1,3-Dipolar Cycloadditions, 102[◇]

Isoquinolinium *N*-Arylimides and Electron-Deficient Ethylene Derivatives☆

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The 1,3-cycloadditions of isoquinolinium *N*-phenylimide (**2a**) and *N*-(2-pyridyl)imide (**2b**) to twelve α,β-unsaturated carboxylic esters and nitriles proceeded at room temp. with high yields; the reactions furnished tetrahydropyrazolo[5,1-*a*]isoquinoline derivatives and could be visually followed by the loss of the red color. In this class of azomethine imines, the imide nitrogen of **2** is the nucleophilic center which determines the regiochemistry of the additions to methyl acrylate, acrylonitrile, and their α-methyl and α-chloro derivatives. The diastereoselectivity is low; pairs of adducts were also formed with dimethyl fumarate and maleate. The configurations were elucidated by ^{1}H NMR analysis, which likewise provided the clue to the favored conformation of the tricyclic system. The *N*-arylimides **5** do not react with ethylene, but the formal ethylene adducts were accessible from the cycloadducts of **5a,b** to triphenylvinylphosphonium bromide by alkaline cleavage. The statistical analysis of the δ_H values of 39 cycloadducts provided a consistent set of substituent increments for the pyrazolidine protons.

Introduction

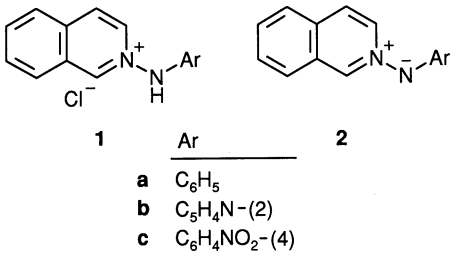
The isoquinolinium *N*-imides are a class of azomethine imines in which the C=N double bond is incorporated into an aromatic ring. The *N*-arylimides which we report here belong to the nucleophilic-electrophilic 1,3-dipoles ("Sustmann's class II"[1]); these combine with electron-deficient *and* electron-rich CC double bonds as dipolarophiles[2].

The study of isoquinolinium *N*-arylimides **2** began in the Munich laboratory in 1960 and ended − after interruptions − in 1984[3]. Apart from two lecture abstracts[4], the results have not yet been published.

Dimethyl Fumarate, Dimethyl Maleate and Related Dipolarophiles

The red isoquinolinium *N*-phenylimide (**2a**) was set free from the colorless aqueous solution of salt **1a** by sodium carbonate and extracted with ether. Although **2a** is not isolable[5], it reacts in the ethereal solution with dimethyl fumarate. In our first experiments, the adduct was purified *via* its picrate. Unexpectedly, an infrared NH absorption indicated a secondary amine. It turned out that the initial adduct is free of NH, but under acid catalysis (here with picric acid), it undergoes a deep-seated rearrangement which will be the subject of a later paper[6]. The cycloadducts of other dipolarophiles are prone to this isomerization to a different degree; some undergo it even in neutral medium.

Salt **1a** was stirred with 1.2 equiv. of *dimethyl fumarate* in dichloromethane; dropwise introduction of 1.1 equiv. of triethylamine liberated the 1,3-dipole **2a** in low stationary



1 **2**

	Ar
a	C_6H_5
b	C_5H_4N-(2)
c	$C_6H_4NO_2$-(4)

concentration. The colorless cycloadduct **3a**, isolated in 80% yield, turned red at about 140°C, signaling a cycloreversion; dimethyl fumarate can be sublimed from **3a** at 150°C/0.15 Torr. The spectra are in agreement with the tetrahydropyrazolo[5,1-*a*]isoquinoline structure **3a**. Besides two carbonyl frequencies, the IR spectrum reveals at 1624 cm^{-1} the C=C vibration of an ene-hydrazine. The doublets of the vinyl protons occur at δ_H = 5.55 (6-H) and 6.23 (5-H, J = 7.8 Hz), separated from the other signals. These doublets served as a diagnostic tool for the 1,2-dihydroisoquinoline system of the *primary* cycloadducts; in the aromatic isoquinoline the corresponding signals appear at δ_H = 8.45 (3-H) and 7.50 (4-H)[7]. The pyrazolidine ring harbors three protons: 10b-H and 2-H are deshielded by the adjacent nitrogen functions and occur at δ = 4.47 and 4.53; the signal of 1-H appears as a dd at 4.13 (Table 1). The reaction of dimethyl 2,3-dideuteriofumarate[3d] with **2a** provided us with the 1,2-dideuterio derivative of **3a**, in which only a broadened s at δ = 4.47 (10b-H) remained of the former three proton signals. Thus, the assignment of the three coupled protons in **3a** is unambiguous.

In the ^{13}C NMR spectrum of **3a**, the three saturated C-atoms of the ring appear as doublets at δ = 56.4, 64.1,

[◇] Part 101: Ref. [5].

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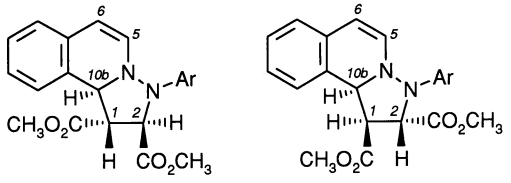
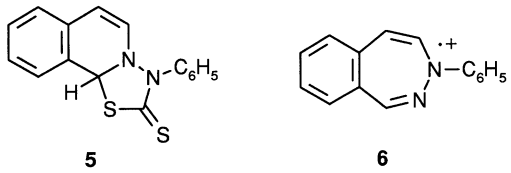


3 **4**

	Ar
a	C_6H_5
b	C_5H_4N-(2)
c	$C_6H_4NO_2$-(4)



5 **6**

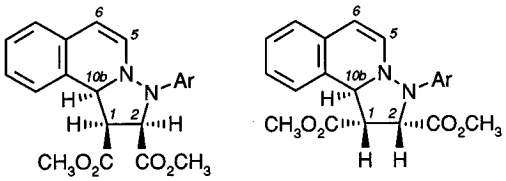
68.4, and the shielded electron-rich C-6 is at δ = 103.4. The application of substituent increments for pyridine and benzene derivatives[7] enabled a far-reaching assignment of the NMR data for aromatic C and H.

The MS showed the molecular ion (*m/z* = 364, 35%), and the base peak (*m/z* = 220) corresponded to $C_{15}H_{12}N_2$, suggesting a cycloreversion. The base peak could be $\mathbf{2a}^{+\bullet}$ or the product of hydrazo rearrangement[6]. If the often postulated analogy between the radical ion and the photo-excited state holds, the diazepine formula **6** is worth discussing. The photochemical conversion of type **2** zwitterions to 1,2-diazepines has attracted much attention[8]. Further fragmentation of $\mathbf{2}^{+\bullet}$ gives rise to isoquinoline$^+$ (41%) and $C_6H_5N^+$ (15%) in accordance with the splitting described for pyridinium and isoquinolinium *N*-acylimides[9]. In the initial cycloreversion of $\mathbf{3a}^{+\bullet}$, part of the positive charge moves with the dipolarophile; *m/z* = 144 (11%) points to the radical cation of dimethyl fumarate and *m/z* = 113 ($C_5H_3O_3^+$, 82%) to the further loss of CH_2OH.

The cycloreversion equilibrium of the carbon disulfide adduct **5** in solution at room temp. generates the 1,3-dipole **2a** in small stationary concentration[5]. In the reaction with dimethyl fumarate in the NMR tube, the red color of **2a** disappeared in 30 min, and besides **3a** a second diastereoisomer became visible in the ^{1}H NMR spectrum: **3a**/**4a** = 85:15. The formation of a different pair of diastereoisomeric cycloadducts from **2a** and dimethyl maleate (see below) demonstrates the retention of configuration in the probably *concerted* cycloaddition. For each of the two dipolarophiles, two differently oriented complexes of the reactants are conceivable, leading to pairs of cycloadducts. Of course, the adducts are racemates; we choose a presentation with the 10b-H on the β-side, *i.e.*, behind the ring system.

Of the ester methyl signals, δ_H = 3.68 and 3.84 for **3a** as well as 3.20 and 3.65 for **4a**, only the signal at δ = 3.20 reveals the shielding influence above the plane of a *cis-vic* aromatic ring. That signal must come from the 1α-CO_2CH_3 of **4a** which is located "before" the benzo ring. As shown below, the condensed ring system favors a configuration with the *N*-phenyl *cis-vic*-located to 2β-CO_2CH_3; however, the *N*-phenyl does not turn the shielding "face" to the *O*-methyl of ester groups in position 2.

The assignment of structures **3a** and **4a** was corroborated by the X-ray analysis[10] of the product that resulted from the acid-catalyzed hydrazo rearrangement of **3a**[6]. The X-ray structure indirectly established the *trans-vic* relation of the three H-atoms in the five-membered ring.



7 **8**

	Ar
a	C_6H_5
b	C_5H_4N-(2)
c	$C_6H_4NO_2$-(4)

The cycloaddition of **2a** onto *dimethyl maleate* afforded the dicarboxylic esters **7a** and **8a** in a ratio of 90:10. Again the CS_2 adduct **5** proved its worth as an acid-free source of the *N*-phenylimide **2a**. The minor adduct **8a** entered the acid-catalyzed hydrazo rearrangement so fast that only the isomerization product was found when **2a** was generated from **1a** mixed with base. In acid-free $CDCl_3$, **8a** had a half-life of 36 h at 25°C; it crystallized after chromatography on basic alumina (6% yield). The main cycloadduct **7a**, isolated in 76% yield, also required the neutral medium. By acid catalysis, the colorless $C_{21}H_{20}N_2O_4$ (**7a**) was converted to bright yellow crystals of $C_{24}H_{22}N_2O_6$ (richer by $C_3H_2O_2$)[3b]; the elucidation of a fascinating polystep sequence[4][11] will be the subject of a later report.

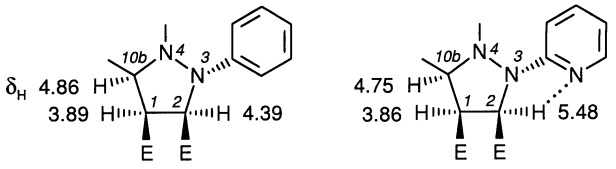
Again, there is one ester methyl in the pair **7a**/**8a** which is shielded by the *cis-vic* benzo system; δ_H = 3.17 points to a 1α-CO_2CH_3 group in **7a**, whereas the 2-CO_2CH_3 signal appears "normal" at 3.77. The two OCH_3 signals of **8a** nearly coincide at δ = 3.66 and 3.67 (Table 1).

The crystalline, storable isoquinolinium *N*-(2-pyridyl)-imide (**2b**)[5] gave a red solution in dichloromethane which was decolorized by dimethyl fumarate within 20 min. The main product **3b** (82% isolated) displayed the OCH_3 signals at δ_H = 3.71 and 3.81, similar to those of **3a**. The minor companion **4b** (about 2%) allowed identification of the 1α-CO_2CH_3 at δ = 3.27.

The MS of the *N*-(2-pyridyl) adduct **3b** reveals the same cycloreversion as described above for **3a**. Amusingly, the base peak here is also at *m/z* = 220, despite a mol. mass of 221 for **2b**. High resolution revealed $C_{14}H_{10}N_3^+$, *i.e.*, [$\mathbf{2b}^+$ − H]; the triazolium ion **12** is a possible candidate. The same *m/z* = 220 was observed in the MS of the dimer of **2b**[5].

The corresponding diastereoisomeric cycloadducts from the *N*-(2-pyridyl)imide **2b** and dimethyl maleate were isolated in yields of 88% (**7b**) and 8% (**8b**). The 1α-CO_2CH_3 of **7b** absorbs at δ_H = 3.17 and the 2α-CO_2CH_3 at 3.74; these data and δ = 3.66 and 3.67 for the ester groups of **8b**

underline the close relationship of the *N*-phenyl and *N*-(2-pyridyl) series.



9 (**7a**) E = CO_2CH_3 **10** (**7b**)

11

12

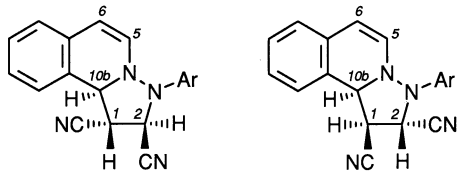
Our study of the scope of these cycloadditions was double-tracked: The use of the *N*-phenylimide **2a** and the *N*-(2-pyridyl)imide **2b** invited comparison of the δ_H of the ring protons in the cycloadducts. The two series differed by less than 0.2 ppm − except for δ(2β-H), as exemplified in the Scheme (**9** and **10**) for the maleic ester adducts **7a** and **7b**: δ(2β-H) for **7b** is 1.1 ppm greater than for **7a**, whereas the δ(2α-H) of both **8a** and **8b** have the same value, 4.99 ppm (Table 1). The same phenomenon occurs in the adducts of dimethyl fumarate: δ(2β-H) = 4.53 in the *N*-phenyl compound **3a** and 5.57 in the *N*-(2-pyridyl) derivative **3b**. In the cycloadduct **3c** of the *N*-(4-nitrophenyl)imide **2c**, δ(2β-H) = 4.69 comes close to the value observed for **3a**. Thus, the increased electron-attraction by the *N*-aryl group cannot be the reason for the down-field shift of 2β-H in the 2-pyridyl series.

According to the molecular model, ring strain is smaller for the *cis*-annellation of the pyrazolidine and dihydropyridine rings, *i.e.*, the lone-pair orbital at N-4 in the perspective formula **11** points "backwards", *cis* to 10b-H. The dihedral angle between the n-orbitals at N-3 and N-4 in **11** may approach 90°, where the lone pair repulsion of hydrazine[12] and its cyclic derivatives[13][14] has its minimum value. The pyramidalization at N-3 and N-4 may be decreased by the aniline and enamine conjugation in **11.** Nevertheless, the lone pair−lone pair interaction should govern the *N*-aryl to the β-side, as shown in **9**−**11**. Furthermore, the aniline-type conjugation favors orthogonality between the n-orbital at N-3 and the plane of the aryl group. Although the rotational barrier of the bond N3−C_{ar} may be small, 2β-H is probably in the deshielding field of the *N*-aryl group. Hydrogen-bonding of the 2β-H with the 2-pyridyl nitrogen (**10**) could well be responsible for the extra down-field shift, a phenomenon known also for *intramolecular* hydrogen bonds; the 2β-H is acidified by the 2α-CO_2CH_3.

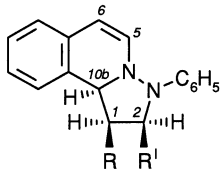
The addition of the *N*-phenylimide **2a** to *fumaronitrile* requires only a few min at room temperature. ^{1}H NMR analysis indicated a 90:10 ratio of **13a** and **14a**; only the major adduct was isolated (71%). In the structural assignment we lose our most valuable argument, *i.e.*, the shielding of the ester methyl above the benzo ring. Besides the analogy with dimethyl fumarate in the diastereoselectivity, indirect evidence comes from the adduct **13b** (72% isolated) of the *N*-(2-pyridyl)imide **2a** to fumaronitrile. The deshielding of the 2β-H by the contact interaction with the pyridine nitrogen reaches its highest value (1.35 ppm) here: δ(2β-H) = 4.62 for **13a** and 5.97 for **13b**.

With *methyl cis-3-cyanoacrylate* as a dipolarophile, regio- and diastereoselectivity allow formation of four products of concerted cycloadditions. The reaction with **5** as a precursor of **2a** in $CDCl_3$ in the NMR tube revealed two cycloadducts in a ratio of 77:23; the preparative separation furnished them in yields of 68% and 19%, respectively. An OCH_3 signal at δ_H = 3.30 in the minor adduct (*vs.* 3.85 for the major) established the presence of an ester group in the shielded position 1α. The coupling constant, $J_{1,2}$ = 8.0 Hz, fits a *cis*-relation, and suggests structure **16** for the minor isomer.

As for the major adduct, we compared its δ_H data (1-H 3.81, 2-H 4.47, 10b-H 4.56) with those calculated for all four *cis*-isomers on the basis of substituent increments (see below); the δ set predicted for **15** (1β-H 3.80, 2β-H 4.72, 10b-H 4.63) showed the best agreement. Thus, both products belong to the 1α,2α series, as does the major adduct of dimethyl maleate.



13a Ar = C_6H_5 **14a**
13b C_5H_4N-(2)



	R	R^I
15	CN	CO_2CH_3
16	CO_2CH_3	CN

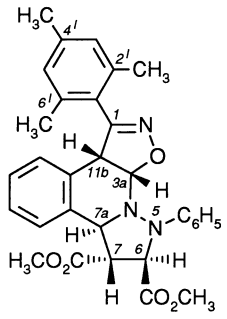
There is *chemical evidence* for the presence of the electron-rich double bond in the 5,6 position of the cycloadducts. The reaction of **3a** with 2,4,6-trimethylbenzonitrile *N*-oxide furnished a 1:1-adduct[3f] in which the ^{1}H NMR pattern of the vinylic 5-H and 6-H is replaced by a new AX spectrum at δ = 6.14 and 4.68. The large difference is consistent with the expectation for 3a-H and 11b-H of **17**. The same regiochemistry is generally obeyed in the cycloadditions of nitrile oxides to enamines[15][16]. Nitrile oxides belong to the electrophilic-nucleophilic 1,3-dipoles[1]; in fact, enamines contained the most active C=C double bonds towards benzonitrile *N*-oxide[17]. Three C-methyl signals in the ^{1}H NMR spectrum of **17** demonstrate the re-

Table 1. ^{1}H NMR data (δ values and *J* [Hz]) for the cycloadducts of **2** to dimethyl fumarate, dimethyl maleate and related dipolarophiles in $CDCl_3$ (E = CO_2CH_3; ester methyl signals in **3** and **8** interchangeable)

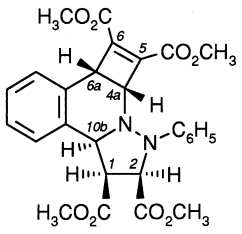
No.	MHz	1α	1β	2α	2β	10b-H	5-H	6-H
3a	400	H 4.13	E 3.68	E 3.84	H4.53	4.47	6.23	5.55
3b	400	H 3.96	E 3.71	E 3.81	H 5.57	4.42	6.31	5.59
3c	60	H 4.08	E 3.71	E 3.84	H 4.69	4.45	6.18	5.66
4a	60	E 3.20	H ?	H ?	E 3.65	4.83	6.17	5.27
7a	60	E 3.17	H 3.89	E 3.77	H 4.39	4.86	6.42	5.30
7b	400	E 3.17	H 3.86	E 3.74	H 5.48	4.75	6.50	5.39
7c	60	E 3.18	H 3.96	E 3.77	H 4.47	4.83	6.30	5.40
8a	400	H 4.02	E 3.66	H 4.99	E 3.67	4.54	6.15	5.60
8b	400	H 4.03	E 3.66	H 4.99	E 3.67	4.82	6.11	5.63
13a	400	H 3.95	CN	CN	H 4.62	4.49	6.29	5.75
13b	60	H 3.83	CN	CN	H5.97	4.32	6.33	5.76
15	60	CN	H 3.81	E 3.85	H 4.47	4.56	6.39	5.53
16	60	E 3.30	H 3.77	CN	H 4.50	4.84	6.33	5.41

J [Hz]	*cis* 1α,2α	*cis* 1β,2β	*cis* 1β,10b	*cis* 5,6	*trans* 1α,2β	*trans* 1α,10b
3a				7.8	7.9	10.0
3b				7.9	7.6	10.0
3c				7.6	7.5	9.8
7a		9.0	7.0	7.8		
7b		9.4	7.9	7.8		
7c		8.6	7.0	8.0		
8a	10.4			7.8		9.6
8b	10.8			7.8		9.2
13a				7.8	7.6	9.6
13b				7.8	9.5	7.0
15		9.2	6.5	7.8		
16		8.0	7.1	7.8		

stricted rotation of the mesityl group; an approach of the nitrile oxide from the unhindered side is assumed.



17



18

The addition of dimethyl acetylenedicarboxylate (DMAD) to cycloadduct **7a** proceeded at room temp. and gave rise to the [2+2] cycloadduct **18**. A new AX spectrum emerged at δ = 4.42 and 4.96; its coupling constant of 4.8 Hz corresponds to $J_{cis\text{-}3,4}$ = 4.4 Hz of cyclobutene[7]. The [2+2] cycloadditions of DMAD to enamines, discovered in 1963[18], have been well-studied, also for cyclic enamines[19]. Such cycloadditions can be followed by electrocyclic ring opening of the cyclobutene or by prototropy giving the β-substituted enamine. The lack of vinyl-H signals excluded these possibilities for **18**.

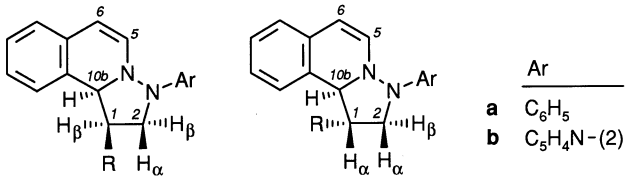
Methyl Acrylate and Acrylonitrile

Each of the termini of a 1,3-dipole can display nucleophilic and electrophilic activity. We expected that the aromaticity of the isoquinolinium cation would favor the anionic charge (and concomitant nucleophilicity) on the N terminus of **2**. We found this confirmed in the addition directions to electrophilic heterocumulenes[5]. We report here that the N-nucleophilicity of **2** likewise dictates the regiochemistry of the cycloadditions to acrylic ester, acrylonitrile, and their derivatives, without exception.

The rapid interaction of **2a** − the CS_2 adduct **5** served as a source − with *methyl acrylate* in dichloromethane afforded the two cycloadducts **19a** and **20a** in a ratio of 57:43. The ester methyl signals appear at δ 3.14 for **19a** and 3.62 for **20a**; thus, **19a** bears the ester group in 1α-position. Separation gave the crystalline **19a** and the oily **20a**.

The number of the protons in the pyrazolidine ring has now grown to four. Three of them (1-H and 2-H_2) in **19a/20a** produced 60 MHz ^{1}H NMR spectra of higher order which can no longer be solved by inspection. The δ and *J* data of **19a**, approximated by intelligent guesses, were subjected to the fine iterative program LAME of Haigh[20] which allows a computer simulation. The doublet of 10b-H (δ = 4.75) occurred at the lowest field, due to the deshielding by N-4 and the benzo ring; the other parameters were adjusted by the program until congruence of experimental

and calculated spectra was achieved. The coupling pattern with $J_{gem} = -12.5$ Hz must belong to 2α-H (δ = 3.80) and 2β-H (3.74); $J_{cis} > J_{trans}$ served the assignment (Table 2).



19 R = CO_2CH_3 **20**
21 CN **22**

In the NMR spectrum (60 MHz) of **20a**, coincidences of the proton signals in positions 1 and 2 reduced the information. If the ester group were located at C-2, a δ(10b-H) lower than 4.47 would be expected. Moreover, we rely on the analogy with the secured acrylonitrile adducts (see below).

Methyl acrylate accepted the *N*-(2-pyridyl)imide **2b**, giving rise to a 60:40 mixture of adducts **19b** and **20b** which were separated by chromatography. Ester methyl signals at $\delta_H = 3.17$ and 3.62 ($CDCl_3$) underline the structural relation to **19a/20a**.

The structures of the *acrylonitrile* adducts were determined unequivocally. The red solutions of **5** and **2b** were decolorized by acrylonitrile within 1 min. The ratios of 56:44 observed for **21a/22a** and 54:46 for **21b/22b** indicate high regioselectivity, but low diastereoselectivity. The 60 MHz spectrum of higher order for **21a** was solved by LAME to perfect congruence; the δ and *J* values were later confirmed by a 400 MHz spectrum (Table 2), which offered more detail and restricted the complexity to the signals of the aromatic protons. No other set of assignments fits the sequence of deshielding effects (N-4 > N-3 > CN) and the occurrence of $J_{gem} = -11.4$ Hz in the two signal groups at δ = 3.62 and 3.98.

The ABCD spectrum of the ring protons of **22a** was likewise solved by computer simulation (Table 2). The general concordance of the spectra leaves no doubt that **21a** and **22a** are not regioisomers, but diastereoisomers. How do we distinguish between the 1α-cyano and the 1β-cyano compound? *cis-vic*-CN deshields the ring-H less than *trans-vic*-CN (0.38 vs. 0.65 ppm, see below); δ(10b-H) and δ(2β-H) are shifted up-field by 0.30 and 0.33 ppm in **22a** compared with **21a**.

Beyer and Thieme[21] cursorily described an adduct of **2b** to acrylonitrile (71% yield); the m.p. corresponds to that found for **21b**, which makes up 54% of the diastereoisomer mixture. The ^{1}H NMR spectra reveal the dramatic deshielding of 2β-H by the interaction with the pyridyl nitrogen, *e.g.*, the shift from δ = 3.55 in **22a** to 4.63 in **22b** ($CDCl_3$). The large δ(2β-H) values of **21b** and **22b** are connected by $J_{gem} = -11.5$ and −11.6 Hz (the sign enters the computer simulation) with δ(2α-H). Thus, the cyano group cannot be located in the 2-position.

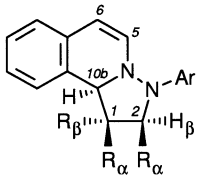
Further Electrophilic Ethylene Derivatives as Dipolarophiles

Some methyl and chloro derivatives of α,β-unsaturated carboxylic esters and nitriles were included in our study; we wished to learn more about the controlling forces of regio- and diastereoselectivity. Moreover, we wanted NMR data

Table 2. ^{1}H NMR data (δ values and *J* [Hz]) for the cycloadducts of **2** to methyl acrylate and acrylonitrile in $CDCl_3$ (* in C_6D_6); E = CO_2CH_3, LA = computer simulation

No.	MHz	1α	1β	2α	2β	10b-H	5-H	6-H
19a	60 LA	E 3.14	H 3.35	H 3.80	H 3.74	4.75	6.22	5.38
19b	400	E 3.17	H 3.39	H 3.69	H 4.77	4.64	6.28	5.47
19b*	60	E 2.92	H 3.02	H 3.80	H 4.92	4.28	6.20	5.32
20b*	60	H ?	E 3.16	H ?	H 4.88	3.62	6.03	5.36
21a	60 LA	CN	H 3.34	H 3.61	H 3.93	4.59	6.29	5.67
21a	400	CN	H 3.39	H 3.62	H 3.98	4.59	6.23	5.62
21b	60	CN	H ?	H ?	H 5.04	4.44	6.28	5.66
21b*	60 LA	CN	H 2.47	H 3.24	H 4.84	3.78	6.02	5.44
22a	100 LA	H 3.44	CN	H 3.69	H 3.55	4.29	6.00	5.44
22b	60	H ?	CN	H 3.60	H 4.63	4.19	6.07	5.53
22b*	60 LA	H 2.95	CN	H 3.19	H 4.60	3.94	5.87	5.35

J [Hz]	*cis* 1α,2α	*cis* 1β,2β	*cis* 1β,10b	*cis* 5,6	*trans* 1α,2β	*trans* 1β,2α	*trans* 1α,10b	*gem* 2α,2β
19a		8.9	8.9	7.5		6.1		−12.5
19b		8.8	9.0	7.8		6.4		−11.5
19b*		8.6	8.9	7.8		6.0		−11.2
20b*					7.8		8.5	
21a		8.9	7.7	8.0		5.6		−11.5
21a		8.8	8.0	7.8		5.6		−11.4
21b			8.1	8.0				
21b*		9.0	8.3	7.8		5.5		−11.5
22a	9.8			7.5	8.1		9.3	−10.8
22b*	10.2			7.5	7.6		9.3	



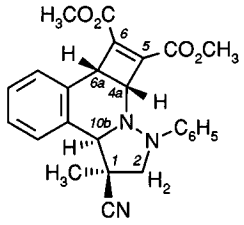
	Ar
a	C_6H_5
b	C_5H_4N-(2)

	1-R_α	1-R_β	2-R_α
23	CO_2CH_3	CH_3	CO_2CH_3
24	Cl	CO_2CH_3	CO_2CH_3
25	CO_2CH_3	CH_3	H
26	CH_3	CO_2CH_3	H
27	CO_2CH_3	Cl	H
28	Cl	CO_2CH_3	H
29	CN	CH_3	H
30	CH_3	CN	H
31	CN	Cl	H
32	Cl	CN	H

to establish increments for methyl and chloro substituents by statistical analysis.

Dimethyl citraconate and *dimethyl 2-chlorofumarate* as trisubstituted ethylenes accepted the *N*-arylimides **2a** and **2b** exclusively in the direction which makes position 1 the persubstituted center in **23/24**, **a** and **b**. The occurrence of an ester group in 2α-position is common to the four cycloadditions. The ^{1}H NMR data of Table 3 again reveal the low-field shift of δ(2β-H) effected by the pyridine ring: 1.1 ppm for **23a/23b** and 0.7 ppm for **24a/24b**. The two doublets of 5-H and 6-H were mentioned as a common feature of all the cycloadducts of **2**. The assumption that the high-field signals are those of the ene-hydrazine β-position 6 was proven here. Since **24a** was not amenable to the hydrazo rearrangement[6], the acid-catalyzed H,D exchange led to the disappearance of the 6-H signal at δ = 5.45, and the d of 5-H at 6.57 became a singlet[3f].

The cycloadditions of **2a** and **2b** to *methyl methacrylate* and *methyl* α-*chloroacrylate* as well as to *methacrylonitrile* and α-*chloroacrylonitrile* furnished the 1,1-disubstituted adducts regioselectively. The diastereoselectivity ranges from 53:47 for **29b/30b** to 85:15 for **27b/28b** in the seven systems studied; the adducts with a CO_2CH_3 or CN group in 1α-position are slightly preferred. Invariably, the ^{1}H NMR spectra are simple: 10b-H gives rise to a singlet, and 2α-H/2β-H form AB or AX spectra with J_{gem} = −10.0 to −13.4 Hz. The diastereoisomer assignment rests for those with 1α-CO_2CH_3 on the shielding by the *cis-vic* benzo ring (Table 3). The chemical shifts of the 1-methyl group demonstrate the same phenomenon, δ(1α-CH_3) < δ(1β-CH_3), to a lower degree, *e.g.*, δ = 1.19 *vs.* 1.33 for **26a/25a** or 1.24 *vs.* 1.47 for **30b/29b**. The differentiation of 2α-H and 2β-H relied on the increments of *cis-vic* and *trans-vic*-substituents (see below), and on the deshielding of 2β-H by the pyridine nitrogen; the alternation of the series **a** (3-phenyl) and **b** (3-α-pyridyl) in Table 3 illustrates this striking effect.



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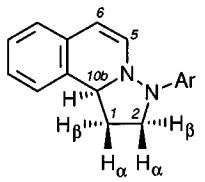


34a Ar = C_6H_5
34b Ar = C_5H_4N-(2)

Although the enamine type reactivity of the 5,6 double bond in our cycloadducts was not systematically studied, a second example of a [2+2] cycloaddition by DMAD may be mentioned in passing. The adduct **29a** prepared from **2a** and methacrylonitrile was converted at room temp. to the tetracyclic cyclobutene **33** (56%). The AB spectrum of 5-H and 6-H in **29a** vanished and gave place to a new one at δ_H 4.69 and 4.77, in analogy with the DMAD adduct **18**.

Preparation of the Formal Ethylene Adducts 34

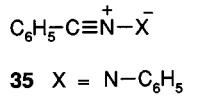
In quantifying ^{1}H NMR substituent effects, the knowledge of the *all*-hydrogen parent system is indispensable. However, neither **2a** nor **2b** reacted with ethylene in the saturated ether solution at 0°C, not even over 3 months. The sacrifice of part of the aromaticity of **2** in the course of the 1,3-cycloaddition slows down the reactivity. Nevertheless, the cycloaddition enthalpy for **2** + ethylene → **34** should have a more negative value than that for the rapid cycloaddition to acrylic ester or acrylonitrile, since no con-

Table 3. Selected ^{1}H NMR data (δ values and *J* [Hz]) of cycloadducts of **2** to various electrophilic ethylenes at 60 MHz ($^+$ 400 MHz) in $CDCl_3$ (E = CO_2CH_3; M = methyl)

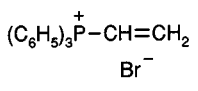
No.	δ 1α	1β	2α	2β-H	10b-H	5-H	6-H	*J*(2α,2β)
23a	E 3.25	M 1.62	E 3.73	3.94	4.33	6.37	5.23	
23b	E 3.24	M 1.66	E 3.72	5.06	4.32	6.50	5.33	
24a	Cl	E 3.87	E 3.85	5.12	5.04	6.57	5.45	
24b	Cl	E 3.83	E 3.76	5.78	5.07	6.52	5.45	
25a	E 3.20	M 1.33	H 4.26	3.27	4.29	6.23	5.31	−10.0
26a$^+$	M 1.19	E 3.63	H 3.28	4.19	4.88	6.31	5.38	−11.1
27a$^+$	E 3.24	Cl	H 4.42	4.09	5.05	6.26	5.44	−12.2
27b	E 3.18	Cl	H 4.26	5.07	4.92	6.27	5.47	−12.2
28a	Cl	E 3.68	H 3.68	4.55	5.00	6.32	5.48	−12.5
28b	Cl	E 3.72	H 3.72	5.45	4.98	6.36	5.52	−12.8
29a$^+$	CN	M 1.49	H 3.98	3.54	4.14	6.26	5.60	−10.8
29b	CN	M 1.47	H 3.78	4.57	3.97	6.25	5.61	−11.8
30a	M 1.22	CN	H 3.35	4.07	4.74	6.26	5.38	−11.4
30b	M 1.24	CN	H 3.19	5.15	4.62	6.28	5.43	−11.8
31a	CN	Cl	H 4.22	4.10	4.82	6.21	5.65	−13.1
31b	CN	Cl	H 3.92	5.29	4.63	6.22	5.65	−13.2
32a	Cl	CN	H 3.92	4.43	4.94	6.32	5.11	−12.6
32b	Cl	CN	H 3.72	5.61	4.77	6.35	5.71	−13.4

jugation energy has to be sacrificed for the dipolarophilic bond. Thus the inertness of **2** to ethylene must be a *kinetic phenomenon*.

The *N*-imides **2** belong to the nucleophilic-electrophilic 1,3-dipoles like diphenylnitrilimine (**35**) and benzonitrile *N*-oxide (**36**). Such 4π systems react fast with electron-poor alkenes, slow with common olefins, and rapidly again with electron-rich double bonds[1][2]. Competition between pairs of dipolarophiles for the reactive **35** and **36** revealed a rate minimum for common alkenes and vinyl ethers[17][22], but **35** and **36** still smoothly combine with ethylene at 0°C[16][23].



35 X = N–C_6H_5
36 X = O



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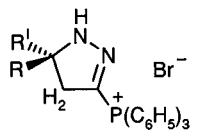

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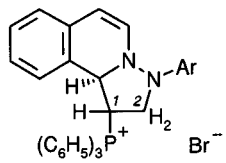


39

The detour of a cycloaddition to triphenylvinylphosphonium bromide (**37**) was chosen. The triarylphosphonio group with $\sigma_p = 1.18$ and $\sigma_m = 1.13$ is a far better electron attractor than the nitro group[24][25]. The effect is not merely inductive as for $(CH_3)_3N^+$; the resonance contribution σ_R also surpasses that of nitro. The addition of diazoalkanes to **37** has been reported, leading to pyrazolinylphosphonium salts **38** which, in turn, were hydrolyzed by alkali to furnish triphenylphosphane oxide and the (not isolated) 2-pyrazolines[26]. Earlier studies had shown that phosphonium hydroxides with alkyl and aryl substituents preferably eliminate alkane[27]. Diazoalkanes add to **37** in the same direction as observed for acrylic ester.

The red solutions of **2a** and **2b** in dichloromethane were quickly decolorized after adding **37**. The adducts **39** were not purified, but treated with aqueous sodium hydroxide at room temp.; after separation of the phosphane oxide and chromatography on alumina, the crystalline ethylene adducts **34a** and **34b** were isolated in 7% and 14% yield, respectively. Regrettably, the desired conversion was only a side reaction, but sufficient material for the spectroscopic characterization was obtained. The isolation and stability of **34a,b** confirmed our assumption of a "kinetic brake" in the system **2** + ethylene.

In the ^{1}H NMR spectrum of **34a** (100 MHz, $CDCl_3$), the doublets of the vinyl-H at δ = 5.26 (6-H) and 5.99 (5-H) served as a diagnostic criterion for the 1,2-dihydroisoquinoline fragment present in all the cycloadducts of **2**. The C=C stretching frequency of the ene-hydrazine group in **34a** gave rise to a strong IR band at 1623 cm^{-1}.

Three groups of ^{1}H NMR signals for the five pyrazolidine protons of **34a** appeared in the integral ratio of 1:2:2. Deshielded by N-4, the benzylic 10b-H occurs at lowest field (dd, δ = 4.05). The 2H multiplet around δ = 3.25 allows the recognition of the ddd pattern expected for 2-H_2; the multiplet could not be evaluated by first order. The very complex signal of 1-H_2 at δ = 1.8–2.6 contains 7 coupling constants. The program LAME[20] provided perfect congruence of calculated and experimental splitting patterns and furnished five δ and eight *J* values (Table 4). The α,β assignment of 1-H_2 and 2-H_2 was based on the experimental δ and *J* values of several structurally secured cycloadducts.

Storable in the crystalline state, **34a** undergoes in $CDCl_3$ or C_6D_6 a hydrazo rearrangement[6]. When the NMR spectrum was recorded again after 6 h, new signals disclosed the beginning conversion.

Table 4. ^{1}H NMR data (calculated by LAME) of 3-aryl-1,2,3,10b-tetrahydropyrazolo[5,1-*a*]isoquinolines **34** in $CDCl_3$ (100 MHz, δ values, *J* [Hz])

No.	δ	1α-H	1β-H	2α-H	2β-H	10b-H	5-H	6-H
34a		2.36	2.07	3.34	3.15	4.05	5.99	5.26
34b		2.34	2.05	3.26	3.98	3.95	5.98	5.32

	J	1α,2α	1β,2β	1β,10b	1α,2β	1β,2α	1α,10b	1α,1β	2α,2β
34a		9.5	8.4	6.3	8.2	2.8	10.6	−11.4	−10.0
34b		9.7	8.5	6.4	8.2	3.0	10.7	−11.4	−10.8

The *N*-(2-pyridyl) compound **34b** does not rearrange. The three signal groups for the pyrazolidine protons appear in the ratio of 2:1:2 in the ^{1}H NMR spectrum. The attribution was simplified by the 1,1-dideuterio derivative. When we treated the primary adduct **39b** with NaOD in D_2O, the crystalline [1,1-D_2]-**34b** was isolated (12%). The complexity of the ^{1}H NMR spectrum of **34b** was reduced here to an AB pattern for 2-H_2 with J_{gem} = 10.8 Hz and a singlet at δ = 3.92 for 10b-H, the signals being somewhat broadened by H,D coupling. The occurrence of the s and dd in [1,1-D_2]-**34b** established the regiochemistry of the cycloaddition to **37**, *i.e.*, the location of the triphenylphosphonio group in position 1 of **39**.

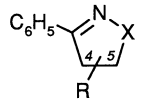
The LAME simulation of the complex ^{1}H NMR pattern of **34b** was successful (Table 4). The δ(2β-H) of **34b** is by 0.83 ppm higher than that of **34a**; the 2β-H signal overlaps now with the dd of 10b-H.

Substituent Increments for δ_H of Ring Protons

The statistical evaluation of substituent increments allows the fitting of NMR data into a consistent order system; moreover, such a set has considerable predictive power. The influence of substituents on the δ_H of ring protons depends to a high extent on ring size, conformation, heteroatoms, centers of unsaturation etc. Published tables of substituent increments for derivatives of benzene, pyridine, cyclohexane and the like[7] may offer first information on direction and magnitude of effects, but will fail to reproduce the interplay on a quantitative basis. In 1967, such substitu-

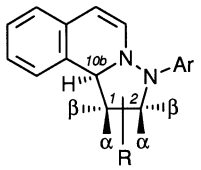
ent parameters have been elaborated for 4- and 5-substituted 1,3-diphenyl-2-pyrazolines (**40**) and 3-phenyl-2-isoxazolines (**41**) which were prepared by cycloadditions of **35** and **36** to olefinic dipolarophiles in the Munich laboratory[28]. The structural similarity of **40** and **41** allowed to establish a combined set of parameters. Despite the resemblance between **40** and the five-membered heterocycle in **34**, a higher conformational flexibility is expected for the latter. The application of the substituent parameters, based on **40**, to derivates of **34** was met by only moderate success.

The statistical analysis of substituent effects was based on 39 cycloadducts of the 1,3-dipoles **2a,b** − mostly of established structure. Besides **34a,b**, 7 mono-, 24 di-, and 6 trisubstituted derivatives **42** were included. The cycloadducts of electron-deficient ethylenes were supplemented by the adducts of 1-pyrrolidinoisobutene; the cycloadducts of enamines will be the subject of a later publication. Twenty-one cycloadducts contain the *N*-phenyl and 17 the *N*-(2-pyridyl) residue.



40 X = N−C_6H_5

41 X = O



42a Ar = C_6H_5

42b Ar = C_5H_4N-(2)

gem, *cis-vic*, and *trans-vic* effects of substituents on the protons of the pyrazolidine ring were distinguished, but the effects of 1-R on 10b-H and 2-H, and those of 2-R on 1-H were set equal; interactions of 2-R with 10b-H, i.e., on protons at the carbon atom after the next one, were neglected. Full additivity of substituent increments in di- and trisubstituted derivatives of **34a** and **34b** was assumed. After the first run, several uncertain regiochemical assignments were corrected.

The 37 substituted derivatives **42** contain 107 protons in the pyrazolidine ring, and 107 equations of type (1) were defined. δ_0 refers to the parent compounds **34a** and **34b**; I_s is the increment of the substituent which occurs *a* times in the same molecule. The experimental δ_H values come from Tables 1−4.

$$\delta_H = \delta_0 + \Sigma a I_s \quad (1)$$

Test runs of the least-square analysis for the *N*-(2-pyridyl) compounds (series **b**) indicated the necessity of a correction term. The δ_H values of **34b** deviate from those of **34a** by 0.83 ppm for 2β-H, and to a lower extent for 2α-H (−0.12 ppm) and 10b-H (−0.10 ppm). We interpreted the 2β-H effect above by a contact interaction with the pyridine nitrogen, probably an intramolecular hydrogen bond. This down-field shift is not constant, but fluctuates between 0.66 and 1.35 ppm amongst the cycloadducts. The highest value was observed for the 1β,2α-dicyano compound for which the most acidic 2β-H is expected.

We introduced correction increments I_β for δ(2β-H) and I_α for δ(2α-H) of **34b**. I_β and I_α average the mentioned deshielding and were included as unknowns in the least-square treatment. Thus, our system of equations of type (1) were solved for 13 quantities: three increments each for *gem*, *cis-vic*, and *trans-vic* interactions of CO_2CH_3 and C≡N, two each for *cis-vic* and *trans-vic* effects of methyl and chlorine, one for *gem*-pyrrolidino, and the two adaptations I_β and I_α for **34b**.

The least-square analysis was carried out with a Fortran IV program and subroutine LEASQ[29], at first separately for the *N*-phenyl series **a** and the *N*-(2-pyridyl) series **b**. As expected, the standard deviations of the substituent increments were greater for the pyridyl than for the phenyl series, due to the variable influence of the hydrogen bond on δ(2β-H); *e.g.*, for *gem*-CO_2CH_3 δ = 0.99 ± 0.071 was found in the phenyl series and 0.92 ± 0.095 in the pyridyl series. However, the substituent increments were identical in both series within the limits of the standard deviations. The combined analysis of the δ_H of phenyl and 2-pyridyl series − all 107 eq. of type (1) − provided the substituent increments and their standard deviations[30] listed in Table 5.

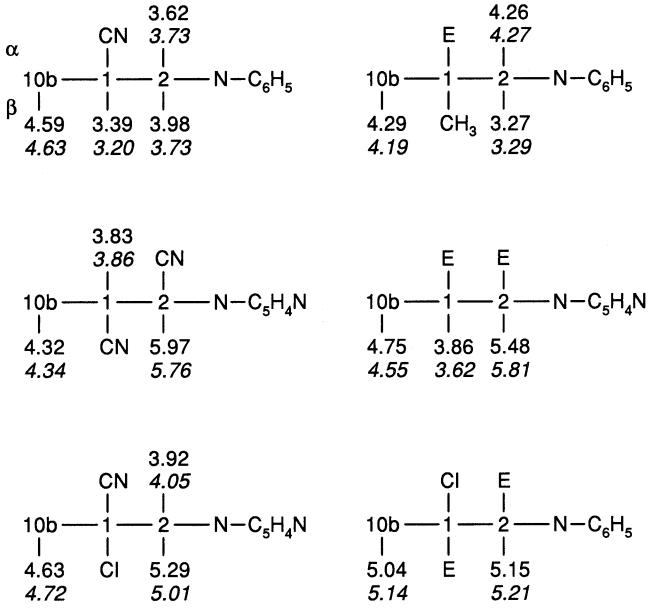
The extra deshielding of 2β-H and 2α-H by the *N*-(2-pyridyl) residue is expressed by the increments:

$$I_\beta = +0.26 \pm 0.06 \text{ ppm}, I_\alpha = -0.17 \pm 0.07 \text{ ppm}$$

Table 5. Increments of substituents in 1- and 2-position on the ^{1}H-chemical shifts (δ_H in $CDCl_3$) of the pyrazolidine protons in 37 compounds **42** and comparison with those of **40** and **41**

Substituent	Number of eq. (1)	Increments I_s for ring H (Δδ, ppm)		
		gem	*cis-vic*	*trans-vic*
	A. 3-Aryl-1,2,3,10b-tetrahydropyrazolo[5,1-a]isoquinolines (**42**)			
Methoxycarbonyl	57	0.97 ± 0.05	0.52 ± 0.05	0.60 ± 0.05
Cyano	45	1.13 ± 0.08	0.39 ± 0.06	0.58 ± 0.06
Methyl	26		−0.46 ± 0.06	0.41 ± 0.07
Chloro	28		0.19 ± 0.07	0.57 ± 0.07
Pyrrolidino	2		1.06 ± 0.17	
	B. 1,3-Diphenyl-2-pyrazolines (**40**) *and 3-phenyl-2-isoxazolines* (**41**)			
Methoxycarbonyl		0.97	0.41	0.37
Cyano		1.12	0.50	0.50
Methyl		0.41	−0.28	0.01
Phenyl		1.30	0.11	0.51

Scheme 1. Comparison of observed δ_H values and those calculated with substituent increments (in italics) for the pyrazolidine protons of some cycloadducts; the horizontal line symbolizes the ring skeleton (E = CO_2CH_3)



Thus, for the calculation of δ_H by eq.(1), we substitute the δ_o values of Table 5 for **34b** by δ(2β-H) = 4.24 and δ(2α-H) = 3.09 (deviations by 0.26 and −0.17 from experimental δ). Scheme 1 compares observed δ_H with those calculated by eq. (1) for some arbitrarily chosen cycloadducts. 37% of the 107 experimental δ_H values are reproduced within 0.10, and 73% within 0.20 ppm; only 13% of the calculated values deviate by ≥ 0.30 ppm. The "trespassers" suggest conformational changes; they occur mainly for the cycloadducts of dimethyl maleate. The δ(2β-H) is often connected with greater deviations for obvious reasons (variable deshielding by pyridyl nitrogen).

The comparison of the substituent increments for the pyrazolidine ring of **42** (series *A* in Table 5) with those for 2-pyrazolines **40** and 2-isoxazolines **41** (series *B*) reveals common features and divergences. The *gem*-increments of cyano and ester group are identical in both series, but *cis-vic* and *trans-vic*-methoxycarbonyl deshield in series *A* stronger than in *B*. The increment for *trans-vic*-CN is greater than for *cis-vic*-CN in series *A*, whereas equal effects were found in series *B*. Chlorine in the *trans-vic* position deshields three times as much as in the *cis-vic* position. The pyrrolidino residue exerts the highest deshielding (1.06 ppm); its increment is based on only two eq. of type (1).

A notable difference concerns the increments of the methyl group, in series *A* −0.46 ppm for the *cis-vic* and +0.41 ppm for the *trans-vic* relation. In series *B,* the *cis-vic*-methyl shifts δ_H by −0.28 ppm, and the near zero value for *trans-vic*-methyl may be the result of cancellation. Closely related, −0.37 for *cis-vic*-CH_3 and −0.01 ppm for *trans-vic*-CH_3, is the effect on δ(3-H) in the more rigid, substituted cyclobutanones[31].

The substituents will alter the conformational equilibria for the pyrazolidine ring of our tricyclic system. For the chair form of cyclohexane, the effects of *equatorial* (*e*) and *axial* (*a*) methyl have been separated[7]. *a*-Methyl shifts the *cis-vic*-H by −0.20 and the *trans-vic*-H by +0.25 ppm. The *e*-methyl shields the *a*-H (*cis-vic*) by 0.31, but the *e*-H (*trans-vic*) only by 0.03 ppm, although the torsion angles are rather similar. Obviously, the interplay of methyl and ring-H is not a simple function of dihedral angle.

vic-Substituent increments for X−CH_2−CH_3[7] are informative in this context: X = CO_2CH_3 0.26, CN 0.45, Cl 0.47, CH_3 0.05 ppm. The effect on 2-H_3 contains 2/3 of *synclinal* and 1/3 of *antiperiplanar* interaction.

H,H Coupling Constants

Besides the dependence of J_{vic} on the torsion angle (the popular "Karplus curve"), the influence of substituents and heteroatoms on $^3J_{H,H}$ is noteworthy[32]. Due to the conformational flexibility of the saturated five-membered ring, *cis-vic* and *trans-vic* coupling constants broadly overlap and their diagnostic value is confined. In cyclopentenes and its hetero derivatives, the dihedral angles between the saturated centers are smaller, and $J_{cis} > J_{trans}$ is the rule. In the 4- and 5-substituted 2-pyrazolines **40**, J_{cis} = 7.7−13.3 Hz and J_{trans} = 2.3−8.7 Hz were observed[28]; despite an overlap zone, $J_{cis} > J_{trans}$ was obeyed by each *cis,trans* pair.

The annellation to a 1,2-dihydroisoquinoline system and the repulsion of the lone-pair orbitals of the N-atoms diminish the flexibility of the pyrazolidine ring in our tricyclic system, compared with cyclopentane derivatives. Table 4 offers the coupling constants for the parent compounds **34a,b**, and Tables 1−3 those of 33 substituted derivatives **42**. The *cis*-couplings $J_{1\alpha,2\alpha}$ and $J_{1\beta,2\beta}$ cover a range of 8.0−10.8 Hz. With $J_{1\alpha,2\beta}$ and $J_{1\beta,2\alpha}$ = 5.5−9.0 Hz, the *trans*-coupling is smaller; **34a** and **34b** with $J_{1\beta,2\alpha}$ = 2.8 and 3.0 Hz are exceptional. With the same regularity that $J_{cis} > J_{trans}$ is obeyed by 1-H/2-H, the opposite was found for $J_{1,10b}$, *i.e.*, 6.3−9.8 Hz for the *cis-vic* and 7.0−10.0 Hz for the *trans-vic* relation. Thus, the ^3J data have limited heuristic value in the structure determination.

J_{gem} = −10.0 to −13.4 Hz was found for 24 of our tricyclic cycloadducts. The negative sign which the fitting of the computer simulation required was assumed for the other J_{gem} values, too. In the substituted 2-pyrazolines **40**, the range was wider: J_{gem} = −9.9 to −17.1 Hz[28]. For cyclopentanes, −12.0 to −15 Hz, and for cyclopentenes $J_{3,3}$ = −15.3 to −18.4 Hz have been reported[33]. It is well-known that an adjacent heteroatom (O > N) diminishes J_{gem} in cyclopentane derivatives.[33]

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Experimental Section

General[5]. NMR: The spectra were recorded on a Varian A60 for ^1H (60 MHz) or on a Varian XL 100 for ^1H (100 MHz) and ^{13}C (25.2 MHz); spectra run on a Varian XR 400S for ^1H (400 MHz) or ^{13}C (100 MHz) are marked. $CDCl_3$ (stored over dry K_2CO_3) served as solvent, if not otherwise stated; TMS was the internal standard. The δ were evaluated by first-order, except for $\delta \leq 4\ J$ (AB). MS: EI spectra with 70 eV, AEI, Manchester, MS 902; supplementary MS were recorded on a Finnigan MAT 90. HR = high resolution; isotope peaks are given in the form ^{13}C calcd./found.

Dimethyl Fumarate, Dimethyl Maleate, and Related Dipolarophiles

Dimethyl (1β,2α,rel-10bβ)-(±)-1,2,3,10b-Tetrahydro-3-phenylpyrazolo[5,1-a]isoquinoline-1,2-dicarboxylate (**3a**)[3b][3d] *and (1α,2β,rel-10bβ)-(±) Diastereoisomer* (**4a**): (a) 3.23 g (12.6 mmol) of pulverized 2-(anilino)isoquinolinium chloride (**1a**)[5][34] were stirred with a solution of 2.20 g (15.3 mmol) of *dimethyl fumarate* in 40 ml of CH_2Cl_2. Triethylamine (2.0 ml, 14.3 mmol) in CH_2Cl_2 was added dropwise within 10 min; after further 15 min the red color of **2a** had disappeared. The triethylammonium chloride was removed by washing with water; cyclohexane was added to the concentrated organic phase. **3a** (3.65 g, 80%) was obtained in two batches; after recrystallization, the colorless cubes showed m.p. 117−118°C. − IR (KBr): $\tilde{\nu}$ = 696 cm^{-1}, 760, 777 st (arom. CH out-of-plane def.), 1170, 1212, 1260 st (C−O), 1492 st, 1600 m (arom. ring vibr.), 1624 m (C=C of enamine), 1734, 1742 st (C=O). − ^1H NMR (400 MHz): Table 1. The assignment of the aromatic ^1H and ^{13}C signals was based on a two-dimensional analysis. δ = 6.94 (dt, 4′-H of C_6H_5−N), 7.03 (d br., 10-H), 7.04 (d br., 7-H), 7.08 (dt, 9-H), 7.14 (dt, 2′-H/6′-H), 7.24 (dt, 8-H), 7.28 (dt, 3′-H/5′-H). − ^{13}C NMR (100 MHz, DEPT): δ = 52.4, 53.0 (2 OCH_3), 56.4 (C-1), 64.1 (C-10b), 68.4 (C-2), 103.4 (C-6), 113.9 (C-2′/C-6′ of N−C_6H_5), 121.3 (C-4′); 125.0, 125.8, 127.2, 128.9 (C-7 to C-10); 130.0, 130.4 (C-10a, C-6a), 139.3 (C-5), 150.1 (C-1′); 171.0, 171.6 (2 C=O). − MS (85°C); *m/z* (%): 364 (35) [M^+, ^{13}C 8/10], 333 (2.1) [$M^+ - CH_3O$, ^{13}C 0.5/0.6], 305 (3) [$M^+ - CO_2CH_3$], 245 (3), 220 (100) [$C_{15}H_{12}N_2^+$, HR calcd. 220.0998/found .1004; **2a**$^+$ or **6**, ^{13}C 16.8/16.2], 144 (11) dimethyl fumarate$^+$], 129 (41) [isoquinoline], 113 (82) [$CH_3O_2C-CH=CH-C\equiv O^+$], 93 (15) [$C_6H_5NH_2^+$], 91 (15) [$C_6H_5N^+$], 85 (35) [$C_4H_5O_2^+$], 77 (15) [$C_6H_5^+$]. − $C_{21}H_{20}N_2O_4$ (364.4): calcd. C 69.22, H 5.53, N 7.69; found C 69.36, H 5.68, N 7.80. − Mol. mass 368 (vapor phase osmometry, benzene 37°C). − (b) CS_2 adduct **5**[5] was reacted with 1.0 equiv. of dimethyl fumarate in $CDCl_3$ in an NMR tube. The integrals of the s (OCH_3) at δ_H = 3.81 and 3.20 indicated **3a/4a** = 85:15. Further ^1H NMR data of **4a**: Table 1. − (c) Thermolysis of **3a**: The colorless melt became red at about 140°C and turned pale yellow on cooling. At 150−160°C (bath)/0.15 Torr, crystals sublimed which were identified as dimethyl fumarate by m.p. 97−99°C and mixed m.p.; yield 22%.

[1,2-D_2]-**3a**[3d]: Reduction of acetylenedicarboxylic acid with Cr(II)SO_4 in D_2O[35][3d] and subsequent esterification with methanol and conc. sulfuric acid afforded dimethyl [2,3-D_2]fumarate; the ^1H NMR integrals pointed to 10% of D_1 compound. 0.65 mmol of **1a** reacted with 0.64 mmol of the dipolarophile and 1.4 mmol of triethylamine in 7 ml of CH_2Cl_2 and furnished 167 mg (72%) of crystalline [D_2]-**3a**. ^1H NMR: The s of 10b-H at δ = 4.47 showed a halfwidth of 5 Hz and is probably an unresolved t, due to coupling with 1-D.

Further Derivatives of (±)-1,2,3,10-Tetrahydropyrazolo[5,1-a]-isoquinoline (full systematic names are no longer repeated)

Dimethyl 3-(2-Pyridyl)-...-1β,2α-dicarboxylate (**3b**): (a) The deep-red color of **2b**[5] (221 mg, 1.00 mmol) in 10 ml of CH_2Cl_2 faded after addition of dimethyl fumarate (144 mg, 1.00 mmol) within 20 min. From ether/petroleum ether, 0.30 g (82%) of **3b** crystallized in colorless platelets, m.p. 123−124°C. − IR (KBr): $\tilde{\nu}$ = 772 cm^{-1} st (arom. CH wagg.), 1198, 1214, 1229 st (C−O); 1438, 1470 st (this pair with little variation was found in all cycloadducts of **2b** and must be connected with 2-pyridyl); 1494 st, 1565 m, 1595 st (arom. ring vibr., C=N), 1630 m (C=C−N); 1733, 1745 st (C=O). − ^1H NMR (400 MHz): Table 1; further data: δ = 6.83 (ddd, 5′-H of 2-pyridyl), 6.99 (d, *J* = 6.8 Hz, 7-H), 7.04 (d, *J* = 8.0 Hz, 10-H), 7.07 (td, *J* = 7.6, 1.2 Hz, 9-H), 7.20 (d, *J* = 9.3 Hz, 3′-H), 7.24 (td, *J* = 7.6 and 1.3 Hz, 8-H), 7.54 (tdd, 4′-H), 8.26 (mc, 6′-H). − ^{13}C NMR (100 MHz, DEPT): δ = 52.4, 52.9 (2 OCH_3), 56.1 (C-1), 63.5 (C-10b), 64.9 (C-2), 104.4 (C-6), 108.7 (C-3′ of pyridyl), 116.6 (C-5′); 125.1, 126.0, 126.9, 128.9 (C-7 to C-10); 129.2, 130.1 (C-6a, C-10a); 138.0, 138.8 (C-5, C-4′), 147.9 (C-6′), 159.6 (C-2′); 171.3, 171.8 (2 C=O). − MS (85°C); *m/z* (%): 365 (6) [M^+, ^{13}C 1.4/1.3], 334 (2.7) [$M^+ - OCH_3$; ^{13}C 0.6/0.7], 306 (13) [$M^+ - CO_2CH_3$; ^{13}C 2.7/2.7], 274 (34) [306 − CH_3OH; ^{13}C 6.5/6.4], 246 (13), 220 (100) [$C_{14}H_{10}N_3^+$, HR 220.0873/.0854, **12**], 201 (53), 169 (35), 143 (5) [$C_6H_7O_4^+$, dimethyl fumarate$^+$ − H], 142 (6), 129 (35) [isoquinoline$^+$], 113 (31) [$C_5H_5O_3^+$], 94 (4) [aminopyridine], 85 (14), 78 (22) [pyridyl$^+$], 59 (8) [$CH_3OC\equiv O^+$]. − $C_{20}H_{19}N_3O_4$ (365.4): calcd. C 65.74, H 5.24, N 11.50; found C 65.81, H 5.38, N 11.52. − (b) When the reactants were combined in $CDCl_3$ in the NMR tube, a small OCH_3 signal at δ_H = 3.27 pointed to the 1α-CO_2CH_3 of a few percent of the diastereoisomer **4b**.

Dimethyl 3-(4-Nitrophenyl)-...-1β,2α-dicarboxylate (**3c**)[3d]: Salt **1c**[5] (0.50 mmol), 0.60 mmol of dimethyl fumarate, and 3 mmol of triethylamine in 12 ml of CH_2Cl_2 were stirred for 3 h at room temp.; after washing with water and removing the solvent, 154 mg (75%) of **3c** crystallized from methanol in colorless needles, m.p. 144−146°C. − IR (KBr): $\tilde{\nu}$ = 740 cm^{-1}, 748, 755, 842 st (arom. CH out-of-plane def.); 1108, 1172, 1245, 1268 (C−O); 1326 vst, 1503 st (NO_2), 1593 st (arom. ring vibr.), 1624 m (C=C−N), 1735 vst (C=O). − ^1H NMR: Table 1. − $C_{21}H_{19}N_3O_6$ (409.4): calcd. C 61.61, H 4.68, N 10.27; found C 61.73, H 4.70, N 10.61.

Dimethyl 3-Phenyl-...-1α,2α-dicarboxylate (**7a**) [3b][3d] *and (1β,2β)-Diastereoisomer* (**8a**): The reaction of 10.0 mmol each of **5** and *dimethyl maleate* in 40 ml of CH_2Cl_2 was finished after 1 h; 76% of **7a** crystallized from $CHCl_3$/ether, m.p. 161−162°C (dec., red). The concentrated mother liquor was quickly put on an alumina (basic, activity grade II) column and eluted with ether/petroleum ether (1:1). From the first fraction (R_f = 0.70) **8a** was isolated, followed by **7a** (R_f = 0.46). Adduct **8a** crystallized from ether/petroleum ether at −18°C in colorless needles (210 mg, 6%), m.p. 113−114°C. In solution, **8a** could be kept only for several h. When the cycloaddition was carried out with **1a** + triethylamine, 66−70% of **7a** was obtained, but no **8a**. In an extra experiment with **5** in the NMR tube, the OCH_3 integrals furnished **7a/8a** = 90:10. − Properties of **7a**. UV ($CHCl_3$): λ_{max} (log δ) = 305 nm (3.93). − IR (KBr): $\tilde{\nu}$ = 1175 cm^{-1}, 1199, 1214 (C−O); 1487 st, 1600 m (arom. ring vibr.), 1628 m (C=C−N); 1728, 1746 vst (C=O). − ^1H NMR: Table 1. − ^{13}C NMR: δ = 51.5, 52.4 (2 q, 2 OCH_3), 58.7 (d, C-1), 62.6 (d, C-10b), 66.8 (d, C-2), 100.3 (d, C-6), C_{ar} and C-5 not assigned; 170.3, 170.4 (2 s, 2 C=O). − MS (70 eV, 90°C): *m/z* (%): 364 (40) [M^+; ^{13}C 9.4/9.4], 333 (3) [$M^+ - OCH_3$], 220 (78) [**2a**$^+$ or **6**; ^{13}C 13/13], 201 (16), 163 (14), 144 (7) [$C_6H_6O_4^+$], 143 (17) [144

− H], 129 (57) [isoquinoline$^+$], 113 (100) [$CH_3O_2C-CH=CH-C\equiv O^+$], 104 (53), 93 (18) [$C_6H_5NH_2^+$], 91 (10) [$C_6H_5N^+$], 77 (47) [$C_6H_5^+$]. − $C_{21}H_{20}N_2O_4$ (364.4): calcd. C 69.21, H 5.53, N 7.69; found for **7a** (**8a**): C 69.23 (69.20), H 5.64 (5.59), N 7.45 (7.63). − Mol. mass: 380 (vapor phase osmometry, benzene, 37°C). − Properties of **8a**. − IR (KBr): $\tilde{\nu}$ = 1180 cm^{-1}, 1206 st (C−O); 1497, 1600 st (ring vibr.), 1634 m (C=C−N), 1738, 1762 vst (C=O). − ^{1}H NMR (400 MHz): Table 1; δ = 6.82−6.86 (m, 2′-H/6′-H, 4′-H of N−C_6H_5), 7.01−7.41 (3 m, 6 arom. H). A second recording, 726 min later, indicated 20.4% hydrazo rearrangement[6]; this corresponds to k_1 = 5.4 10^{-6} s^{-1} (half-life 36 h) in $CDCl_3$ at 25°C. − ^{13}C NMR (100 MHz, DEPT): δ = 52.2, 52.5 (2 OCH_3), 53.4 (C-1); 61.2 (C-10b), 61.9 (C-2), 105.6 (C-6), 114.2 (C-2′/C-6′ of N−C_6H_5), 119.8 (C-4′); 125.0, 126.3, 127.6, 128.8 (C-7 to C-10), 129.4 (C-3′/C-5′); 129.5, 130.2 (C-6a, C-10a), 136.8 (C-5), 144.7 (C-1′); 169.3, 170.3 (2 C=O).

Dimethyl 3-(2-Pyridyl)-...-1α,2α-dicarboxylate (**7b**) *and 1β,2β-Diastereoisomer* (**8b**): The red solution of 3.00 g (13.6 mmol) of **2b** and 2.00 g (13.9 mmol) of dimethyl maleate in 30 ml of CH_2Cl_2 faded in 45 min. 4.37 g (88%) of **7b** as pale yellow needles, m.p. 139−140°C, crystallized from ether/petroleum ether. The residue of the mother liquor was subjected to CC on alumina (ether/petroleum ether 1:1); the first fraction gave 0.39 g (8%) of **8b** as colorless needles, m.p. 144−145°C. − Properties of **7b**. − IR (KBr): $\tilde{\nu}$ = 776 cm^{-1} st (arom. CH out-of-plane def.), 1200 st, 1292 m (C−O); 1432, 1470 st (pyridyl), 1567, 1595 st (arom. ring vibr.), 1628 m (C=C−N), 1741, 1763 st (C=O). − ^{1}H NMR (400 MHz): Table 1; δ = 6.81 (dd, J = 5.4 and 6.7 Hz, 5′-H of pyridyl), 6.97 (d, J = 7.3 Hz, 7-H), 7.02 (d br., J = 8.5 Hz, 10-H), 7.07 (t br., 9-H), 7.17 (d br., 3′-H), 7.18 (t, overlap, 8-H), 7.53 (dt, 4′-H), 8.22 (d br., 6′-H). − ^{13}C NMR: δ = 51.4, 52.3 (2 q, 2 OCH_3), 57.8 (d, C-1), 61.1 (d, C-2), 63.4 (d, C-10b), 101.6 (d, C-6); 108.4 (d, C-3′ of pyridyl), 116.4 (d, C-5′), 124.7, 125.2, 127.0, 127.4 (4 d, C-7 to C-10); 128.5, 131.4 (2 s, C-6a, C-10a); 137.7, 138.5 (2 d, C-5, C-4′), 147.5 (d, C-6′), 160 (s, C-2′); 170.1, 170.4 (2 s, 2 C=O). − $C_{20}H_{19}N_3O_4$ (365.4): calcd. C 65.74, H 5.24, N 11.50; found for **7b** (**8b**): C 65.90 (65.65), H 5.34 (5.32), N 11.30 (11.63). − Properties of **8b**. − IR (KBr): $\tilde{\nu}$ = 765 cm^{-1} st (arom. CH out-of-plane def.), 1208, 1292, 1337 (C−O), 1446, 1470 st (pyridyl), 1568 m, 1593 st (ring vibr.), 1631 m (C=C−N), 1745 vst, br (C=O). − ^{1}H NMR (400 MHz): Table 1; δ = 6.67 (ddd, 5′-H of pyridyl), 6.97 (d, J = 8.5 Hz, 7-H), 7.03 (d br., J = 7.4 Hz, 10-H), 7.10 (td, 9-H), 7.19 (d br., 3′-H), 7.23 (td, 8-H), 7.52 (ddd, 4′-H), 8.11 (mc, 6′-H).

Dimethyl 3-(4-Nitrophenyl)-...-1α,2α-dicarboxylate (**7c**)[3b]: Salt **1c**, dimethyl maleate, and triethylamine reacted, as described for **3a**. Adduct **7c** (74%) was obtained as yellow needles (benzene), m.p. 178−180°C (dec.). − IR (KBr): $\tilde{\nu}$ = 1110 cm^{-1}, 1214 (C−O), 1325 vst, 1499 st (NO_2), 1600 st (arom. ring vibr.), 1633 m (C=C−N), 1744 (C=O). − ^{1}H NMR: Table 1. − $C_{21}H_{19}N_3O_6$ + C_6H_6 (409.4 + 78.1): calcd. C 66.52, H 5.17; found C 66.75, H 5.12.

3-Phenyl-...-1β,2α-dicarbonitrile (**13a**) *and 1α,2β-Diastereoisomer* (**14a**): (a) Triethylamine (0.80 ml, 5.7 mmol) was added to **1a** (600 mg, 2.35 mmol) and *fumaronitrile* (240 mg, 3.1 mmol) in 25 ml of CH_2Cl_2 under stirring; the red color vanished in a few minutes. The usual workup furnished 495 mg (71%) of colorless **13a** ($CHCl_3$/methanol), m.p. 149−150°C. − IR (KBr): $\tilde{\nu}$ = 692 cm^{-1}, 755, 772 st (arom. CH out-of-plane def.), 1497, 1601 (arom. ring vibr.), 1632 st (C=C−N), 2240 m (C≡N). − ^{1}H NMR (400 MHz): Table 1; δ = 7.07 (t, 4′-H of C_6H_5), 7.08 (d br., J = 7.9 Hz, 2′-H/6′-H), 7.15 (d br., J = 7.6 Hz, 7-H), 7.22 (td, J = 7.3, 1.0 Hz, 9-H), 7.29 (d br., J = 7.1 Hz, 10-H), 7.36 (dd, m, 3′-H/5′-H, 8-H). − ^{13}C NMR (100 MHz, DEPT): δ = 43.6 (C-1), 56.2 (C-2), 64.7 (C-10b), 105.8 (C-6), 114.2 (C-2′/C-6′of C_6H_5), 115.8, 117.0 (2 CN), 123.1 (C-4′), 125.8, 127.18, 127.21, 130.2 (C-7 to C-10), 129.9 (C-3′/C-5′), 136.7 (C-5), 125.9, 129.4 (C-10a, C-6a), 148.1 (C-1′). − MS (70 eV, 85°C); *m/z* (%): 298 (15) [M$^+$, ^{13}C 3.3/3.3], 220 (100) [$C_{15}H_{12}N_2$, **2**$^+$ or **6**; ^{13}C 17/16], 129 (76) [isoquinoline$^+$], 102 (14) [129 − HCN], 93 (9) [$C_6H_5NH_2^+$], 91 (11) [$C_6H_5N^+$], 77 (12) [$C_6H_5^+$]. In contrast to the MS of **3a** and **3b**, no fragments coming from the dipolarophile were observed. − $C_{19}H_{14}N_4$ (298.3): calcd. C 76.49, H 4.73, N 18.78; found C 76.57, H 4.72, N 18.75. − Mol. mass: 308 (vapor phase osmometry, benzene, 37°C). − (b) The reaction of CS_2 adduct **5** with fumaronitrile in $CDCl_3$ in the NMR tube indicated **13a/14a** 90:10 (d, of 6-H at δ = 5.70 and 5.65). Due to superposition, only part of the ^{1}H NMR signals of **14a** was visible: δ = 5.00 (d, $J_{1,2}$ = 6.5 Hz, 2α-H); 5.65, 6.11 (2 d, $J_{5,6}$ = 8.0 Hz, 6-H, 5-H).

3-(2-Pyridyl)-...-1β,2α-dicarbonitrile (**13b**): From 1.00 mmol each of *N*-(2-pyridyl)imide **2b** and fumaronitrile, 216 mg (72%) of colorless **13b** (ether/petroleum ether) was obtained, m.p. 150−151°C. − IR (KBr): $\tilde{\nu}$ = 686 cm^{-1} m, 760, 784, 799 st (arom. CH out-of-plane def.); 1439, 1466 st (pyridyl); 1498, 1576, 1595 st (arom. ring vibr.), 1638 st (C=C−N), 2250 m (C≡N). − ^{1}H NMR: Table 1. − $C_{18}H_{13}N_5$ (299.3): calcd. C 72.22, H 4.38, N 23.40; found C 72.23, H 4.50, N 23.41.

Methyl 1α-Cyano-3-phenyl-...-2α-carboxylate (**15**) *and Methyl 2α-Cyano-3-phenyl-...-1α-carboxylate* (**16**): (a) The red color rapidly disappeared, when **1a** and *methyl cis-3-cyanoacrylate*[36] (10 mmol of each) were stirred in 50 ml of CH_2Cl_2 with 11 mmol of triethylamine. Workup gave a pale yellow oil which crystallized from ether: 2.24 g (68%) of colorless **15**, m.p. 163−164°C was obtained. − IR (KBr): $\tilde{\nu}$ = 1205 cm^{-1}, 1291 (C−O); 1493, 1600 st (arom. ring vibr.), 1630 st (C=C−N), 1761 (C=O), 2240 w (C≡N). − ^{1}H NMR: Table 1. − $C_{20}H_{17}N_3O_2$ (331.4): calcd. C 72.49, H 5.17, N 12.68; found C 72.26, H 5.22, N 12.70. − On CC (ether/petroleum ether 1:1), the first fraction from the ethereal mother liquor of **15** provided **16** (0.60 g, 19%), which was isolated as colorless needles ($CHCl_3$/ether at −10°C), m.p. 121−123°C. − IR (KBr): $\tilde{\nu}$ = 1176 cm^{-1}, 1203, 1291 (C−O), 1490, 1598 (arom. ring vibr.), 1631 (C=C−N), 1741 (C=O), 2240 (C≡N). − ^{1}H NMR (Table 1). − (b) The cycloaddition was run with **5** in $CDCl_3$ in the NMR tube. The d of 6-H at δ = 5.53 for **15** and 5.41 for **16** were suitable for the comparison of the integrals (77:23).

Dimethyl (3aα,6α,7β,rel-7aβ,11bα)-(±)-3a,5,6,7,7a,11b-Hexahydro-5-phenyl-1-(2,4,6-trimethylphenyl)pyrazolo[5,1-a]isoxazolo[5,4-c]isoquinoline-6,7-dicarboxylate (**17**)[3f]: Adduct **3a** (180 mg, 0.49 mmol) and 2,4,6-trimethylbenzonitrile *N*-oxide[37] (90 mg, 0.56 mmol) in 3 ml of benzene were refluxed for 5 h; **17** (145 mg, 56%) was obtained as colorless needles, m.p. 225−226°C, from $CHCl_3$/methanol. − IR (KBr): $\tilde{\nu}$ = 1171 cm^{-1}, 1198, 1257, 1288 st (C−O, C−N), 1500, 1603 (arom. ring vibr.), 1735 st br (C=O). − ^{1}H NMR (400 MHz): δ = 1.53 (s, 4′-CH_3 of mesityl); 2.31, 2.38 (2 s, 2′-CH_3/6′-CH_3); 3.79, 3.91 (2 s, 2 OCH_3), 4.15 (dd, $J_{7,7a}$ = 7.3 Hz, $J_{6,7}$ = 11.3 Hz, 7α-H), 4.51 (d, $J_{6,7}$ = 11.3 Hz, 6β-H), 4.78 (d, $J_{7,7a}$ = 7.3 Hz, 7aβ-H), 4.68 and 6.14 (AX, $J_{3a,11b}$ = 8.7 Hz, 11b-H, 3a-H), 6.48 (br d, J = 7.5 Hz, arom.H), 6.78 (br s, 1 arom.H), 6.92−6.96 (m, 2 arom.H), 7.01−7.07 (m, 2 arom.H), 7.20−7.30 (m, 4 arom.H). − $C_{31}H_{31}N_3O_5$ (525.6): calcd. C 70.84, H 5.95, N 8.00; found C 71.12, H 5.91, N 8.16.

Tetramethyl (1α,2α,4aα,6aα,rel-10bβ)-(±)-1,2,3,4a,6a,10b-Hexahydro-3-phenylcyclobuta[c]pyrazolo[5,1-a]isoquinoline-1,2,5,6-tetracarboxylate (**18**): **7a** (1.00 g, 2.74 mmol) and DMAD (0.50 g, 3.5 mmol) in 5 ml of ether were kept at room temp. for 12 h. Four recrystallizations from $CHCl_3$/ether at −10°C gave 430 mg (31%)

of **18** as lustrous, pale yellow platelets, m.p. 160−162°C. − IR (KBr): $\tilde{\nu}$ = 1202 cm^{-1} vst, 1250, 1285 st (C−O), 1485, 1595 (arom. ring vibr.), 1645 m (C=C); 1730 br vst, 1756 (C=O). − ^1H NMR: δ = 3.13 (s, 1α-CO_2CH_3), 3.32, 3.75, 3.81 (3 s, 3 OCH_3), 4.02 (dd, $J_{1\beta,2\beta}$ = 9.5 Hz, $J_{1\beta,10b}$ = 7.0 Hz, 1-H), 4.59 (d, 10b-H), 4.60 (d, 2-H), 4.42 and 4.96 (AX, $J_{4a,6a}$ = 4.8 Hz, 6a-H, 4a-H), 6.8-7.3 (m, 9 arom. H). − $C_{27}H_{26}N_2O_8$ (506.5): calcd. C 64.02, H 5.17, N 5.53; found C 63.98, H 5.11, N 5.53.

Methyl Acrylate, Acrylonitrile, and Derivatives

Further (±)-1,2,3,10b-Tetrahydropyrazolo[5,1-a]isoquinolines: Methyl 3-Phenyl-...-1α-carboxylate (**19a**) *and 1β-Diastereoisomer* (**20a**): The reaction of **5** (1.48 g, 5.00 mmol) with freshly distilled *methyl acrylate* (470 mg, 5.5 mmol) in 10 ml of CH_2Cl_2 required only a few minutes. After removal of the solvent, CC (basic Al_2O_3, ether/petroleum ether 1:1) afforded 0.21 g (14%) of **20a** (colorless oil) as the first fraction (R_f = 0.74); the second fraction (R_f = 0.57) consisted of 0.58 g (38%) of **19a** as a pale yellow oil which crystallized from ether/petroleum ether at −18°C and gave 0.32 g of colorless prisms, m.p. 73−74°C. − Properties of **19a**. − IR (KBr): $\tilde{\nu}$ = 1169 cm^{-1}, 1190 st, br (C−O); 1375, 1436, 1460; 1498 st, 1573 m, 1604 st (arom. ring vibr.), 1634 st (C=C−N), 1740 st br (C=O). − ^1H NMR: Table 2. − $C_{19}H_{18}N_2O_2$ (306.3): calcd. C 74.49, H 5.92, N 9.15; found C 74.64, H 5.86, N 9.18.− ^1H NMR of **20a**: δ = 3.62 (s, OCH_3), 3.57−3.83 (superimposed and little resolved 1α-H and 2-H_2), 4.47 (m, 10b-H), 5.51 and 6.17 (2 d, $J_{5,6}$ = 7.8 Hz, 6-H, 5-H), 7.4-6.8 (m, 9 arom. H). − (b) The reaction in $CDCl_3$ in the NMR tube allowed the determination of the ratio **19a**/**20a** (57:43) from the integrals of the isolated signals of 10b-H (δ 4.75, 4.47).

Methyl 3-(2-Pyridyl)-...-1α-carboxylate (**19b**) *and 1β-Diastereoisomer* (**20b**): (a) The red solution of 1.00 (4.52 mmol) of **2b** and 0.50 g (5.8 mmol) of methyl acrylate in 20 ml of CH_2Cl_2 was decolorized after 2 min. CC (basic alumina, ether/petroleum ether) provided 0.32 g (23%) of oily **20b**, followed by 0.72 g (52%) of **19b** which crystallized from $CHCl_3$/ether at −10°C, m.p. 78−80°C. − Properties of **19b**. − IR (KBr): $\tilde{\nu}$ = 1167 cm^{-1}, 1188 (C−O); 1430, 1455 (pyridyl), 1470, 1568, 1594 (arom. ring vibr.), 1629 st (C=C−N), 1734 (C=O). − ^1H NMR (400 MHz): Table 2; δ = 6.79 (m, 5′-H of pyridyl), 6.98 (d br., J = 7.6 Hz, 7-H), 7.04 (d, 10-H), 7.06 (m, 9-H), 7.17 (m, 3′-H), 7.18 (m, 8-H), 7.52 (m, 4′-H), 8.24 (m, J = 4.8 Hz, 6′-H); the assignment was based on two-dimensional techniques[38]. For comparison, the 60 MHz spectrum in C_6D_6 is included in Table 2; the signals are shifted to higher field (ASIS)[39]. − ^{13}C NMR (100 MHz, DEPT): δ = 49.2 (C-2), 51.4 (OCH_3), 53.7 (C-1), 62.5 (C-10b), 103.7 (C-6), 109.0 (C-3′ of pyridyl), 116.2 (C-5′); 124.8 (C-7), 125.3 (C-9), 128.0 (C-10a), 128.1 (C-10), 128.4 (C-8), 131.4 (C-6a), 137.9 (C-5), 138.0 (C-4′), 147.7 (C-6′), 160.9 (C-2′), 172.5 (C=O). − $C_{18}H_{17}N_3O$ (307.3): calcd. C 70.34, H 5.58, N 13.67; found C 70.30, H 5.69, N 13.51. − ^1H NMR of **20b**: The gross overlap of signals thwarted the computer simulation; δ = 3.60 (s, 1β-CO_2CH_3), 4.42 (m, 10b-H), 4.50 (m, 2β-H), 5.53 and 6.16 (AX, $J_{5,6}$ = 7.7 Hz, 6-H, 5-H); (C_6D_6): Table 2. − (b) When the reaction was run in $CDCl_3$ in the NMR tube, the d of 6-H indicated a ratio of **19b**/**20b** = 60:40.

3-Phenyl-...-1α-carbonitrile (**21a**) *and 1β-Diastereoisomer* (**22a**): (a) The reaction of **5** (2.96 g, 10.0 mmol) and *acrylonitrile* (0.55 g, 10.4 mmol) in 25 ml of benzene was finished within 1 min. Colorless needles of **21a** (0.89 g, 31%, m.p. 110−112°C) were isolated from ether/petroleum ether after 8 d at 4°C. After CC (alumina, ether/petroleum ether), the residue of the mother liquor gave **22a** (0.59 g, 22%) as a pale yellow oil of limited stability (hydrazo rearrangement). The reaction, run in C_6D_6 in an NMR tube, indicated **21a**/**22a** = 56:44 (d, 5-H); no further products were visible. − Properties of **21a**. − IR (KBr): $\tilde{\nu}$ = 1493 cm^{-1} st, 1570 w, 1600 st (arom. ring vibr.), 1630 st (C=C−N), 2240 w (C≡N). − UV ($CHCl_3$): λ_{max} (log δ) = 297 (3.81). − ^1H NMR (400 MHz): Table 2; δ = 6.94 (tt, 4′-H of C_6H_5), 7.02 (d br., 2′-H/6′-H), 7.04 (d br., 7-H), 7.12 (d br., 10-H), 7.15 (td, 9-H), 7.27 (dd, J = 7.3, 8.7 Hz, 3′-H/5′-H), 7.28 (td, 8-H). Three recordings with 9, 40, and 90 mg of **21a** per 0.5 ml of $CDCl_3$ indicated δ values decreasing by 0.04−0.11 ppm; intermolecular shielding by the aromatic rings is probably responsible for this. − ^{13}C NMR (100 MHz, DEPT): δ = 39.5 (C-1), 55.1 (C-2), 60.8 (C-10b), 105.4 (C-6), 114.3 (C-2′/C-6′ of N−C_6H_5), 118.9 (C≡N), 121.5 (C-4′); 125.6, 126.4, 127.3, 129.4 (C-7 to C-10); 126.8, 131.3 (C-6a, C-10a), 136.8 (C-5), 149.1 (C-1′). − $C_{18}H_{15}N_3$ (273.3): calcd. C 79.09, H 5.53, N 15.38; found C 79.23, H 5.81, N 15.11. − ^1H NMR of **22a** (Table 2); data of ring protons computer-simulated. − (b) Adduct **21a** undergoes the hydrazo rearrangement[6] slowly in neutral medium at 25°C. A second 400 MHz ^1H NMR spectrum after 48.5 h showed 28% conversion, corresponding to k_1 = 2 10^{-6} s^{-1} (half-life 101 h) in $CDCl_3$.

3-(2-Pyridyl)-...-1α-carbonitrile (**21b**) *and 1β-Diastereoisomer* (**22b**): **2b** (0.44 g, 2.0 mmol) rapidly reacted with acrylonitrile (0.15 g, 2.8 mmol) in 10 ml of CH_2Cl_2. From $CHCl_3$/ether **21b** (0.21 g, 39%) crystallized as colorless needles, m.p. 157−158°C (ref: light yellow, m.p. 157−158°C[21]). CC (basic alumina, ether/petroleum ether) of the mother liquor furnished 0.13 g (24%) of **22b** as a colorless oil. When the reaction took place in $CDCl_3$ in the NMR tube, the 5-H doublets indicated **21b**/**22b** = 54:46; no impurities visible. − Properties of **21b**. − IR (KBr): $\tilde{\nu}$ = 1435 cm^{-1}, 1468 st (pyridyl), 1562 m, 1592 st (arom. ring vibr.,), 1630 st (C=C−N), 2240 m (C≡N). − ^1H NMR: Table 2. The overlap of the signals at δ 3.13−3.77 was so strong that the data of 1β-H and 2α-H could not be determined. δ = 4.44 (d, J = 7.3 Hz, 10b-H), 5.04 (dd, 2β-H), 5.66 and 6.08 (2d, $J_{5,6}$ = 8.0 Hz, 6-H, 5-H), 6.70−8.33 (m, 8 arom. H). In C_6D_6 (Table 2), the signal groups of 1β-H, 2α-H, 10b-H and 2β-H were so far separated, that evaluation by first-order was feasible; the signal of 1β-H showed all 8 lines and 3 coupling constants. − ^{13}C NMR: δ = 38.8 (d, C-1), 50.4 (dd, C-2), 61.7 (d, C-10b), 106.0 (d, C-6), 109.0 (d, C-3′ of pyridyl), 116.7 (d, C-5′), 119.0 (s, CN); 125.5, 126.4, 127.0, 129.2 (4 d, C-7 to C-10); 126.4, 130.9 (2 s, C-6a, C-10a), 136.5, 138.1 (d, C-5, C-4′), 147.4 (d, C-6′ of pyridyl), 159.6 (s, C-2′). − $C_{17}H_{14}N_4$ (274.3): calcd. C 74.43, H 5.14, N 20.43; found C 74.61, H 5.28, N 20.45. − ^1H NMR of **22b**: δ = 5.53, 6.07 (2 d, $J_{5,6}$ = 7.5 Hz, 6-H, 5-H); the complex spectrum of the 4 H at the pyrazolidine ring in C_6D_6 was easier to disentangle for simulation by LAME (Table 2).

Dimethyl 1β-Methyl-3-phenyl-...-1α,2α-dicarboxylate (**23a**)[3d]: *Dimethyl citraconate* and salt **1a** (5.0 mmol of each) were stirred with triethylamine in 10 ml of CH_2Cl_2; the reaction was still incomplete after 24 h. The usual workup was followed by CC on neutral alumina. − ^1H NMR: Table 3.

Dimethyl 1β-Methyl-3-(2-pyridyl)-...-1α,2α-dicarboxylate (**23b**): Analogous reaction with **2b** in $CDCl_3$ in the NMR tube. − ^1H NMR: Table 3; no second isomer visible.

Dimethyl 1α-Chloro-3-phenyl-...-1β,2α-dicarboxylate (**24a**)[3d][3f]: The reaction with 5.0 mmol of *dimethyl 2-chlorofumarate*[40] − same procedure as for **23a** − was complete after 20 min; m.p. 124−126°C (methanol). − ^1H NMR: Table 3. − After refluxing with picric acid in methanol, **24a** was reisolated unchanged. − **24a** (0.1 g) and some crystals of 4-toluenesulfonic acid in 3 ml of CH_3OD were refluxed for 3 h. At −25°C [6-D]-**24a** crystallized; the d at δ = 5.45 (6-H) had disappeared, and the 5-H signal at 6.54 was a singlet.

The analogous *3-(2-pyridyl)* compound **24b** was prepared with **2b** in $CDCl_3$ in the NMR tube; after 12 h the color had faded. − ^{1}H NMR (Table 3).

Methyl 1β-Methyl-3-phenyl-...-1α-carboxylate (**25a**) *and Diastereoisomer* **26a**: (a) The yellow oil, obtained from **5** (1.48 g, 4.99 mmol) and *methyl methacrylate* (0.50 g, 5.0 mmol) in 10 ml of CH_2Cl_2, was separated by CC (basic alumina, ether/petroleum ether, 1:5). The first fraction (R_f = 0.81) furnished **26a** (0.29 g, 8%) as colorless cubes; m.p. 86−87°C (petroleum ether, −10°C). The second fraction (R_f = 0.56) gave **25a** (0.55 g, 34%) as colorless needles, m.p. 67−69°C, from petroleum ether. − Properties of **25a**. − IR (KBr): $\tilde{\nu}$ = 1126 cm^{-1}, 1142, 1230, 1246, 1281 (C−O); 1492, 1600 (arom. ring vibr.), 1626 st (C=C−N), 1733 (C=O). − ^{1}H NMR: Table 3. − MS (85°C); *m/z* (%): 320 (22) [M^+, ^{13}C 4.8/4.7], 289 (1.2) [$M^+ - OCH_3$], 220 (100) [$C_{15}H_{12}N_2^+$, **2a**$^+$ or **6**; ^{13}C 17/15], 219 (11) [220 − H], 129 (22) [isoquinoline], 102 (3), 77 (6) [$C_6H_5^+$]. − $C_{20}H_{20}N_2O_2$ (320.4): calcd. C 74.96, H 6.29, N 8.74; found for **25a** (**26a**) C 75.14 (75.16), H 6.27 (6.39), N 8.62 (8.84). − Properties of **26a**. − IR (KBr): $\tilde{\nu}$ = 1093 cm^{-1}, 1148, 1220, 1258, 1280, 1290 (C−O), 1489, 1599 (arom. ring vibr.), 1630 st (C=C−N), 1727 (C=O). − ^{1}H NMR (400 MHz): Table 3; δ = 6.88 (tt, *J* = 7.3, 1.0 Hz, 4′-H of C_6H_5), 6.99 (d br., *J* = 7.7 Hz, 7-H), 7.03 (dd, 2′-H/6′-H), 7.07 (m, 9-H, 10-H), 7.19 (m, 8-H), 7.25 (dd, *J* = 7.3, 8.8 Hz, 3′-H/5′-H). − ^{13}C NMR (100 MHz, DEPT): δ = 19.9 (1α-CH_3), 52.3 (OCH_3), 59.6 (C-1), 62.6 (C-2), 64.3 (C-10b), 102.0 (C-6), 114.1 (C-2′/C-6′ of N−C_6H_5), 120.5 (C-4′); 124.6, 125.7, 127.6, 128.3 (C-7 to C-10), 129.1 (C-3′/C-5′), 129.2 (C-10a), 132.3 (C-6a), 139.0 (C-5), 150.1 (C-1′), 175.2 (C=O). − (b) When the reaction was carried out in $CDCl_3$ in the NMR tube, the integrals of 1-CH_3 established **25a/26a** = 73:27. If a small third methyl signal at δ_H = 1.47 belongs to a regioisomer, the product ratio would be 69:25:6.

Methyl 1β-Chloro-3-phenyl-...-1α-carboxylate (**27a**) *and Diastereoisomer* **28a**: (a) CS_2 adduct **5** and *methyl 2-chloroacrylate*[41] (10.0 mmol of each) in 30 ml of CH_2Cl_2 reacted in a few min at room temp.; colorless **27a** (2.20 g, 65%), m.p. 100−101°C, crystallized from ether/petroleum ether at −10°C. − IR (KBr): $\tilde{\nu}$ = 1248 cm^{-1}, 1258, 1283 (C−O); 1496, 1603 st (arom. ring vibr.), 1636 st (C=C−N), 1735 (C=O). − ^{1}H NMR (400 MHz): Table 3; δ = 6.95 (tt, *J* = 7.3, 1.1 Hz, 4′-H of C_6H_5), 7.00 (d br., *J* = 7.6 Hz, 7-H), 7.09 (dd, 2′-H/6′-H), 7.10 (td ?, overlap, 9-H), 7.23 (td, *J* = 7.5, 1.2 Hz, 8-H), 7.27 (d br., 10-H), 7.29 (dd, *J* = 7.3, 8.5 Hz, 3′-H/5′-H). − ^{13}C NMR (100 MHz, DEPT): δ = 53.1 (OCH_3), 64.3 (C-2), 73.1 (C-10b), 77.2 (C-1), 102.5 (C-6), 114.1 (C-2′/C-6′ of N−C_6H_5), 121.2 (C-4′); 124.8, 125.6, 127.7, 129.7 (C-7 to C-10); 125.7 (C-10a), 131.2 (C-6a), 137.3 (C-5), 149.5 (C-1′), 168.8 (C=O). − $C_{19}H_{17}ClN_2O_2$ (340.8): calcd. C 66.96, H 5.03, N 8.22; found C 67.01, H 5.17, N 8.22. − (b) An experiment in $CDCl_3$ in the NMR tube showed **27a/28a** = 82:18 by the integrals of the OCH_3 signals at δ = 3.19 and 3.68; further NMR data of **28a** in Table 3.

Methyl 1β-Chloro-3-(2-pyridyl)-...-1α-carboxylate (**27b**) *and Diastereoisomer* **28**: The reaction with **2a** and methyl 2-chloroacrylate in $CDCl_3$ in the NMR tube afforded **27b/28b** = 85:15 (d of 2α-H); ^{1}H NMR in Table 3.

1β-Methyl-3-phenyl-...-1α-carbonitrile (**29a**) *and Diastereoisomer* **30a**: (a) The deep-red solution of **5** and *methacrylonitrile* (10.0 mmol of each) in 10 ml of CH_2Cl_2 was decolorized after 5 h; **29a** (1.07 g, 37%) was isolated as colorless crystals, m.p. 126−127°C (ether/petroleum ether, −10°C). − IR (KBr): $\tilde{\nu}$ = 756 cm^{-1} st (arom. CH out-of-plane def.); 1495, 1602 (arom. ring vibr.), 1633 st (C=C-N), 2230 m (C≡N). − $C_{19}H_{17}N_3$ (287.4): calcd. C 79.41, H 5.96, N 14.62; found C 79.33, H 5.97, N 14.45. − ^{1}H NMR (400 MHz): Table 3; δ = 6.92 (t, *J* = 7.5 Hz, 4′-H of N−C_6H_5), 7.00 (d, *J* = 7.9 Hz, 2′-H/6′-H), 7.06 (d br., 7-H), 7.14 (d br., 10-H), 7.15 (t br., 9-H), 7.27 (dd, 3′-H/5′-H), 7.28 (td, 9-H). − ^{13}C NMR (100 MHz, DEPT): δ = 23.2 (1β-CH_3), 48.4 (C-1), 62.6 (C-2), 68.2 (C-10b), 104.8 (C-6), 113.9 (C-2′/C-6′ of N−C_6H_5), 121.1 (C-4′), 122.1 (C≡N); 125.6, 126.2, 126.7, 129.6 (C-7 to C-10); 126.9, 131.4 (C-10a, C-6a), 129.4 (C-3′/C-5′), 137.3 (C-5), 149.7 (C-1′) − (b) The reaction in $CDCl_3$ in the NMR tube revealed **29a/30a** = 56:39 (integrals of the methyl signals at δ_H = 1.49 for **29a**, 1.22 for **30a**). It is left open whether a third methyl-singlet at δ 1.58 belongs to 5% of a regioisomer. Compound **30a** was not isolated.

1β-Methyl-3-(2-pyridyl)-...-1α-carbonitrile (**29b**) *and 1α,1β-Diastereoisomer* (**30b**): An experiment was carried out with **2** and methacrylonitrile in $CDCl_3$ in the NMR tube (no product isolation). The methyl integrals, δ_H = 1.47 for **29b** and 1.24 for **30b**, indicated an adduct ratio of 53:47. − ^{1}H NMR in Table 3.

1β-Chloro-3-phenyl-...-1α-carbonitrile (**31a**) *and 1α,1β-Diastereoisomer* (**32a**): (a) **5** (3.60 g, 12.1 mmol) and *2-chloroacrylonitrile* (1.10 g, 12.6 mmol) in 25 ml of CH_2Cl_2 afforded **32a** (2.11 g, 57%) as colorless needles, m.p. 103−104°C (ether/petroleum ether). − IR (KBr): $\tilde{\nu}$ = 756 cm^{-1}, 762 (arom. CH wagg.); 1492, 1599 st (arom. ring vibr.), 1628 st (C=C−N), 2230 w (C≡N). − ^{1}H NMR: Table 3. − $C_{18}H_{14}ClN_3$ (307.8): calcd. C 70.24, H 4.59, N 13.65; found C 70.13, H 4.65, N 13.56. − (b) After reaction in $CDCl_3$ in the NMR tube, the s of 10b-H at δ_H = 4.82 for **31a** and 4.94 for **32a** enabled the determination of the 68:32 ratio. ^{1}H NMR of **44a**: Table 3.

1β-Chloro-3-(2-pyridyl)-...-1α-carbonitrile (**31b**) *and 1α,1β-Diastereoisomer* (**32b**): (a) The red color of the solution of **2a** (2.00 g, 9.04 mmol) and 2-chloroacrylonitrile (0.80 g, 9.14 mmol) in 20 ml of CH_2Cl_2 was pale yellow after 1 min. Colorless needles of **31b** (1.94 g, 70%), m.p. 110−111°C, came from $CHCl_3$/ether. − IR (KBr): $\tilde{\nu}$ = 778 cm^{-1}, 786 (arom. CH out-of-plane def.); 1438, 1473 st (pyridyl); 1570, 1596 st (arom. ring vibr.), 1633 m (C=C−N), 2245 w (C≡N). − ^{1}H NMR: Table 3. − $C_{17}H_{13}ClN_4$ (308.8): calcd. C 66.13, H 4.24, N 18.15; found C 66.24, H 4.25, N 18.41. − (b) An experiment in $CDCl_3$ in the NMR tube established **31b/32b** = 76:24 (s of 10b-H at δ_H = 4.63 and 4.77).

Dimethyl (1α,4aα,6aα,rel-10bβ)-(±)-1-Cyano-1,2,3,4a,6a,10b-hexahydro-1-methyl-3-phenylcyclobuta[c]pyrazolo[5,1-a]isoquinoline-5,6-dicarboxylate (**33**): A suspension of **29a** (1.00 g, 3.48 mmol) in 5 ml of ether was stirred with DMAD (1.00 g, 7.04 mmol) for 12 h at room temp.; after removal of the volatile up to 40°C/0.1 Torr, the brown residue crystallized from $CHCl_3$/ether: 0.84 g (56%) of **33** was obtained as colorless prisms, m.p. 156−157°C. **33** is stable in boiling toluene (no ring expansion). − IR (KBr): $\tilde{\nu}$ = 695 cm^{-1}, 756 (arom. CH out-of-plane def.); 1205, 1254, 1313, 1324 (C−O); 1494, 1603 st (arom. ring vibr.), 1653 st (C=C); 1719, 1733 (C=O), 2230 w (C≡N). − ^{1}H NMR (C_6D_6): δ = 0.81 (s, 1β-CH_3), 3.18, 3.35 (2 s, 2 OCH_3), 2.80, 3.97 (AX, J_{gem} = −10.6 Hz, 2α-H and 2β-H), 3.38 (s, 10b-H), 4.69, 4.77 (AB, $J_{4a,6a}$ = 4.5 Hz, 4a-H, 6a-H), 7.3−7.6 (m, 8 arom. H), 7.9−8.1 (m, 1 arom. H). ($CDCl_3$): 3.38, 3.81 (2 s, 2 OCH_3). − $C_{25}H_{23}N_3O_4$ (429.5): calcd. C 69.91, H 5.40, N 9.79; found C 69.92, H 5.39, N 9.75.

Triphenylvinylphosphonium Bromide and the Formal Ethylene Adducts

1,2,3,10b-Tetrahydro-3-phenylpyrazolo[5,1-a]isoquinoline (**34a**): 2-Anilinoisoquinolinium chloride (**1a**, 2.57 g, 10.0 mmol) was dissolved in 15 ml of water, basified with saturated aqueous Na_2CO_3, and extracted with CH_2Cl_2. After short drying of the organic phase

with $MgSO_4$, vinyltriphenylphosphonium bromide[42] (**37**, 3.80 g, 10.3 mmol) was added; the red color of **2a** turned to yellow-brown. After removal of the solvent, the residue (**39a**) was shaken with 12 ml of 7% aqueous NaOH for 45 min at room temp. The dark sticky mixture was extracted with 3 × 50 ml of ether; after concentration, triphenylphosphane oxide crystallized from the ether solution after seeding. The mother liquor was put on a column of basic alumina and eluted with petroleum ether. The first fraction (R_f = 0.89) was followed by an unidentified substance which turned brown on air; the first fraction (0.66 g) crystallized from petroleum ether at −10°C: 0.17 g (7%) of colorless **34a**, m.p. 74−76°C, was obtained. − IR (KBr): $\tilde{\nu}$ = 692 cm^{-1}, 752, 763, 782 st (*cis*-CH=CH and arom. CH out-of-plane def.); 1492, 1603 st, 1569 m (arom. ring vibr.), 1623 st (C=C−N). − ^1H NMR (100 MHz, $CDCl_3$, fresh solution): Table 4; δ = 6.81−7.18 (m, 9 arom. H). − ^{13}C NMR (25.2 MHz, $CDCl_3$): δ = 35.3 (t, C-1), 50.0 (t, C-2), 58.8 (d, C-10b), 102.2 (d, C-6), 113.6 (d, C-2′/C-6′ of N−C_6H_5), 119.6 (d, C-4′), 124.4, 125.3, 126.4, 127.7 (4 d, C-7 to C-10), 128.9 (d, C-3′/C-5′); 130.2, 131.8 (2 s, C-6a, C-10a), 139.4 (d, C-5), 151.3 (s, C-1′); smaller signals for the product of the hydrazo rearrangement were visible. − $C_{17}H_{16}N_2$ (248.3): calcd. C 82.22, H 6.50, N 11.28; found C 82.13, H 6.26, N 11.30.

1,2,3,10b-Tetrahydro-3-(2-pyridyl)pyrazolo[5,1-a]isoquinoline (**34b**): **2b** (2.21 g, 10.0 mmol) was dissolved in 50 ml of CH_2Cl_2; the deep-red color faded upon addition of 3.80 g (10.3 mmol) of **37** within 2 min. The work-up with alkaline hydrolysis of the orange primary adduct followed the description for **34a**. Colorless crystals of **34b** (0.34 g, 14%), m.p. 75−78°C, came from ether/petroleum ether at −18°C. − IR (KBr): $\tilde{\nu}$ = 710 cm^{-1}, 740 m, 765, 785 st (*cis*-CH=CH- and arom. CH out-of-plane def.), 1430, 1460 st (pyridyl vibr.), 1563 m, 1595 st (arom. ring vibr.), 1625 m (C=C−N). − ^1H NMR (100 MHz, $CDCl_3$): Table 4; δ = 6.44−8.16 (m, 8 arom. CH); (C_6D_6, 60 MHz): δ = 1.40−2.58 (m, 1-H_2), 3.26 (m, 2α-H), 3.76 (dd, 10b-H), 4.27 (m, 2β-H), 5.29, 6.01 (AB, $J_{5,6}$ = 8.0 Hz, 6-H and 5-H), 6.30−7.33 (m, 7 arom. CH), 8.25 (m, 6′-H of pyridyl). − ^{13}C NMR (25.2 MHz, $CDCl_3$, comparison of H-decoupled and off-resonance spectrum): δ = 34.6 (t, C-1), 45.7 (dd, C-2), 59.7 (C-10b), 103.3 (d, C-6), 108.4 (d, C-3′ of pyridyl), 114.9 (d, C-5′); 124.5, 125.5, 126.3, 127.7 (4 d, C-7 to C-10); 129.9, 131.9 (2 s, C-6a, C-10a), 137.3 (d, C-5), 138.9 (d, C-4′), 147.5 (d, C-6′), 161.3 (s, C-2′). − $C_{16}H_{15}N_3$ (249.3): calcd. C 77.08, H 6.06, N 16.86; found C 77.10, H 6.18, N 16.83.

[1,1-D_2]-**34b**: The above procedure for **34b** was followed on the same 10 mmol scale, but a 7% solution of NaOD in D_2O was used for the hydrolysis of **39b**; 0.30 g (12%), m.p. 78−80°C, crystallized from ether/petroleum ether. − IR (KBr): $\tilde{\nu}$ = 2003 cm^{-1} w (C−D). − ^1H NMR (60 MHz, $CDCl_3$): δ = 3.25 and 4.01 (AB, $J_{2\alpha,2\beta}$ = 10.8 Hz, 2α-H, 2β-H), 3.92 (s, 10b-H, coincides with the high-field signal for the d of 2β-H), 5.32, 5.98 (AB, $J_{5,6}$ = 8.0 Hz, 6-H and 5-H). (C_6D_6, 60 MHz): δ = 3.25, 4.28 (AB, $J_{2\alpha,2\beta}$ = 10.8 Hz, 2α-H, 2β-H), 3.75 (s, 10b-H), 5.31, 6.02 (AB, $J_{5,6}$ = 8.0 Hz, 6-H, 5-H). − $C_{16}H_{13}D_2N_3$ (251.3): calcd. C 76.46, H/D 6.81, N 16.72; found C 76.54, H/D 6.17, N 16.49.

Statistical Analysis: The increments I_s of equation (1) were calculated by standard matrix algebra leading to a minimal least-squares fit of the model equation to the experimental data. In order to find out the standard errors, the Variance-Covariance matrix was determined. The square root of its diagonal elements are the standard errors of the fitted parameters[32].

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