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Isoquinolinium *N*-Arylimides and Electrophilic Ethylenes: Structures and NMR Spectra of Cycloadducts [1]

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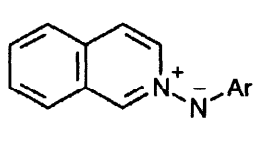
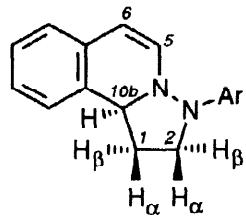
Abstract: The title compounds furnish high yields of substituted 3-aryl-1,2,3,10b-tetrahydropyrazolo[5,1-a]isoquinolines of type **2**. The structural conclusions from ^{1}H NMR spectra are confirmed by X-ray analyses of cycloadducts **3b** and **4a**. The lone pair repulsion of the two nitrogen atoms freezes the N-inversion in the bicyclic hydrazines and determines the conformation; the torsion angle of the n-orbitals is close to the optimum of 90°. An intramolecular hydrogen bond of the weakly acidic 2ß-H to the pyridyl nitrogen of **3b** was established, corroborating previous ^{1}H NMR evidence. The ^{13}C NMR spectra of 14 cycloadducts reveal the contributions of substituents to δ_C. Two-dimensional NMR techniques secure the assignments of all ^{1}H and ^{13}C signals of selected cycloadducts.

Introduction

The cycloadditions of isoquinolinium *N*-arylimides [2] - mainly the *N*-phenylimide **1a** and the *N*-(2-pyridyl)-imide **1b** - to twelve α,ß-unsaturated carboxylic esters and nitriles proceeded at room temp. with high yields. The 1,3-dipoles **1a,b** did not react with ethylene; however, the alkaline cleavage of the cycloadducts with triphenylvinylphosphonium bromide, an electrophilic dipolarophile, provided the formal ethylene adducts **2a** and **2b**.[3]



1



2

a Ar = C_6H_5
b Ar = C_5H_4N-(2)

The entirety of the ^{1}H NMR data allowed the structural assignment of about forty cycloadducts. The supposition that the imide nitrogen of **1** would be the nucleophilic terminus of the 1,3-dipole was confirmed; the methoxycarbonyl of methyl acrylate and the cyano group of acrylonitrile were located in 1α- or 1ß-position of the diastereoisomeric cycloadducts.[3] In the ^{1}H NMR spectra, the methyl group of 1α-CO_2CH_3 was shielded in the cycloadducts by the benzo ring of the dihydroisoquinoline system, whereas 2α-CO_2CH_3 did not lie in the shielding cone of the *N*-aryl residue. On comparing the ^{1}H NMR

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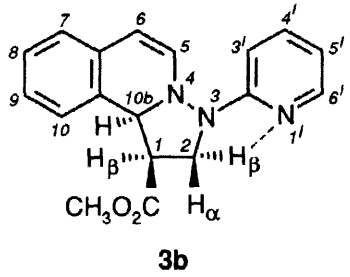
spectra of the *N*-phenyl series **a** and *N*-(2-pyridyl) series **b**, i.e., **2a** and **2b** as well as their mono-, di-, and trisubstituted derivatives, we noticed a shift to higher frequency of the 2ß-H signal in the *N*-(2-pyridyl) series **b** by 0.66 - 1.35 ppm. This phenomenon suggested an intramolecular hydrogen bond of 2ß-H to the pyridyl nitrogen.

Several configurations of the hydrazine system in the cycloadducts **2** and their derivatives are conceivable. However, the ^{1}H NMR evidence suggested a strong preference for a structure which corresponds to a *cis*-annellation of the pyrazolidine ring to the dihydroisoquinoline system, the *N*-aryl being turned "backwards".[3]

We wanted a *direct confirmation* of the structural model which dates from 1980 [4] and was based on the ^{1}H NMR spectra only.

X-Ray Structures of Cycloadducts

We chose the methyl acrylate adduct **3b** as an example of the *N*-(2-pyridyl) series and found the predictions based on NMR criteria fully confirmed by the X-ray analysis. In Figure 1 as well as in the numbered formulae, the racemic cycloadducts are illustrated by the enantiomer with 10bß-H.



3b

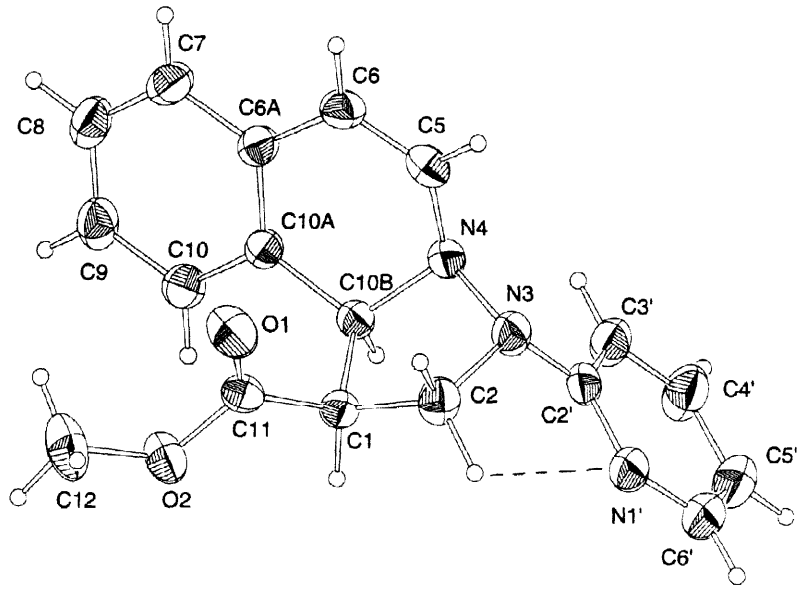


Figure 1. X-ray structure of cycloadduct **3b**; ZORTEP plot (thermal ellipsoids represent 30% probability)

The pyrazolidine ring assumes an envelope conformation with N3 as the flap. This is indicated by the dihedral angles; with 10.6°, the torsion angle at C1-C10b is the smallest (Table 1).

1,3-Cyclohexadiene (gas phase) has a half-chair conformation (C_2) with torsion angles of 17.5° at C2-C3 and 45° at C5-C6.[5] The corresponding dihedral angles for the 6-membered heteroring of **3b** are 8.1° for C5-C6-C6a-C10a and 31.9° for C5-N4-C10b-C10a. The half-chair is deformed; N4 juts out of the quasi-plane stronger than C10b. The driving force comes mainly from keeping the repulsion potential of the lone pairs at N3 and N4 at a minimum. The hydrazine group has a key function in determining the structure.

Table 1. X-ray Structures of Methyl 1,2,3,10b-Tetrahydro-3-(2-pyridyl)pyrazolo[5,1-*a*]isoquinoline-1α-carboxylate (**3b**) and Methyl 1ß-Chloro-1,2,3,10b-tetrahydro-3-phenylpyrazolo[5,1-*a*]isoquinoline-1α-carboxylate (**4a**); Selected Bond Lengths and Angles (in parentheses standard deviations on the last decimal)

Bond lengths (Å)	**3b**	**4a**		**3b**	**4a**
C1-C2	1.540(3)	1.532(3)	C5-C6	1.316(3)	1.323(3)
C2-N3	1.478(3)	1.470(3)	N4-C5	1.398(3)	1.391(3)
N3-N4	1.423(3)	1.425(2)	N3-C2'	1.406(3)	-
N4-C10b	1.473(3)	1.466(3)	N3-C1'	-	1.425(3)
C10b-C1	1.580(3)	1.589(3)	N1'-C2'	1.327(3)	-
C1-Cl	-	1.799(2)	C1'-C2'	-	1.386(3)
Bond angles (°)					
C1-C2-N3	105.8(2)	106.2(2)	C2-H-N1'	105.2(2)	-
C2-N3-N4	105.1(2)	104.5(2)	C10b-N4-C5	117.5(2)	118.2(2)
N3-N4-C10b	106.2(2)	106.6(2)	N4-C5-C6	122.6(2)	122.4(2)
N4-C10b-C1	104.5(2)	103.9(2)	C5-C6-C6a	121.0(2)	121.1(2)
C10b-C1-C2	102.7(2)	102.5(2)	C6-C6a-C10a	118.2(2)	118.6(2)
C2-N3-C2'	118.3(2)	-	C6a-C10a-C10b	120.4(2)	120.1(2)
C2-N3-C1'	-	118.6(2)	C10a-C10b-N4	112.8(2)	113.2(2)
Dihedral angles (°)					
C1-C2-N3-N4	33.6(2)	34.0(2)	N4-C5-C6-C6a	5.3(4)	5.1(4)
C2-N3-N4-C10b	-41.5(2)	-42.2(2)	C5-C6-C6a-C10a	8.1(3)	6.3(3)
N3-N4-C10b-C1	32.0(2)	32.5(2)	C6-C6a-C10a-C10b	0.2(3)	1.7(3)
N4-C10b-C1-C2	-10.6(2)	-10.8(2)	C6a-C10a-C10b-N4	-19.5(3)	-19.0(2)
C10b-C1-C2-N3	-13.2(2)	-13.5(2)	C10a-C10b-N4-C5	31.9(2)	29.8(3)
C2-N3-C2'-N1'	-41.3(3)	-	C10b-N4-C5-C6	-26.5(3)	-24.2(3)
C2-N3-C1'-C2'	-	-45.9(3)			

The enamine resonance in C6-C5-N4 and the amidine resonance in N3-α-pyridyl tend to planarize the bond systems of N3 and N4. However, the N-atoms have still distinctly pyramidal bond systems. The three bond angles at N3 furnish a sum of 336.7°, whereas those at N4 add up to 337.3°. The bond angles sum up in ammonia to 320.4° and at each of the N-atoms of gaseous hydrazine to 325°.[6] Another measure of pyramidalization is provided by the distance of the N-atom from the plane of its three ligands [7]. N3 is located 0.41 Å above the plane of C2, C2', and N4; the distance of N4 from the plane of N3, C5, and C10b amounts to 0.40 Å.

Bipyramidal hydrazines prefer a torsion angle of 90° according to ab initio calculations.[8] The joint analysis of electron diffraction data and rotational constants for gaseous hydrazine provided 91± 2° as torsion angle;[6] 87.0° was found for N3 and N4 of our cyclic hydrazine **3b**,[9] *i.e.*, the favoured orthogonality of the lone pair orbitals is well approximated.

The π-orbital at N4 cuts the plane determined by the atoms C6, C5, and N4 at an angle of 92.2°. This close approach to 90° warrants full enamine type resonance; the C5-C6 bond, *i.e.*, the double bond

of the enamine group, is somewhat lengthened to 1.316 Å, and N4-C5 is shortened to 1.398 Å, the latter compared with 1.473 Å for N4-C10b. The effect is small compared with that in an enamino-ß-ketocarboxylic ester which we recently described: C=C 1.324 Å and C-N 1.421 Å.[10]

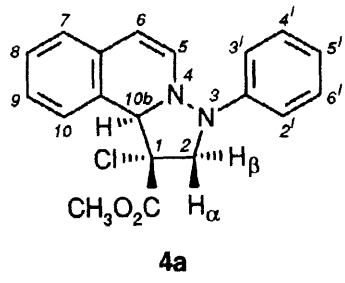
Similar structural conditions should permit the amidine type resonance in the 2-aminopyridine system involving N3. The lone pair-orbital at N3 forms an angle of 79.5° with the plane defined by atoms N1', C2', and N3. The deviation from 90° is caused by the hydrogen bond C2ß-H···N1'.

The position of the 2ß-H was approximated by differential Fourier transform. The distance between 2ß-H and N1' is 2.36 Å, *i.e.*, lower than the sum of the van der Waals radii [2.7]; the distance between C2 and N1', anchor points of the intramolecular hydrogen bond, is 2.82 Å. Joesten and Schaad [11] give the following H···B bond lengths in Å, based on neutron diffraction data, which we compare with the calculated sum of van der Waals radii [Å]:

O-H···O 1.7 [2.6], N-H···O 1.9 [2.6], C-H···O 2.3 [2.6], O-H···N 1.9 [2.7], N-H···N 2.2 [2.7]

Extrapolation to C-H···N yields a bond length which is in the range of our experimental value (2.36 Å).

To what extent does the hydrogen bond between 2ß-H and N1' in **3b** influence the conformation of the 5-membered heterocycle ? For a second structure analysis, the *N*-phenyl compound **4a** was chosen which contains 1ß-chlorine atom in addition to the 1α-CO_2CH_3 (Figure 2). The bond lengths and angles turned out to be rather similar to those of **3b**; the structural data of **3b** and **4a** are compared in Table 1.



4a

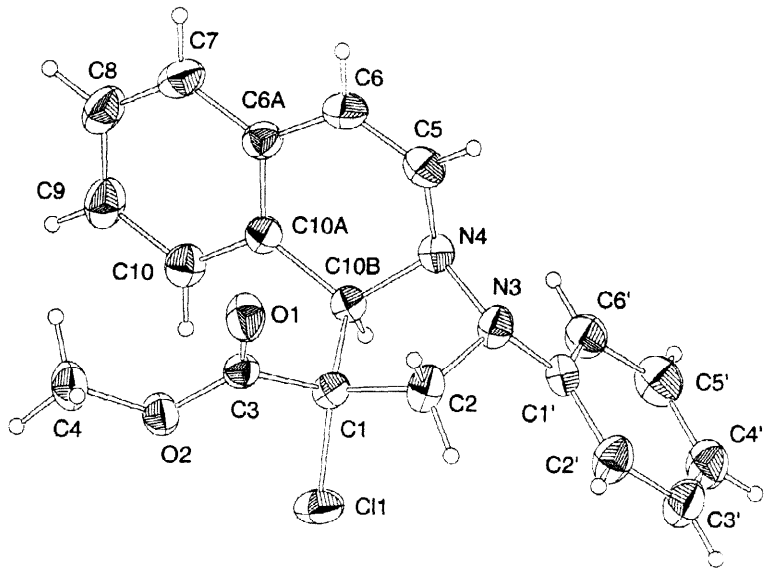


Figure 2. X-ray analysis of cycloadduct **4a**; ZORTEP plot (thermal ellipsoids represent 30% probability

Like the *N*-(2-pyridyl) ring in **3b**, the *N*-phenyl in **4a** allows an effective aniline-type resonance. The n-orbital at N3 cuts the benzene plane in **4a** at an angle of 79.6°. The enamine resonance in the six-membered heteroring is also well established, as shown by an angle of 93.6° between the n-orbital at N4 and the σ-bond plane of the C5-C6 double bond. Angle sums of 337.1° at N3 and 339.0° at N4 emphasize the structural similarity of **4a** with **3b**. The torsion angle between the lone-pair orbitals at N3 and N4 amounts to 93.6°, again not far from the optimal value for hydrazine, 90°.

The dihedral angle of C2-N3-C1'-C2' (45.9°) in **4a** is somewhat larger than that of C2-N3-C2'-N1' (41.3°) in **3b**; that increases the distance from 2.82 Å for C2 and N1' in **3b** to 2.97 Å for C2 and C2' in **4a**. As a result, the collision of the van der Waals radii of 2ß-H and 2'-H in **4a** is diminished, although this H,H-distance of 2.10 Å is the smallest in the molecule.

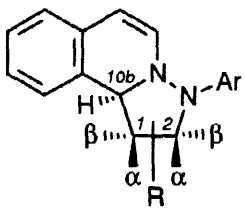
Thus, the hydrogen bond between C2 and N1' in **3b** neither requires an enhancement of the lone pair repulsion at N3 and N4, nor does it impose an increase of conformational strain in the two hetero-rings. The conditions for the engagement of the C2ß-H - despite its low acidity - in an *intramolecular hydrogen bond* with N1' are optimal, also from the viewpoint of entropy.

Substituent Effects in ^{13}C NMR Spectra

The assignment of the δ_C is unproblematic for the saturated C-atoms of the formal ethylene adducts **2a** and **2b** (Table 2). The CH_2 at lowest frequency (δ = 35.3, 34.6) must be C-1; the second CH_2 is deshielded by N-3 and appears at δ = 50.0 and 45.7, respectively. The CH signal of C-10b is deshielded by N-4 and benzylic resonance (δ = 58.8, 59.7). We reported that δ(2ß-H) of the *N*-phenyl compound **2a** was *increased* by 0.8 ppm in the *N*-(2-pyridyl) parent compound **2b**.[3] Interestingly, the hydrogen bond with the pyridine nitrogen leads to a *decrease* of δ(C-2) by 4.3 ppm, when **2b** is compared with **2a**.

We observed that the ^{13}C-H coupling of the methylene group C-2 in **2b** does not produce a triplet, but rather a dd as a consequence of the considerable difference of δ(2α-H) and δ(2ß-H). The 1α-carboxylic ester **3b** is a derivative of **2b**; here we found apparent J_{CH} values (X part of ABX) of 144.2 and 149.6 Hz for C-2. Large δ_H differences (≥ 0.5 ppm) of methylene protons are one of the prerequisites for the dd being resolved in the ^{13}C-H coupling.[12]

Table 2. ^{13}C Chemical Shifts (δ_C in $CDCl_3$) of the Saturated C-Atoms of 3-Aryl-1,2,3,10b-tetrahydropyrazolo-[5,1-*a*]isoquinolines (25 or 100 MHz); **a** = 3-Phenyl, **b** = 3-(2-Pyridyl). In Parentheses: Substituent Effects ($\delta_s - \delta_2$), E = CO_2CH_3.



2 – 11

a Ar = C_6H_5
b Ar = C_5H_4N-(2)

No.	Substituents	δ(C-1)	δ(C-2)	δ(C-10b)
2a	none	35.30	49.96	58.76
2b	none	34.59	45.65	59.65
3b	1α-E	53.71 (19.1)	49.16 (3.5)	62.48 (2.8)
4a	1α-E, 1ß-Cl	77.23 (41.9)	64.31 (14.4)	73.12 (14.4)
5a	1α-CN	39.54 (4.2)	55.14 (5.2)	60.77 (2.0)
5b	1α-CN	38.84 (4.3)	50.44 (4.8)	61.66 (2.0)
6a	1α-CH_3, 1ß-E	59.59 (24.3)	62.64 (12.7)	64.34 (5.6)
7a	1α-CN, 1ß-CH_3	48.42 (13.1)	62.59 (12.6)	68.20 (9.4)
8a	1ß-E, 2α-E	56.40 (21.1)	68.44 (18.5)	64.07 (5.3)
8b	1ß-E, 2α-E	56.10 (21.5)	64.87 (19.2)	63.53 (3.9)
9a	1α-E, 2α-E	58.69 (23.4)	66.79 (16.8)	62.63 (3.9)
9b	1α-E, 2α-E	57.79 (23.2)	61.09 (15.4)	63.36 (3.7)
10a	1ß-E, 2ß-E	53.42 (18.1)	61.88 (11.9)	61.23 (2.5)
11a	1ß-CN, 2α-CN	43.55(8.3)	56.20(6.2)	64.73(6.0)

As well as **2a,b**, Table 2 contains three more pairs which allow the δ_C comparison of the *N*-phenyl series **a** and the *N*-(2-pyridyl) series **b** of cycloadducts; $\delta_a - \delta_b$ = 0.3 – 0.9 ppm for C-1 and 3.6 - 5.7 ppm for C-2 of **5**, **8**, and **9** were found. Thus, the low frequency shift of δ(C-2) by the intramolecular hydrogen bond in the *N*-(2-pyridyl) series appears to be general.

When a methoxycarbonyl group is introduced into position 1 of **2b**, the changes of the three δ_C values in **3b** are the "substituent effects", listed in parentheses for **3b** in Table 2. The shift to high frequency of δ(C-1) by 19.1 ppm is the *gem*-CO_2CH_3 effect, and *vic*-CO_2CH_3 increases δ(C-2) by 3.5 and δ(C-10b) by 2.8 ppm. A much smaller influence of *gem*-CN is derived from **5a** and **2a** ($\Delta\delta$ = 4.2 ppm) as well as from **5b** and **2b** ($\Delta\delta$ = 4.3 ppm). The influence of *vic*-CN should be similar for C-2 and C-10b; $\Delta\delta_C$ = 5.2 and 2.0 ppm for **5a**, and 4.8 and 2.0 ppm for **5b** reveal consistency, but not equality. The substituents influence conformational equilibria and modify δ_C as a consequence.

The *e*-CO_2CH_3 shifts C-1 and C-2 of the cyclohexane chair to high frequency by 16.5 and 2.5 ppm, respectively;[13] that compares well with $\Delta\delta_C$ = 19.1 ppm for C-1, 3.5 for C-2, and 2.8 for C-10b of the carboxylic ester **3b**. A smaller influence of C≡N on δ_C is well-known,[13] amounting to 0.5 and 2 ppm for C-1 and C-2 of cyclohexane. The effects found for **5a** and **5b** are somewhat higher.

A 1-methyl group in combination with 1-CO_2CH_3 in **6a** (1-CN in **7a**) leads to the sums of substituent effects shown in parentheses in Table 2. When additivity of substituent increments is assumed and those for *gem*- and *vic*-CO_2CH_3 (CN) are subtracted, methyl effects of 5.2 (8.9) ppm for C-1, 9.2 (7.4) ppm for C-2, and 2.8 (7.4) ppm for C-10b result. Methyl increments of 5.8 ppm for C-1 and 8.4 ppm for C-2 of cyclohexane were reported.[14] *e*-Chlorine increases δ(C-1) of cyclohexane by 32 and δ(C-2) by 10 ppm.[14] The comparison of **4a** with **3b** reveals 23 ppm as increment of *gem*-Cl, and 11 (C-2) and 12 ppm (C-10b) as increments of *vic*-Cl.

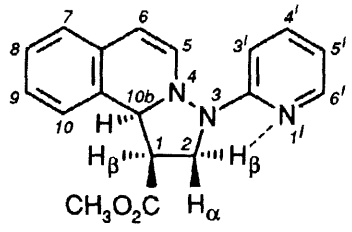
In the 1,1-disubstituted cycloadducts **4a**, **6a**, and **7a**, the multiplicity of the ^{13}C signals establishes a unique assignment of C-1, C-2, and C-10b. This is no longer true for the 1,2-diesters **8-10**. Applying the increments for *gem*- and *vic*-CO_2CH_3 (**3b**) to the 1,2-diesters, the following sums of substituent increments (full additivity assumed) would be expected: 23 ppm for C-1 and C-2, and 2.8 for C-10b. The δ_C values (in parentheses in Table 2) are in fair agreement for C-1 and C-10b of **8-10**, but the *cis*-diesters **9a**, **9b**, and **10a** show only $\Delta\delta$(C-2) = 12 - 17 ppm. Considerable conformational changes are concluded for the *cis*-1,2-diesters; the latter also disclosed rather large deviations in the δ(1-H) and δ(2-H) from those calculated with substituent increments.[3] Two-dimensional NMR techniques helped in distinguishing C-2 and C-10b.

Two-Dimensional NMR Techniques

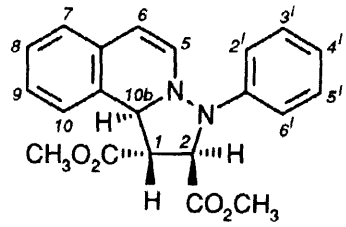
The heteronuclear shift correlation of ^{13}C and ^{1}H signals of the adducts **3b** and **8a** was achieved by the HETCOR method.[15] Table 3 presents the data for **3b**; the X-ray analysis (Figure 1) makes **3b** a suitable test object. The assignments of the saturated C-atoms (preceding section) and their H-ligands was confirmed. The AB or AX pattern of the 5-H and 6-H signals (enamine bond) is unmistakable and was corroborated by chemical conversions (cycloadditions to the enamine bond).[3] The attribution of the sp^2-hybridized C-atom at lowest frequency to the enhydrazine ß-position 6 was unproblematic, too.

Tables of substituent increments for mono- and 1,2-disubstituted benzenes as well as for 2-substituted pyridines, [13,14] combined with general considerations, allow tentative assignments of many aroma-

tic C-atoms and protons. Signal overlap (9-H/10-H, 3'-H/8-H for **3b** and 7-H/10-H for **8a**), the complex pattern of the benzo protons (7-H to 10-H), and the narrow δ region for C-7 to C-10 created difficulties.



3b



8a

A DQF-COSY [16] experiment (Table 3) gave the desired information and allowed the ordering of the four benzo protons in a sequence. There is no coupling in the pairs 6-H/7-H and 10-H/10b-H (U shaped long-range system). The weak coupling between 6-H and 10-H is reminiscent of the small $J_{1,5}$ of substituted naphthalenes.[13] The direction of 7-H to 10-H was established by a NOESY [17] experiment which indicates the spatial proximity of 6-H/7-H (2.53 Å in **3b**) and 10-H/10b-H (2.51 Å in **3b**). Furthermore, DQF-COSY indicates a coupling of 5-H with 10b-H which is not resolved in the 400 MHz spectrum; it is open, whether it is mediated by N-4 or by the conjugated chain of C-atoms.

Electron release by N-4 generates the low frequency shift of δ(C-6), part of it should be conducted to C-7 and C-9. Indeed, δ(C-9) is lower by 3.2 ppm than δ(C-8) in the spectra of **3b** and **8a**. The same is true for the ^{1}H signals: δ(9-H) < δ(8-H) by 0.13 (**3b**) and 0.17 ppm (**8a**). Six further cycloadducts of series **a** and **b** were examined and showed the same regularity in their δ_C and δ_H values.

In contrast to δ_H of 7-H to 9-H, δ(10-H) is sensitive to the anisotropy of substituents in position 1. δ(10-H) = 7.04 was found for **3b** (1α-CO_2CH_3), 7.02 for **8a** (1ß-CO_2CH_3, 2α-CO_2CH_3), 7.12 for **5a** (1α-CN), 7.14 for **7a** (1α-CN, 1ß-CH_3), and 7.27 ppm for **4a** (1α-CO_2CH_3, 1ß-Cl).

The X-ray structure of **3b** provides the torsion angles at C-C bonds. We expected a correlation of $^3J_{H,H}$ for the pyrazolidine protons with the dihedral angles. The outcome was unsatisfactory.

The chemical shifts of the *N*-(2-pyridyl) C-atoms of **3b** are very similar to those of 2-aminopyridine:[13]

δ_C (ppm) of	C-2'	C-3'	C-4'	C-5'	C-6'
Cycloadduct **3b**	160.9	109.0	138.0	116.2	147.7
2-Aminopyridine	161.1	110.5	138.0	113.0	148.9

The electron release by N-3 leads to a stronger decrease of δ_C in position 3' than in position 5'. The resonance effect of N-3 likewise decreases δ(3'-H) and δ(5'-H), but the effect is now stronger for 5'-H.

δ_H (ppm) of	3'-H	4'-H	5'-H	6'-H
Cycloadduct **3b**	7.17	7.52	6.28	8.24
2-Aminopyridine	6.70	7.44	6.60	8.11

These shifts to low frequency are smaller for **3b** than for 2-aminopyridine, suggesting that N-3 (hydrazine type) is a weaker donor than NH_2.

Amusingly, the NOESY experiment showed a proximity relation between 3'-H of the pyridyl and 10b-H in the pyrazolidine ring which the projection formula **3b** does not reveal. The X-ray data indicate

a distance of 2.76 Å to which NOESY still responds.

The δ_C of the *N*-phenyl in **8a** correspond well with the signals of phenylhydrazine [13] (in parentheses): C-1' 150.1 (151.3), C-2' 113.9 (112.0), C-3' 129.3 (129.0), C-4' 121.3 ppm (118.9). The positional sequence of the phenyl protons was established by HETCOR, DQF-COSY, and splitting pattern. The agreement of the δ_H of **8a** with those of phenylhydrazine is less close: 2'-H 7.14 (6.66), 3'-H 7.28 (7.18), 4'-H 6.94 ppm (6.71). The electron release of N-3 to positions 2' and 4' in **8a** appears to be weaker than that in phenylhydrazine. The anisotropy effects of the 5,6 double bond and of 2-substituents may be partially responsible for the deviations.

The X-ray data of **4a** indicated the close vicinity of 2ß-H and 2'-H (2.10 Å); the NOESY experiment testifies to the strong interaction of these protons in **8a** as a model.

In cases of overlapping ^1H signals of higher order, the computer simulation by DavinX [18] produced congruent signal shapes and gave precise δ_H and *J* values. Finally, the CH couplings over two and three bonds, elucidated by COLOCS,[19] allowed the distinction of the quaternary C-6a and C-10a in **3b** and **8a** and confirmed the high δ(C-2') in **3b** and δ(C-1') in **8a**.

EXPERIMENTAL

X-Ray Diffraction Analyses

Methyl 1,2,3,10b-Tetrahydro-3-(2-pyridyl)pyrazolo[5,1-a]isoquinoline-1α-carboxylate (**3b**, Figure 1, Table 1): [20] Mol. mass 307.4 for $C_{18}H_{17}N_3O_2$, monoclinic. Space group $P2_1/c$, No. 14. Unit cell dimensions: a = 9.292(1), b = 8.959(2), c = 19.067(3) Å, ß = 95.004(13)°, volume 1581.1 (4) Å^3, Z = 4, D_c = 1.291 mg/ml; $F(000)$ = 648, T = 294 (2) K, μ (Mo-K_α) = 0.086 mm^{-1}. Data collection: CAD4 Diffractometer, pale yellow plate (.27 x .33 x .47 mm), mounted in a glass capillary, cell constants from 25 centered reflections. Mo-K_α radiation, λ = 0.71073 Å, graphite monochromator, ω-2Θ-scan, scan width (0.56 + 0.56 tan Θ)°, maximum measuring time 60 sec, intensity of three standard reflections checked every two hours, Θ range 2.14 - 22.97° for all $-h$, $+k$, $\pm l$, 2338 reflections measured, 2183 unique and 1747 with $I > 2\sigma(I)$. Structure solution by SHELXS-86 and refinement by SHELXL-93,[21] non-hydrogen atoms refined anisotropically, hydrogen with U_i = 1.2 x U_{eq} of the adjacent carbon atom. Full-matrix refinement against F^2. Final $R1$ = 0.0449 and $wR2$ = 0.1155 for 1747 reflections with $I > 2\sigma(I)$ and 209 variables. $R1$ = 0.0603 and $wR2$ = 0.1260 for all data. Weight: SHELXL-93. Maximum and minimum of the final difference Fourier synthesis 0.185 and -0.247 e Å^{-3}. ZORTEP plot.[22]

Methyl *1ß-Chloro-1,2,3,10b-tetrahydro-3-phenylpyrazolo[5,1-a]isoquinoline-1α-carboxylate* (**4a**, Figure 2, Table 1): [20] $C_{19}H_{17}ClN_2O_2$, mol. mass 340.8, monoclinic. Space group $P2_1/n$, No. 14. Unit cell dimension: a = 13.906 (7), b = 8.373 (2), c = 14.472 (2) Å, ß = 98.67 (2)°, volume 1665.8 (9) Å^3, Z = 4, D_c = 1.359 mg/ml; $F(000)$ = 712, T = 294 (2) K, μ (Mo-K_α) = 0.243 mm^{-1}. Data collection: CAD4 Diffractometer, pale yellow bloc (.33 x .47 x .57 mm), mounted in a glass capillary, cell constants from 25 centered reflections. Mo-K_α radiation, λ = 0.71073 Å, graphite monochromator, ω-2Θ-scan, scan width (0.63 + 0.51 tan Θ)°; maximum measuring time 60 sec, intensity of three standard reflections checked every two hours, Θ range 2.82 - 23.99° for all $-h$, $+k$, $\pm l$, 2729 reflections measured, 2611 unique and 2142 with $I > 2\sigma(I)$. Structure solution by SHELXS-86 and refinement by SHELXL-93, non-hydrogen atoms refined anisotropically, hydrogens with U_i = 1.2 x U_{eq} of the adjacent carbon atom. Full-matrix

refinement against F^2. Final $R1$ = 0.0376 and $wR2$ = 0.0928 for 2142 reflections with $I > 2\sigma(I)$ and 218 variables. $R1$ = 0.0493 and $wR2$ = 0.1007 for all data. Weight: SHELXL-93. Maximum and minimum of the final difference Fourier synthesis 0.184 and -0.230 e $Å^{-3}$.

NMR Experiments

Instruments: The spectra were recorded on a Varian XR 400S for ^1H (400 MHz) and ^{13}C (100 MHz with DEPT). Some of the ^{13}C spectra were run on Varian XL 100 (25.2 MHz); the multiplicities came from the comparison of H-decoupled and off-resonance spectrum. Acid-free $CDCl_3$ was used.

Simulation of ABCD ^1H Spectra by DavinX:[18] The computer iteration produced line shapes identical to the experimental with the following data for **3b**: δ = 6.98 (7-H), 7.04 (10-H), 7.06 (9-H), 7.18 (8-H); J(Hz) = 7.63 (for 7,8); 1.18 (7,9), 0.64 (7,10), 7.55 (8,9), 1.23 (8,10), 7.60 (9,10). **8a**: δ = 7.03 (10-H), 7.05 (7-H), 7.08 (9-H), 7.24 (8-H); J(Hz) = 7.49 (for 7,8), 1.20 (7,9), 0.61 (7,10), 7.63 (8,9), 1.28 (8,10), 7.49 (9,10).

Table 3. NMR Data of Methyl 1,2,3,10b-Tetrahydro-3-(2-pyridyl)-pyrazolo[5,1-a]isoquinoline-1α-carboxylate (**3b**) in $CDCl_3$

Position No.	δ_H ppm	Multiplicity	DQF-COSY	NOESY	δ_C ppm	COLOCS $^3J_{CH}(^2J_{CH})$
OCH_3	3.17	s		10 (small)	51.42	
1ß	3.39	ddd	10b, 2ß > 2α	10b > 2ß	53.71	(10b)
2α	3.69	dd	2ß > 1ß	2ß	49.16	
2ß	4.77	dd	2α > 1ß	2α > 1ß	"	
10b	4.64	dd	1ß > 5	1ß > 10 > 3'	62.48	5, 10
6	5.47	d	5 > 10	5, 7	103.66	7, (5)
5	6.28	d	6 > 10b	6	137.93	10b, (6)
7	6.98	d br.	8 > 9	6, 8	124.76	6, 9
10	7.04	dd br.	9 > 8	(9), 10b	128.07	8, 10b
9	7.06	td	8 > 10	8, (10)	125.26	7
8	7.18	td	7 > 9 > 10	9, 7	128.41	10
5'	6.79	ddd	4', 6' > 3'	4', 6'	116.22	3', (6')
3'	7.17	dt	4' > 5'	4' > 10b	108.99	5'
4'	7.52	ddd	3', 5' > 6'	3', 5'	138.04	6'
6'	8.24	ddd br.	5' > 4' > 3'	5'	147.70	4', (5')
2'					160.86 s	6'
6a					131.41 s	5, 8, 10
10a					127.98 s	6, 7, 9,(10b)
C=O					172.50 s	OCH_3, 10b, (1)

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