

Stereochemistry of Cycloadducts from 3,4-Dihydro-6,7-dimethoxyisoquinoline Ylide and Olefins

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Cycloaddition of 2-methoxycarbonylmethyl-3,4-dihydro-6,7-dimethoxyisoquinolinium ylide with various *E*-substituted olefin type dipolarophiles gave products of 10b-H, 1-H, 2-H and 3-H $\alpha, \alpha, \beta, \beta$ -relative configuration with one exception. Relative configuration of compounds prepared has been determined by 1D and 2D ^1H and ^{13}C nmr techniques. It has also been detected that a triple *trans* \rightleftharpoons *cis-1* \rightleftharpoons *cis-2* conformation equilibrium exists in solution.

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Earlier we reported on the 1,3-dipolar cycloaddition of azomethine ylide **2** obtained from *N*-methoxycarbonylmethyl-3,4-dihydro-6,7-dimethoxyisoquinolinium bromide (**1**) on treatment with base [1-4]. Reactions of methylene **2** with olefin and azomethine type dipolarophiles were investigated and the structure of the cycloadducts obtained was elucidated. It was established that the substituents of the azomethines and the olefins influence the stereochemistry of the products. Generally "endo" type cycloadducts were obtained with olefins except for dimethyl fumarate which gave an "endo-exo" mixture [3]. In our present studies the influence of the further modification of the substituent of the olefin on the configuration and con-

formation of adducts prepared has been investigated.

Results and Discussion.

Our model compounds were olefins possessing ester, acetyl of a partly substituted benzoyl group and an aromatic or heteroaromatic ring in the *E* (*trans*) position beside the reacting double bond (Scheme 1).

For the structure elucidation of cycloadducts **16-29** determination of the relative configuration of centres of chirality C(10b), C(1), C(2), and C(3) was not enough since owing to the presence of the N(4) bridgehead nitrogen atom a triple conformation equilibrium can develop (Scheme 2).

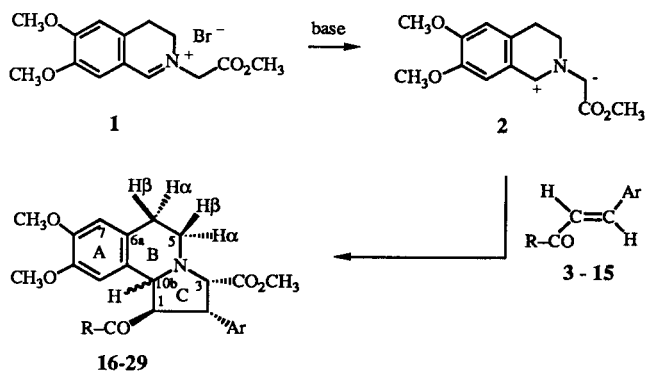
For the nmr assignment results of our previous studies [3,4] were utilized in the course of which various 1,2-disubstituted-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic acid methyl esters were investigated. The higher field strength and more modern techniques used in the present studies made possible a better assignment and a more precise analysis. Characteristic ^1H and ^{13}C data are summarized in Tables 1-4.

Proton signals of the pyrrolidine ring (ring C) appeared separately and were analyzed according to the first order. Signals at 3-H and 10b-H of equal multiplicity were assigned on the basis of the carbon-proton correlation spectrum and by means of the allyl coupling (approximately 1 Hz) between the 10b-H and 10-H [3].

Of 5- H_2 and 6- H_2 methylene protons those adjacent to the nitrogen atom appear with higher chemical shift but in the case of compound **29** this rule is invalid according to the 2D carbon-proton correlation measurements. Since the *cis-1* *cis-2* conformation equilibrium results in the exchange of the axial and equatorial 5 and 6 methylene protons only the α/β designation of these protons is reasonable at all.

It has been observed that chemical shift values of 7-H

Scheme 1



	R	Ar
3, 16	methoxy	phenyl
4, 17	methoxy	4'-nitrophenyl
5, 18	methoxy	3'-nitrophenyl
6, 19	methoxy	4'-methoxyphenyl
7, 20	methoxy	3',4',5'-trimethoxyphenyl
8, 21	methoxy	thienyl
9, 22	methoxy	furyl
10, 23	methyl	3',4'-methylenedioxyphenyl
11, 24	methyl	furyl
12, 25	phenyl	phenyl
13, 26	phenyl	4'-nitrophenyl
14, 27	phenyl	furyl
15, 28, 29	4'-nitrophenyl	furyl

Scheme 2

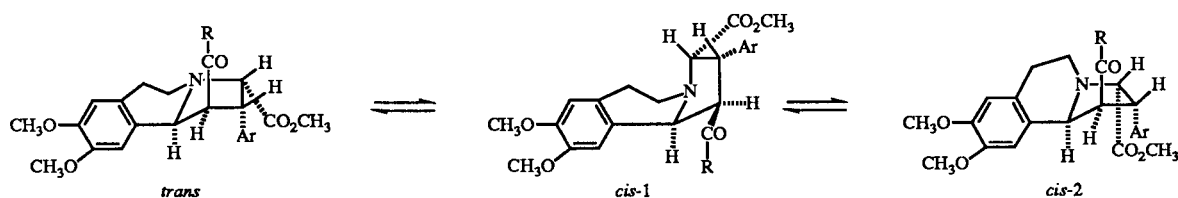


Table 2
Results of NOE Measurements from Compounds 16,22,25,27-29

	Proton irradiated	NOE observed
(16)	1-H	2-H (1%), 10-H (9.6%), 10b-H (14.5%), 2'6'-H (11.3%)
	3-H	2-H (15.8%), 5-H α (3.6%), 5-H β (2.6%), 6-H β (5.7%), 2'6'-H (1.4%)
	5-H α	3-H (45.1%), 5-H β (13.3%), 6-H α (9.3%), 10b-H (4.1%)
	6-H β	3-H (12.5%), 5-H β (6.5%), 6-H α (31.3%), 7-H (6.5%)
	10b-H	1-H (17.6%), 5-H α (1.9%), 10-H (10.8%), 2'6'-H (10.7%)
(22)	2-H	1-H (3.8%), 3-H (9.8%), 3'-H (4.1%)
	3-H	2-H (11.9%), 5-H β (1.5%), 5H α (1.5%), 6-H (1.5%)
	10b-H	1-H (18.5%), 10-H (12.0%)
(25)	2-H	1-H (1.5%), 3-H (14.1%), 2'6'-H (18.1%)
	3-H	2-H (24.1%), 6H β (2.4%)
	5-H α	3-H (13.4%), 6-H α (3.1%), 10b-H (4.0%)
	9-OCH ₃	10-H (27.0%)
	10b-H	3-H (14.8%), 5-H β (5.1%), 6-H α (38.0%), 7-H (5.0%)
(27)	1-H	2-H (14.4%), 10-H (13.0%), 2'6'-H (9.6%), 2''6''-H (2.2%)
	3-H	2-H (3.1%), 10b-H (14.1%), 3'-H (4.7%), 2''6''-H (29.4%), 3''5''-H (4.4%)
	5-H α	2-H (9.4%), 5-H α (1.5%), 5-H β (1.5%), 6H β (1.5%)
	9-OCH ₃	2-H (0.5%), 3-H (4.6%), 5-H β (12.9%), 6-H β (6.0%), 6-H α (1.5%), 10b-H (2.6%)
	6-H β	10-H (5.9%)
	10-H	3-H (17.6%), 5-H β (7.5%), 6-H α (15.0%), 7-H (11.6%)
	10b-H	1-H (1.0%), 10b-H (7.1%), 2''6''-H (2.1%)
(28)	2-H	1-H (14.0%), 5-H α (0.9%), 10-H (9.8%), 3'-H (0.9%)
	3-H	1-H (3.0%), 3-H (7.9%), 3''-H (3.8%), 2'6'-H (1.2%)
	5-H α	2-H (10.0%), 5-H α (3.1%), 6-H β (4.1%), 3''-H (0.8%)
	6-H β	3-H (4.6%), 6-H α (7.4%), 10b-H (2.7%)
	10b-H	3-H (7.2%), 6-H α (14.9%), 7-H (5.3%)
(29)	1-H	1-H (12.7%), 10-H (8.7%), 3''-H (1.3%)
	2-H	10-H (4.3%), 3''-H (2.2%), 2'6'-H (20.7%)
	3-H	3-H (6.3%), 3''-H (4.0%)
	8-OCH ₃	2-H (3.8%), 5-H β (3.5%), 10b-H (4.8%)
	10b-H	7-H (2.8%) 3-H (6.5%), 5-H β (6.3%), 10-H (3.1%)

Table 4
Characteristic Proton-Proton and Proton-Carbon Couplings (Hz)

	16	17	18	19	20	21	22	23	24	25	26	27	28	29
J (10b-H, 10b-C)	146.0						148.3			145.0		148.4	149.0	135.0
J (1-H, 1-C)	140.7						140.5			134.0		135.8	134.0	142.0
J (2-H, 2-C)	133.7						135.5			136.0		137.9	137.0	136.2
J (3-H, 3-C)	141.7						143.4			140.6		142.6	141.7	138.5
J (1-H, 2-H)	5.2	5.0	5.1	5.1	6.1	4.8	6.2	?	4.7	6.6	7.0	6.9	6.0	8.5
J (2-H, 3-H)	7.8	7.5	7.6	7.8	8.1	7.4	7.7	7.3	7.9	8.5	8.3	8.2	8.0	9.7
J (1-H, 10b-H)	8.2	8.5	8.3	8.3	8.1	8.5	8.4	7.3	7.6	7.7	7.8	8.2	8.0	9.8
J (5-H α , 5-H β)	12.3						11.5			12.6		12.3	12.1	
J (6-H α , 6-H β)	16.1						15.4			15.7		15.6	15.7	
J (5-H α , 6-H α)	4.5						4.4			4.1		4.2	4.2	
J (5-H α , 6-H β)	8.4						7.2			9.1		8.1	8.1	
J (5-H β , 6-H α)	5.4						5.8			4.7		5.4	5.6	
J (5-H β , 6-H β)	4.3						4.4			4.2		4.1	4.4	

and 8-MeO were unchanged but those of 10-H and 9-MeO were strongly dependent on the change of the substituent R. If R is an aromatic ring it results in a strong diamagnetic shift of 10-H and 9-MeO, the reason for which is the well-known anisotropic effect of the phenyl group. Assignment of the 8-MeO and 9-MeO signals was corroborated by 1D nOe difference measurements by the irradiation of signals 7-H and 10-H.

For the assignment of the ^{13}C signals 2D carbon-proton correlation measurements and proton-coupled ^{13}C spectra were utilized. Assignment of the quarternary carbon atom was corroborated by INAPT measurements [5] utilizing the fact among others that $J(\text{C},\text{H-metha})$ is approximately 7 Hz in the aromatic ring [6]. INAPT measurements optimized for the 7 Hz coupling constant value indicated the C(9) and C(10a) signals on irradiation of 7-H and signals C(8) and C(6a) on the irradiation of 10-H. Characteristic coupling constants of approximately 7 Hz were observed between the protons of methoxy groups 8 and 9 and the connecting C(8) and C(9) carbon atoms, between 10b-H, C(10), and C(1)-CO atoms, 5-H and the vicinal C(10b), C(3), and C(6a).

On the basis of the ^1H and ^{13}C shift analogies it can be concluded that the relative configuration of compounds **16-28** is the same while that of substance **29** is different. Despite the high flexibility and pseudorotation of the five-membered ring α/β character of its substituents can be deduced from nOe difference measurements. The nOe observed between protons in positions 1 and 3 of the five-membered ring proves that they are on the same side [7].

Despite the other cases, irradiation of signal 10b-H resulted in intensity enhancement of signal 3-H only in compound **29** indicating that both protons are α in this case. This was corroborated by the fact that irradiation of 3-H caused intensity enhancement on the 10b-H. Since no nOe was observed on signal 1-H as a result of the irradiation of 10b-H and *vice versa*, *trans* antiperiplanar arrangement of those protons and, therefore, α -configuration of 1-H is obvious. β -Arrangement of 2-H is confirmed by the fact that owing to the spatial proximity of the 3-H of β -position considerable nOe was detected between these two atoms and no intensity enhancement was detected on the 1-H, positioned on the other side, on the saturation of the 2-H. The nOe was observed between 10b-H and 3-H being in the 1,3-position but no such effect could be detected between 10b-H and 2-H which indicates that in the predominant conformation of the five-membered ring the intramolecular distance of the latter is greater than that of the former.

In our case the conformation equilibrium is shifted to the direction of *trans* B/C ring junction. Since spatial proximity of 10b-H and 5-H(β) or 3-H and 5-H(β) are proved by the measured 6.3% and 3.5% intensity enhancements,

presence of *cis*-2 conformation in the conformation equilibrium is negligible. In the *cis*-1 10b-H and 1-H should be in spatial proximity which was not corroborated by nOe measurements, and furthermore, the great distance of 3-H and 5-H(β) is inconsistent with the measured nOe. Considerable presence of this conformer is excluded by the $J(10\text{b-H}, 1\text{-H}) = 9.8$ Hz coupling constant since approximately 90° dihedral angle exists in the above-conformer. Inspection of the Dreidling models also shows that of the three possible conformers the *cis*-1 is the most packed in the case of the given configuration. *Trans* conformation and the antiperiplanar arrangement of the 10b-H, 3-H protons, and the lone electron pair of the nitrogen atom of compound **29** is confirmed by the expected [8,9] small $^1\text{J}(\text{C},\text{H})$ coupling (135 Hz and 138.5 Hz, respectively) and the pronounced downfield shift [9,10] ($\Delta\delta$ 1.29 ppm and 1.12 ppm, respectively) originating from the protonation. It should be mentioned that the $^1\text{J}(\text{C},\text{H})$ and $\Delta\delta$ data are of direct diagnostic value only for conformationally homogeneous or semihomogeneous systems.

On the basis of the modified Karplus equation taking also the electronegativity into consideration [11] $^3\text{J}(\text{H},\text{H})$ coupling constants summarized in Table 4 gave dihedral angle values of $160^\circ + 10^\circ$, $150^\circ \pm 10^\circ$, and $10^\circ \pm 10^\circ$ for 10b-H, 1-H, 2-H, and 3-H.

Configuration of cycloadducts **16-28** was equal and, therefore, 10b-H, 1-H, 2-H, and 3-H have $\alpha,\alpha,\beta,\beta$ arrangements which differ from (**29**) only at C-10b.

Spatial proximity of 10b-H and 1-H was corroborated by approximately 15% nOe. Coupling of these two protons is between 7.3-8.5 Hz which on the basis of the modified Karplus equation on the above-mentioned nOe measurements reflects a 20-40° dihedral angle value. All those prove that 10b-H and 1-H are on the same side. Protons 2-H and 3-H are also on the same side according to the 8-24% nOe and 7.3-8.5 Hz coupling which indicate a 20-40° dihedral angle as well.

The 4.7-6.9 Hz coupling constant values observed between the 1-H and 2-H refer to 40-50° or 125-135° dihedral angles and the relatively low nOe data (1.0-3.8%) prove the *trans* orientation of these two protons as well.

In accordance with the above-mentioned structure no nOe was observed between the *trans* 10b-H/3-H and 1-H/3-H protons.

If compounds (**16**)-(28) have a predominant conformation then between the *trans* and vicinal protons of ring B characteristically different $J_{\text{ax,ax}}$ and $J_{\text{eq,eq}}$ couplings (approximately 11 and 2 Hz) are expected [12]. The measured 7.2-9.1 Hz values indicate the presence of a conformation equilibrium with commensurable amounts of the possible conformers. Taking into account that the 5-H(α) and 6-H(β) protons are *trans* diaxial both in the *trans* and *cis*-1 conformers, and diequatorial in the *cis*-2,

the measured coupling constants reflect the presence of 21-42% *cis*-2. The presence of this conformer is also corroborated by the nOe measured between the 3-H and 5-H(α) since these two protons can exist in spatial proximity only in this conformer.

Characteristic intensity enhancement was observed at 3-H (7.2-17.6%) on the irradiation of 6-H(β) and *vice versa* (1.5-5.7%). Since these two protons are in spatial proximity only in conformer *cis*-1, on the basis of our measurement, considerable amount (58-79%) of conformer *cis*-1 should be present in the equilibrium.

It is known that the chemical shift of C(6) can advantageously be used to investigate the character of the B/C ring junction since owing to the γ -gauche effect 5 ppm diamagnetic shift can be measured in *cis*-1 conformer [3]. Chemical shift of C(6) is 29.0 ppm [13] without the γ -gauche effect as it was found in the case of substance **29**.

Since C(6) is 25.3-26.5 ppm in compounds **16**, **22**, **25**, **27**, and **28** rate of the *cis*-1 is 50-74%. All these facts made possible a semiquantitative analysis of the conformation equilibrium of these substances.

Compound	16	22	25	27	28
<i>cis</i> -1	60%	50%	74%	62%	50%
<i>cis</i> -2	29%	42%	21%	32%	32%
<i>trans</i>	11%	8%	5%	6%	18%

On all these basis the characteristic decrease of the $^1\text{J}(\text{C}(10\text{b}), \text{H})$ and $^1\text{J}(\text{C}(3), \text{H})$ coupling constants in comparison with those measured for *trans* (**29**) is understandable. Since in *cis*-1 of relatively high population the lone electron pair of the nitrogen atom is antiperiplanar to the 3-H it is not surprising that the difference of the $^1\text{J}(\text{C}(3), \text{H})$ values is lower (2-5 Hz) than those of the $^1\text{J}(\text{C}(10\text{b}), \text{H})$ (10-14 Hz) if compared to data measured for the *trans* **29**.

Although detailed high field nmr measurements were performed only in the case of six compounds but on the basis of the analogy of the measured data it is doubtless that similar conformation equilibrium should exist in the other cases as well.

It can be concluded that the 1,2,3-trisubstituted-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinolines depending on the character of the substituents, exist in a characteristic triple *trans* \rightleftharpoons *cis*-1 \rightleftharpoons *cis*-2 conformation equilibrium in solution. It is interesting that a single product of equal configuration was obtained in each case but one, therefore, the reaction is highly stereoselective. Further studies are in progress to investigate the reaction mechanism and to elucidate whether the formation of **29** is a primary or secondary process.

EXPERIMENTAL

Melting points were determined with a Gallenkamp apparatus and are uncorrected. The ir spectra were measured on a SPECORD 75 instrument and uv spectra were recorded on a SPECORD M40 spectrometer. The tlc performed on Kieselgel 60 F₂₅₄ (Merck) layer using acetone:hexane = 2:3 developing mixture. The nmr spectra were recorded on Bruker AC-250 and Jeol FX-100 spectrometers at room temperature. Chemical shifts were determined on the δ scale. In the 1D measurements 32 K data points were used for the FID. For homonuclear nOe experiments a delay time of 3 s was applied. The nOe difference and two-dimensional carbon-proton correlated experiments were recorded by using the Bruker software package. In the 2D experiments 1K x 1K data matrixes were transformed. For the INAPT-measurements a selectivity of 25 Hz and $J_{\text{CH}} = 7$ Hz were applied.

General Procedure for the Preparation of Cycloadducts **16-21** and **26**.

3,4-Dihydro-6,7-dimethoxy-*N*-(methoxycarbonylmethyl)isoquinolinium bromide (**1**) (1 g, 2.9 mmoles) was suspended in methylene chloride (20 ml) then the dipolarophile (3 mmoles) and triethylamine (0.3 g, 3 mmoles) were added. The mixture was left to stand for 48 hours, the solvent evaporated under reduced pressure and the residue crystallized from methanol.

2-Phenyl-1,2,3,5,6,10b-hexahydro-8,9-dimethoxypyrrolo[2,1-*a*]isoquinoline-1,3-dicarboxylic acid methyl ester derivatives (**16**)-(20).

Unsubstituted Derivative **16**.

The yield was 0.7 g (56%), mp 158°; ir (potassium bromide): 2960, 2800 cm^{-1} (ν CH), 1705, 1690 (ν C=O), 1595 (ν C=C), 1260, 1240, 1170 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 207 nm (2.91), 291 (1.95).

Anal. Calcd. for C₂₄H₂₇NO₆ (425.5): C, 67.5; H, 6.40; N, 3.29. Found: C, 67.98; H, 6.64; N, 3.43.

2-(4-Nitrophenyl) Derivative **17**.

The yield was 1.0 g (76%), mp 139°; ir (potassium bromide): 2920, 2810 cm^{-1} (ν CH), 1710, 1705 (ν C=O), 1590 (ν C=C), 1500, 1340 (ν NO₂), 1260, 1240, 1180 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 205 nm (2.91), 287 (2.12); $R_f = 0.43$.

Anal. Calcd. for C₂₄H₂₆N₂O₈ (470.5): C, 61.27; H, 5.57; N, 6.87. Found: C, 61.23; H, 5.47; N, 6.63.

2-(3-Nitrophenyl) Derivative **18**.

The yield was 0.9 g (66%), mp 165°; ir (potassium bromide): 2930, 2879, 2840, 2810 cm^{-1} (ν CH), 1740, 1720 (ν C=O), 1605 (ν C=C), 1520, 1350 (ν NO₂), 1250, 1145 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 205 nm (2.89), 286 (2.09).

Anal. Calcd. for C₂₄H₂₆N₂O₈ (470.5): C, 61.27; H, 5.57; N, 6.87. Found: C, 61.27; H, 5.49; N, 6.66.

2-(4-Methoxyphenyl) Derivative (**19**).

The yield was 0.5 g (40%), mp 158°; ir (potassium bromide): 2905, 2800 cm^{-1} (ν CH), 1695 (ν C=O), 1585 (ν C=C), 1220, 1180-1140 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 206 nm (2.78), 286 (2.10); $R_f = 0.67$.

Anal. Calcd. for C₂₅H₂₉NO₇ (455.5): C, 65.92; H, 6.42; N, 3.08. Found: C, 65.81; H, 6.28; N, 2.91.

2-(3,4,5-Trimethoxyphenyl) Derivative (**20**).

The yield was 0.45 g (30%), mp 159°; ir (potassium bromide): 2915, 2800 cm⁻¹ (ν CH), 1705, 1700 (ν C=O), 1575 (ν C=C), 1240, 1220, 1175, 1150 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 206 nm (2.84), 287 (2.12); R_f = 0.35.

Anal. Calcd. for C₂₇H₃₃NO₉ (515.6): C, 62.90; H, 6.45; N, 2.72. Found: C, 62.89; H, 6.45; N, 2.75.

2-Thienyl-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-1,3-dicarboxylic Acid Methyl Ester (**21**).

The yield was 0.5 g (40%), mp 136°; ir (potassium bromide): 2920, 2805 cm⁻¹ (ν CH), 1705 (ν C=O), 1600 (ν C=C), 1240, 1150 (ν C-O-C); uv (ethanol): λ max (log ϵ) 208 nm (2.74), 290 (1.75); R_f = 0.38.

Anal. Calcd. for C₂₂H₂₅NO₆S (431.5): C, 61.24; H, 5.84; N, 3.25; S, 7.43. Found: C, 61.16; H, 5.82; N, 3.25; S, 7.49.

1-Benzoyl-2-(4-nitrophenyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic Acid Methyl Ester **26**.

The yield was 0.6 g (53%), mp 200°; ir (potassium bromide): 2900, 2820 cm⁻¹ (ν CH), 1720, 1705 (ν C=O), 1585 (ν C=C), 1500, 1350 (ν NO₂), 1240, 1160 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 205 nm (2.87), 287 (2.15); R_f 0.42.

Anal. Calcd. for C₂₉H₂₈N₂O₇: C, (516.6): C, 67.43; H, 5.46; N, 5.42. Found: C, 67.67; H, 5.48; N, 5.45.

General Procedure for the Preparation of Cycloadducts **22-25**, **27** and **29**.

A mixture of 3,4-dihydro-6,7-dimethoxy-*N*-(methoxycarbonylmethyl)isoquinolinium bromide (**1**) (1 g, 2.9 mmoles), dipolarophile (**3** mmoles), triethylamine (0.3 g, 3 mmoles), and methanol (15 ml) was stirred, the residue filtered off, washed with methanol and recrystallized from methanol.

1-Acetyl-2-(3,4-methylenedioxyphenyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic Acid Methyl Ester (**23**).

The yield was 0.65 g (49%), mp 145°; ir (potassium bromide): 2920-2860 cm⁻¹ (ν CH), 1715, 1680 (ν C=O), 1600 (ν C=C), 1260-1150 (ν C-O-C); λ max (log ϵ) = 204 nm (2.70), 293 (1.95); R_f = 0.35.

Anal. Calcd. for C₂₃H₂₇NO₇ (453.5): C, 66.21; H, 6.00; N, 3.09. Found: C, 65.99; H, 5.97; N, 2.82.

1-Benzoyl-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic Acid Methyl Ester Derivatives **25** and **27**.

2-Phenyl Derivative **25**.

The yield was 1.0 g (73%), mp 188°; ir (potassium bromide): 2910, 2800 cm⁻¹ (ν CH), 1720, 1650 (ν C=O), 1600 (ν C=C), 1250, 1195, 1180, 1160 (ν C-O-C); UV (EtOH): λ max (log ϵ) = 206 nm (2.28), 291 (1.85); R_f = 0.16.

Anal. Calcd. for C₂₉H₂₉NO₅ (471.5): C, 73.87; H, 6.20; N, 2.97. Found: C, 73.98; H, 6.51; N, 3.16.

2-Furyl Derivative **27**.

The yield was 0.8 g (59%), mp 186°; ir (potassium bromide): 2960, 2800 cm⁻¹ (ν CH), 1720, 1645 (ν C=O), 1600 (ν C=C), 1240, 1200, 1150 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 205 nm (2.76), 290 (1.78); R_f = 0.42.

Anal. Calcd. for C₂₇H₂₇NO₆ (461.5): C, 70.26; H, 5.90; N, 3.03. Found: C, 70.25; H, 6.14; N, 3.15.

2-Furyl-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic Acid Methyl Ester Derivatives **22** and **24**.

1-Carboxylic Acid Methyl Ester Derivative **22**.

The yield was 0.6 g (50%), mp 150°; ir (potassium bromide): 2920, 2800 cm⁻¹ (ν CH), 1720, 1705 (ν C=O), 1600 (ν C=C), 1280-1225, 1180 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 206 nm (2.78), 290 (2.33); R_f = 0.38.

Anal. Calcd. for C₂₂H₂₅NO₇ (415.4): C, 63.61; H, 6.07; N, 3.37. Found: C, 63.84; H, 6.14; N, 3.42.

1-Acetyl Derivative **24**.

The yield was 0.6 g (51%), mp 149°; ir (potassium bromide): 2905, 2800 cm⁻¹ (ν CH), 1720, 1680 (ν C=O), 1600 (ν C=C), 1240, 1220, 1150 (ν C-O-C); uv (ethanol) λ max (log ϵ) = 206 nm (2.90), 291 (2.05); R_f = 0.42.

Anal. Calcd. for C₂₂H₂₅NO₆ (399.4): C, 66.15; H, 6.31; N, 3.51. Found: C, 65.95; H, 6.11; N, 3.48.

2-Furyl-1-(4-nitrobenzoyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic Acid Methyl Ester (**29**).

The yield was 0.85 g (58%), mp 142°; ir (potassium bromide): 2910, 2800 cm⁻¹ (ν CH), 1715, 1700 (ν C=O), 1605 (ν C=C), 1505, 1360 (ν NO₂), 1230, 1210, 1160 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 206 nm (2.85), 287 (2.10); R_f 0.55.

Anal. Calcd. for C₂₇H₂₆N₂O₈ (506.5): C, 64.03; H, 5.17; N, 5.53. Found: C, 63.92; H, 5.08; N, 5.43.

2-Furyl-1-(4-nitrobenzoyl)-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylic Acid Methyl Ester (**28**).

Preparation.

A mixture of 3,4-dihydro-6,7-dimethoxy-*N*-(methoxycarbonylmethyl)isoquinolinium bromide (**1**) (1 g, 2.9 mmoles), 1-(4-nitrophenyl)-3-furylpropenone (0.7 g, 2.9 mmoles), triethylamine (0.3 g, 3 mmoles), and methylene chloride (20 ml) was stirred for one day then washed with water, the organic phase dried and the solvent evaporated. The residue was stirred with a 3:2 mixture of hexane:ethyl methyl ketone and the precipitate filtered off, yield 0.6 g (41%), mp 136°; ir (potassium bromide): 2920, 2800 cm⁻¹ (ν CH), 1720, 1700 (ν C=O), 1600 (ν C=C), 1500, 1350 (ν NO₂), 1230, 1200, 1160 (ν C-O-C); uv (ethanol): λ max (log ϵ) = 205 nm (2.90), 285 (2.10); R_f = 0.41.

Anal. Calcd. for C₂₇H₂₆N₂O₈ (506.5): C, 64.03; H, 5.17; N, 5.53. Found: C, 63.85; H, 5.43; N, 5.42.

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