(±)-1,2,3,10b-Tetrahydro-1,1-dimethyl-3-phenyl-2α-pyrrolidinopyrazolo[5,1-*a*]isoquinoline (**5**).

1-Pyrrolidinoisobutene [21] (1.30 g, 10.4 mmoles) and 1.10 g (10.9 mmoles) of triethylamine were added to a stirred suspension of 2.56 g (10.0 mmoles) of *N*-anilinoisoquinolinium chloride (**1a**) [2,22] in 25 ml of dichloromethane. The deep-red color disappeared within a few minutes. After washing with water and evaporation of the organic solvent, the residue was crystallized from diethyl ether/petroleum ether to give 2.11 g (61%) of **5**. Recrystallization afforded long, pale-yellow needles, mp 109-110° (which turned red above 90°, due to cycloreversion); ir: ν 695, 742, 755, 771 (aromatic CH out-of-plane deformations), 1493 st, 1569 m, 1595 st (aromatic ring vibrations), 1621 cm^{-1} st (C=C of enhydrazine); uv (chloroform): λ max 330 nm (log ε 3.77), 265 (4.00); in chlorobenzene at 60°, the absorption tails into the visible at 400-550 nm, due to the presence of **2a**; ^{1}H nmr (400 MHz): δ 1.07, 1.11 (2 s, 2 CH_3), 1.81 (m, 3"-H_2/4"-H_2), 2.97-3.09 (m, 2"-H_2/5"-H_2), 4.17 (s, 10b-H), 4.21 (s, 2β-H), 5.19, 6.34 (AX, $J_{5,6}$ = 7.6 Hz, 6-H, 5-H), 6.87 (br d, 10-H), 6.89 (tt, 4'-H), 6.93 (br d, 7-H), 7.00 (td, 9-H), 7.06 (br d, 2'-H/6'-H), 7.15 (td, 8-H), 7.25 (td, 3'-H/5'-H); ^{13}C nmr (100 MHz, DEPT): δ 18.3, 26.9 (2 CH_3), 24.7 (C-3"/C-4"), 50.0 (C-2"/C-5"), 54.6 (C-1), 67.9 (C-10b), 90.4 (C-2), 99.2 (C-6), 113.8 (C-2'/C-6'), 120.2 (C-4'), 124.3, 125.0, 126.2, 127.9 (C-7 to C-10), 129.0 (C-3'/C-5'), 130.0, 132.9 (C-6a, C-10a), 140.2 (C-5), 151.9 (C-1').

Anal. Calcd. for $C_{23}H_{27}N_3$ (345.5): C, 79.96. H, 7.88; N, 12.16. Found: C, 80.08; H, 7.96; N, 12.00.

1,2,3,10b-Tetrahydro-1,1-dimethyl-3-(2-pyridyl)-2α-pyrrolidinopyrazolo[5,1-*a*]isoquinoline (**6**).

Isoquinolinium *N*-(2-pyridyl)imide [2] (**2b**, 221 mg, 1.00 mmole) and 150 mg (1.20 mmoles) of 1-pyrrolidinoisobutene were combined in 5 ml of dichloromethane at 20°. The deep orange-red color faded over a period of 12 hours, but the solution did not become colorless. After evaporation of the solvent, pale orange-yellow needles (141 mg, 45%) of **6** crystallized

from diethyl ether/chloroform, mp 129-132° dec. On redissolving **6**, an orange color indicated some reversion to **2b** in the equilibrium. The cycloreversion thwarted the preparation of an analytically pure specimen; the crystals still smelled of pyrrolidinoisobutene; ir: ν 683, 765 (aromatic CH out-of-plane deformations), 1434, 1477 st (2-pyridyl vibration [4]), 1498, 1568, 1591 st (aromatic ring vibrations), 1634 cm^{-1} st (C=C stretching); uv-vis (chlorobenzene): λ max 308 nm (4.23) in fresh solution; within 1 hour this band diminished while the absorptions of **2b** at 450 and 468 nm intensified; ^1H nmr (signals of dissociation products subtracted): δ 1.06 (br s, 2 CH_3), 1.72 (m, 3"-H_2/4"-H_2), 3.06 (m, 2"-H_2/5"-H_2), 4.02 (s, 10b-H), 4.94 (br s, 2β-H), 5.23 and 6.33 (AX, $J_{5,6}$ = 7.8 Hz, 6-H, 5-H), 6.53-7.57 (7 aromatic H), 8.17 (m, 6'-H).

1,2,3,10b-Tetrahydro-1,1-dimethyl-2α-morpholino-3-phenylpyrazolo[5,1-*a*]isoquinoline (**7**).

Compound **2a** (1.10 mmoles), liberated from **1a** in 15 ml of dichloromethane as described above, was reacted with 1-morpholinoisobutene [21] (200 mg, 1.42 mmoles). Workup afforded **7** as colorless cubes (293 mg, 74%), mp 155-157° dec, after recrystallization from methanol; ^1H nmr (400 MHz): δ 1.12, 1.13 (2 s, 2 CH_3), 2.91-3.08 (m, 3"-H_2/5"-H_2 of morpholino), 3.73 (m, 2"-H_2/6"-H_2 of morpholino), 3.99 (s, 10b-H), 4.19 (s, 2β-H), 5.21 and 6.31 (AX, $J_{5,6}$ = 7.6 Hz, 6-H and 5-H), 6.86 (br d, 10-H), 6.93 (tt, 4'-H), 6.94 (dd, 7-H), 7.02 (td, 9-H), 7.17 (td, 8-H), 7.18 (dd, 2'-H/6'-H), 7.28 (tt, 3'-H/5'-H); ^{13}C nmr (100 MHz, DEPT): δ 18.2, 27.1 (2 CH_3), 50.0 (br, C-3"/C-5"), 54.6 (C-1), 67.8 (C-2"/C-6"), 68.0 (C-10b), 93.2 (C-2), 99.7 (C-6), 114.0 (C-2'/C-6'), 120.6 (C-4'), 124.4, 125.2, 126.2, 128.1 (4 CH, C-7 to C-10), 129.1 (C-3'/C-5'), 129.6 (C-10a), 132.8 (C-6a), 139.9 (C-5), 151.8 (C-1').

Anal. Calcd. for $C_{23}H_{27}N_3O$ (361.5): C, 76.42; H, 7.53; N, 11.63. Found: C, 76.49; H, 7.72; N, 11.39.

2-Ethylidene-1,2,3,10b-tetrahydro-1β-methyl-3-phenylpyrazolo[5,1-*a*]isoquinoline (**9**).

Salt **1a** (2.56 g, 10 mmoles) was suspended in 25 ml of dichloromethane, and 1.10 g (10.9 mmoles) of triethylamine and 1.71 g (11.0 mmoles) of 3-morpholino-2-pentene, freshly prepared from diethyl ketone and morpholine [23], were added to the stirred suspension. After 12 minutes, the brown mixture was washed with water; evaporation of the volatiles at 40°/0.1 Torr left **9** as an oily residue which did not crystallize; ^1H nmr: δ 1.10 (d, J = 7.0 Hz, 1β-CH_3), 1.47 (m, CH_3 of ethylidene), 2.25 (dq, 6 lines visible, 1α-H), 3.73 (br d, J = 10.0 Hz, 10b-H), 5.18 (m, vinyl-H of ethylidene), 5.37 and 6.30 (AB, J = 7.4 Hz, 6-H and 5-H), 6.55-7.10 (m, **9** aromatic H). The spectrum suggests a mixture of *cis,trans* isomers with respect to the ethylidene group. The dissociation equilibrium did not allow the purification of **9** by chromatography, hence crude **9** was directly converted to **13**.

2-(6,7-Diacetyl-6,6a,7,11b-tetrahydro-5*H*-indolo[2,3-*c*]isoquinolin-5-yl)pentane-3-one (**13**).

A solution of crude **9** (3.16 g) in 33 ml of acetic anhydride and 17 ml of acetic acid was stored for 4 weeks at room temperature; long, colorless needles of **13** (0.98 g, 25%) precipitated, mp 231-232° (chloroform); ir: ν 756 st, 785 m; 1090, 1122, 1279, 1312, 1357, 1383, 1417, 1464, 1483 st; 1668 st br (amide I), 1710 cm^{-1} st (C=O, ketone); ^1H nmr (100 MHz): δ 0.74 (d, J = 7.0 Hz, 1'-CH_3), 1.00 (t, J = 7.3 Hz, CH_3-4'), 2.22 and 2.36 (2 s, 2 CH_3 of N-Ac), 7.5-8.1 (m, -CH-CO-CH_2-, not resolved), 4.76 (d, J = 11 Hz, 11b-H), 4.91 (br d, J = 11 Hz, 5-H), 6.8-7.4 (m, 7 aromatic CH, 6a-H), 8.20 (d, J = 8 Hz, 1 aromatic H); ^{13}C nmr (25 MHz): δ 7.4, 17.0 (2 q, 2 CH_3), 22.8, 24.3 (2 q, 2 $COCH_3$), 43.6, 47.4 (2 d, C-5, C-1'), 59.8 (d, C-11b), 67.6 (d, C-6a), 117.7 (d, C-8), 124.3-129.8 (7 d, 7 arom CH), 133.6, 134.9, 135.8, 142.2 (4 s, 4 quaternary C), 171.2, 172.7 (2 s, 2 C=O, amide), 212.6 (s, C=O, ketone); ms: (70 eV, 125°) m/z (%): 390 (33) [M^+], 347 (45) [M^+-$COCH_3$], 305 (10) [M^+ - C_5H_9O], 263 (100) [305 - CH_2=C=O], 232 (10), 221 (17) [305 - 2 CH_2=C=O], 220 (11) [$C_{15}H_{12}N_2^+$], 219 (28), 204 (32), 130 (4) [isoquinolinium$^+$].

Anal. Calcd. for $C_{24}H_{26}N_2O_3$ (390.5): C, 73.82; H, 6.71; N, 7.18. Found: C, 73.76; H, 6.68; N, 7.21.

8,9,10,11,11a,11b-Hexahydro-8a-morpholino-8-phenyl-8*H*-cyclopenta[3,4]pyrazolo[5,1-*a*]isoquinoline (**14**).

Salt **1a** (10.0 mmoles) and 1-morpholinocyclopentene (1.56 g, 10.2 mmoles) [23] were allowed to react as described for **5**, affording 1.62 g (43%) of **14**, which was obtained as colorless crystals, mp 129-130°, from diethyl ether/petroleum ether. Solutions show reversible thermochromism on warming, ir: ν 699, 752, 1118 st; 1269, 1284 m; 1456, 1496, 1600 st; 1624 cm^{-1} st (C=C stretching of enehydrazine); ^1H nmr: δ 1.4-2.3 (m, 9-H_2, 10-H_2, 11-H_2), 2.77 (m, 3"-H_2/5"-H_2), 3.2-3.6 (m, 11a-H), 3.72 (m, 2"-H_2/6"-H_2), 4.23 (d, $J_{11a,11b}$ = 9.7 Hz, 11b-H), 5.29 and 6.14 (AB, J = 7.5 Hz, 6-H and 5-H).

Anal. Calcd. for $C_{24}H_{27}N_3O$ (373.5): C, 77.18; H, 7.29; N, 11.25. Found: C, 76.99; H, 7.45; N, 11.30.

8,10,11,12,12a,12b-Hexahydro-8-phenylindazolo[3,2-*a*]isoquinoline (**15**).

A suspension of 2.56 g (10.0 mmoles) of **1a** in 25 ml of dichloromethane was treated with 1.71 g (10.2 mmoles) of 1-morpholinocyclohexene [23] and 10.9 mmoles of triethylamine. The usual workup afforded a slowly crystallizing fraction; after 8 days at 4°, 0.52 g (12%) of the rearrangement product **16**, mp 230-235°, was deposited from a solution in petroleum ether. The mother liquor contained the initial cycloadduct **15**, which was not obtained in a pure state; ^1H nmr of **15**: δ 3.42 (m, 12a-H), 4.11 (d, $J_{12a,12b}$ = 11.0 Hz, 12b-H), 5.20 (br s, 9-H), 5.35 and 6.17 (AB, $J_{5,6}$ = 8.0 Hz, 6-H and 5-H).

6,6a,7,11b,14,15,16,17-Octahydro-5*H*-5,7[1',2']benzenoindolo[2,3-*c*]isoquinoline (**16**).

Recrystallization of the above-mentioned specimen gave pure **16**, mp 240-245° dec; ^1H nmr (100 MHz): δ 1.63 (m, 15-H_2, 16-H_2), 2.15 (m, 14-H_2, 17-H_2), 2.50 (br s, NH), 3.94 (br s, 5-H), 4.12 (d, $J_{6a,11b}$ = 6.4 Hz, 11b-H), 5.31 (dd, ^3J = 6.4 Hz, $^4J_{5,6a}$ = 1.6 Hz, 6a-H; on irradiation at δ 3.94, the signal becomes a doublet with J = 6.4 Hz), 6.85-7.56 (m, 8 aromatic H).

Anal. Calcd. for $C_{21}H_{20}N_2$ (300.4): C, 83.96; H, 6.71; N, 9.33. Found: C, 83.84; H, 6.73; N, 9.11.

N-Acetyl Derivative **17**.

(a) The reaction of 1.50 g (*ca.* 5 mmoles) of oily **15** with 13 ml of acetic anhydride and 7 ml of acetic acid was slightly exothermic. After a few days at room temperature, 840 mg (*ca.* 50%) of colorless **17** had crystallized from chloroform/diethyl ether; mp 271-274° dec; ir: ν 768 st, 1450 br st, 1655 cm^{-1} st br (amide I);

^{1}H nmr (some signals split because of hindered rotation at the amide bond, ratio 70:30): δ 1.60 (m, 15-H_2, 16-H_2), 2.12 (m, 14-H_2, 17-H_2), superimposed by 2.12 (s, $COCH_3$), 4.25 + 4.28 (2 d, $J_{6a,11b}$ = 6.5 Hz, 11b-H), 4.76 + 5.60 (2 d, $^4J_{5,6a}$ = 2.5 Hz, 5-H), 6.03 + 6.75 (2 dd, J = 6.5, 2.5 Hz, 6a-H); thus, δ(5-H) and δ(6a-H) are influenced most by the amide configuration.

Anal. Calcd. for $C_{23}H_{22}N_2O$ (342.4): C, 80.67; H, 6.48; N, 8.18. Found: C, 80.60; H, 6.50; N, 8.34.

(b) One hundred mg (0.33 mmole) of **16** was dissolved in 2 ml of acetic anhydride. After 2 days at room temperature, the excess of the reagent was removed. Compound **17** (92 mg, 81%) was crystallized from chloroform/diethyl ether, mp 269-273° (mixed mp without depression).

10,11,12,13,13a,13b-Hexahydro-8-phenyl-8*H*-cyclohepta-[3,4]pyrazolo[5,1-*a*]isoquinoline (**19**).

Salt **1a** (3.90 g, 15.2 mmoles), 2.90 g (16.0 mmoles) of 1-morpholinocycloheptene [23], and 1.70 g (16.8 mmoles) of triethylamine in 30 ml of dichloromethane were converted to 5.4 g of a brown oil from which the colorless **19** (1.12 g, 23%) crystallized after a month at room temperature, mp 100-102° (chloroform/-diethyl ether); ir: ν 690, 748, 755, 763 st, 921, 1235, 1248 m, 1489, 1595 st, 1630 cm^{-1} st (C=C of enamine); ^{1}H nmr (400 MHz): δ 1.19, 1.41, 1.83, 2.04, 2.14, 2.38 (6 m, ratio 1:2:2:1:1:1, 10-H_2 to 13-H_2), 3.25 (m, 13 lines resolved, 13a-H), 3.82 (d, $J_{13a,13b}$ = 9.7 Hz, 13b-H), 5.49 and 6.23 (AX, $J_{5,6}$ = 7.7 Hz, 6-H and 5-H), 5.79 (ddd, J_{allyl} = 2.4 Hz, J_{vic} = 4.1, 8.8 Hz, 9-H), 6.90-7.39 (9 aromatic CH).

Anal. Calcd. for $C_{22}H_{22}N_2$ (314.4): C, 84.04; H, 7.05; N, 8.91. Found: C, 84.12; H, 7.04; N, 8.85.

6-Acetyl-5,6,6a,14,15,16,17,18-octahydro-7*H*,11b*H*-5,7[1',2']-cycloheptindolo[2,3-*c*]isoquinoline (**18**).

Upon storage of a solution of 1.00 g (3.18 mmoles) of **19** in 20 ml of acetic anhydride/acetic acid (2:1) for 3 days at room temperature, 680 mg (60%) of colorless **18** crystallized, mp 218-221°; after repeated recrystallization from chloroform, mp 224-225°; ir: ν 706, 728, 760 st; 952, 1220, 1244 st; 1440 st br; 1635-1660 cm^{-1} st br (amide I); ^{1}H nmr: rotamer ratio 72:28 with respect to hindered amide bond; δ 2.19 (s, $COCH_3$), 4.26 + 4.21 (2 d, $J_{6a,11b}$ = 6.3 Hz, 11b-H), 5.71 + 4.88 (2 d, $J_{5,6a}$ = 2.5 Hz, 5-H), 6.00 + 6.72 (2 dd, J = 6.3, 2.5 Hz, 6a-H).

Anal. Calcd. for $C_{24}H_{24}N_2O$ (356.5): C, 80.86; H, 6.79; N, 7.86. Found: C, 80.78; H, 6.88; N, 7.85.

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