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On irradiation in the solid state the 4-aryl-1,4-dihydropyridines **1** undergo [2+2] cycloaddition to centrosymmetric head-to-tail dimers **3** and **4a**. The almost exclusive formation of the cage dimers **3** via the C₂-symmetric *syn*-dimers **2** takes place in nearly quantitative yields, in contrast with the cycloaddition reaction of the *anti*-dimer **4a**, which is accompanied by photooxidation to pyridine **5a**.

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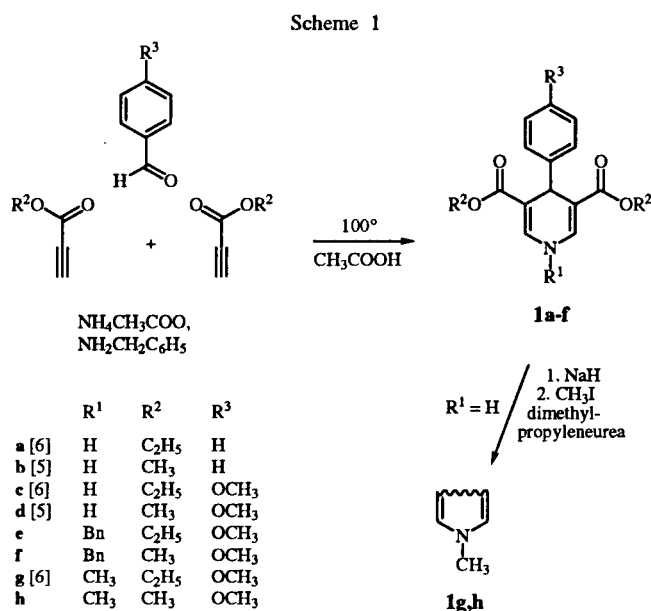
4-Aryl substituted 1,4-dihydropyridines of the nifedipine-type are of great interest because of their Ca²⁺-antagonistic and -agonistic activities [1]. Photochemical investigations have been made to analyse their light sensitivity [2], which proved to be high in the case of nifedipine yielding an *o*-nitrosophenylpyridine [3].

During efforts to produce *N*-substituted 1,4-dihydropyridines without substituents in the 2- and 6-positions the resulting derivatives were found to be highly light sensitive in the solid state, their spectroscopical analyses indicating formation of dimers. As such dimeric 4-aryl-1,4-dihydropyridines with suitable substituents are of interest as novel potential inhibitors of the symmetric, dimeric HIV-1 protease [4], thus systematic investigations have been undertaken in order to examine the photochemical properties of 2- and 6-unsubstituted 1,4-dihydropyridines.

The 1,4-dihydropyridines **1a-f** with R¹ = H and benzyl were synthesized by cyclocondensation in glacial acetic acid from an aromatic aldehyde, alkyl propiolate and ammonium acetate or benzylamine following the method of Chennat and Eisner [5]. The *N*-methyl derivatives **1g** and **h** were produced by methylation of the 1,4-dihydropyridine anions in dimethylpropyleneurea in excellent yields.

On irradiation with Ultra-Vitalux^R lamps, which produce a light spectrum corresponding to sunlight, the crystalline 1,4-dihydropyridines **1** with λ_{max} between 359 and 376 nm firstly cyclize to head-to-tail *syn*-dimers **2** excepting **1f** that remains unchanged. Further irradiation of **2** leads to cage dimers **3** by reaction of the remaining neighbouring double bonds under excitation of the vinylogous carbamide ester chromophore with an absorption at 278-294 nm.

The symmetric structure of **2** and **3** with both aryl substituents either pseudoaxial or pseudoequatorial was established by their ¹H nmr spectra which consist of only one set of signals for both 1,4-dihydropyridines in the dimers. The spectra of **2** show beside two ester group signals the singlet for the 8b-H of one monomer between 3.5 and 4.5

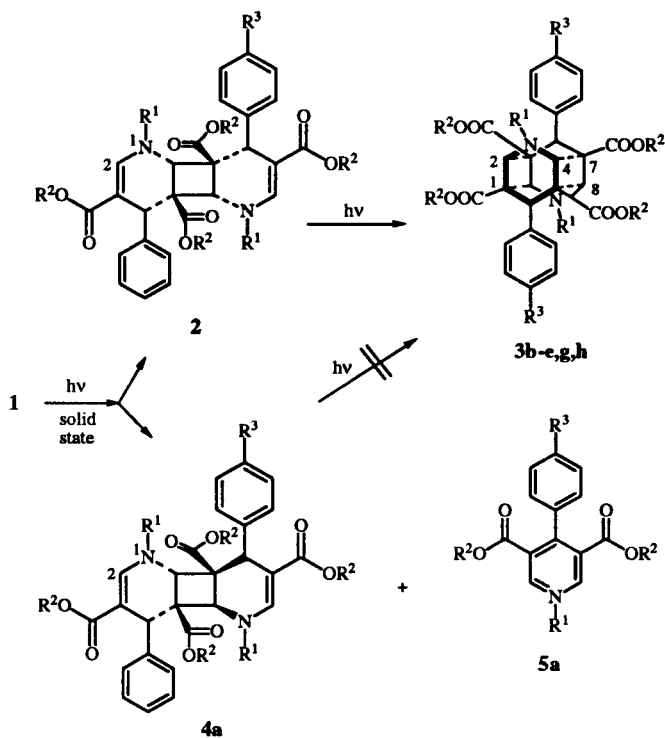


ppm and the one for the 2-H between 7.3 and 8.3 ppm. In the cage dimers **3** with only one ester group signal both protons form one singlet between 3.5 and 4.0 ppm.

Furthermore, dimers **2** are characterized by the ir-spectra with two carbonyl bands. The non conjugated C=O was observed at 1720-1739 cm⁻¹; and the conjugated C=O at 1660-1690 cm⁻¹ and a strong absorption between 1611 and 1650 cm⁻¹. As this band is not found in the spectra of the cage dimers **3**, which have yet one carbonyl bond (1720-1731 cm⁻¹), it is assigned to the C=C bond of the vinylogous carbamide esters of **2**. The mass determination of both dimers was accomplished using electrospray ionisation (ESI) or field desorption (FD) as smooth ionisation methods, while electron ionisation (EI-70eV) yielded only monomeric molecular peaks caused by dimers-fragmentation.

In contrast with the reaction of the other derivatives, **1a** forms a photoadduct that remains stable on further irradiation with spectroscopic properties resembling those found

Scheme 2



for the *syn*-dimers **2** (see Experimental). It has been demonstrated to have a centrosymmetric *anti*-structure **4a** by X-ray crystal structure analysis.

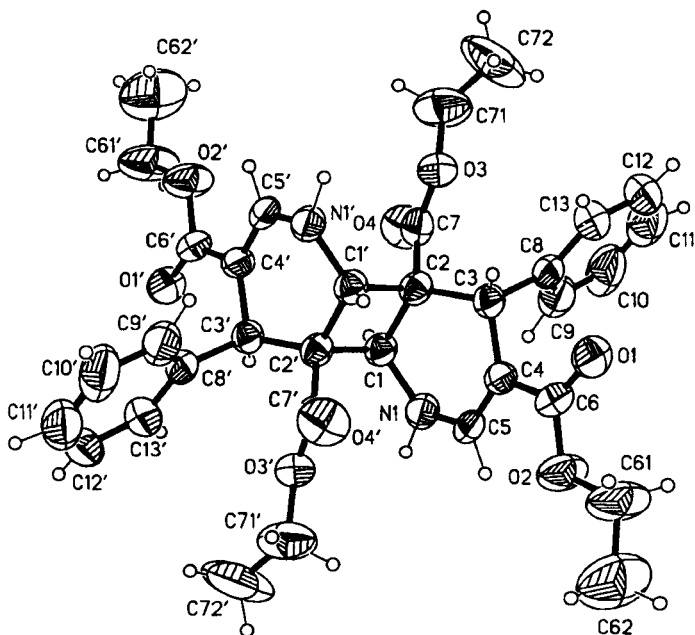


Figure 1. ORTEP Drawing of tetraethyl 1,5,8,8 β -tetrahydro-4,8-diphenylcyclobuta[1,2-*b*:3,4-*b'*]dipyridine-3,4 α ,7,8 $\alpha\beta$ (4H,4 β H)-tetracarboxylate (**4a**).

Table 1
Bond Lengths (Å) and Bond Angles (deg) for **4a**

O(1)-C(6)	1.215(4)	O(2)-C(6)	1.349(4)
O(2)-C(61)	1.456(6)	O(3)-C(7)	1.335(4)
O(3)-C(71)	1.456(5)	O(4)-C(7)	1.193(4)
N(1)-C(5)	1.352(4)	N(1)-C(1)	1.437(5)
N(1)-H(1N)	0.99(5)	C(1)-C(2)	1.550(4)
C(1)-C(2)#1	1.601(4)	C(1)-H(1)	0.93(3)
C(2)-C(7)	1.518(5)	C(2)-C(3)	1.550(5)
C(2)-C(1)#1	1.601(4)	C(3)-C(4)	1.512(5)
C(3)-C(8)	1.528(5)	C(3)-H(3)	0.97(3)
C(4)-C(5)	1.354(5)	C(4)-C(6)	1.438(5)
C(5)-H(5)	0.98(3)	C(8)-C(13)	1.369(6)
C(8)-C(9)	1.391(6)	C(9)-C(10)	1.374(6)
C(9)-H(9)	0.99(4)	C(10)-C(11)	1.329(8)
C(10)-H(10)	1.10(4)	C(11)-C(12)	1.358(9)
C(11)-H(11)	0.97(5)	C(12)-C(13)	1.425(8)
C(12)-H(12)	0.78(6)	C(13)-H(13)	0.89(3)
C(61)-C(62)	1.417(6)	C(61)-H(61A)	0.97
C(61)-H(61B)	0.97	C(62)-H(62A)	0.96
C(62)-H(62B)	0.96	C(62)-H(62C)	0.96
C(71)-C(72)	1.360(7)	C(71)-H(71A)	0.97
C(71)-H(71B)	0.97	C(72)-H(72A)	0.96
C(72)-H(72B)	0.96	C(72)-H(72C)	0.96
C(6)-O(2)-C(61)	117.0(3)	C(7)-O(3)-C(71)	116.9(3)
C(5)-N(1)-C(1)	120.2(3)	C(5)-N(1)-H(1N)	114(3)
C(1)-N(1)-H(1N)	119(2)	N(1)-C(1)-C(2)	115.5(3)
N(1)-C(1)-C(2)#1	116.9(3)	C(2)-C(1)-C(2)#1	90.8(3)
N(1)-C(1)-H(1)	111(2)	C(2)-C(1)-H(1)	111(2)
C(2)#1-C(1)-H(1)	110(2)	C(7)-C(2)-C(1)	111.7(3)
C(7)-C(2)-C(3)	111.2(3)	C(1)-C(2)-C(3)	117.3(3)
C(7)-C(2)-C(1)#1	111.9(3)	C(1)-C(2)-C(1)#1	89.2(3)
C(3)-C(2)-C(1)#1	113.9(3)	C(4)-C(3)-C(8)	109.9(3)
C(4)-C(3)-C(2)	111.7(3)	C(8)-C(3)-C(2)	112.9(3)
C(4)-C(3)-H(3)	109(2)	C(8)-C(3)-H(3)	106(2)
C(2)-C(3)-H(3)	108(2)	C(5)-C(4)-C(6)	120.5(3)
C(5)-C(4)-C(3)	120.6(3)	C(6)-C(4)-C(3)	118.5(3)
N(1)-C(5)-C(4)	123.7(4)	N(1)-C(5)-H(5)	118(2)
C(4)-C(5)-H(5)	118(2)	O(1)-C(6)-O(2)	121.1(4)
O(1)-C(6)-C(4)	125.1(4)	O(2)-C(6)-C(4)	113.8(3)
O(4)-C(7)-O(3)	125.1(4)	O(4)-C(7)-C(2)	125.0(4)
O(3)-C(7)-C(2)	109.8(3)	C(13)-C(8)-C(9)	118.2(4)
C(13)-C(8)-C(3)	121.1(4)	C(9)-C(8)-C(3)	120.8(4)
C(10)-C(9)-C(8)	121.2(5)	C(10)-C(9)-H(9)	119(3)
C(8)-C(9)-H(9)	120(3)	C(11)-C(10)-C(9)	120.2(6)
C(11)-C(10)-H(10)	125(2)	C(9)-C(10)-H(10)	115(2)
C(10)-C(11)-C(12)	121.6(6)	C(10)-C(11)-H(11)	124(3)
C(12)-C(11)-H(11)	115(3)	C(11)-C(12)-C(13)	119.1(6)
C(11)-C(12)-H(12)	130(6)	C(13)-C(12)-H(12)	110(6)
C(8)-C(13)-C(12)	119.7(6)	C(8)-C(13)-H(13)	116(2)
C(12)-C(13)-H(13)	124(2)	C(62)-C(61)-O(2)	108.2(4)
C(62)-C(61)-H(61A)	110.1(4)	O(2)-C(61)-H(61A)	110.1(3)
C(62)-C(61)-H(61B)	110.1(4)	O(2)-C(61)-H(61A)	110.1(3)
H(61A)-C(61)-H(61B)	108.4	C(61)-C(62)-H(62A)	109.5(4)
C(61)-C(62)-H(62B)	109.5(3)	H(62A)-C(62)-H(62B)	109.5
C(61)-C(62)-H(62C)	109.5(4)	H(62A)-C(62)-H(62C)	109.5
H(62B)-C(62)-H(62C)	109.5	C(72)-C(71)-O(3)	112.5(5)
C(72)-C(71)-H(71A)	109.1(5)	O(3)-C(71)-H(71A)	109.1(2)
C(72)-C(71)-H(71B)	109.1(4)	O(3)-C(71)-H(71B)	109.1(2)
H(71A)-C(71)-H(71B)	107.8	C(71)-C(72)-H(72A)	109.5(3)
C(71)-C(72)-H(72B)	109.5(5)	H(72A)-C(72)-H(72B)	109.5
C(71)-C(72)-H(72C)	109.5(4)	H(72A)-C(72)-H(72C)	109.47(6)
H(72B)-C(72)-H(72C)	109.5		

Symmetry transformations used to generate equivalent atoms #1 -*x*+1, -*y*+1, -*z*+1.

Table 2

Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters, U_{eq} ($\text{\AA}^2 \times 10^3$)

	x	y	z	$U_{eq}[a]$
O(1)	2476(2)	7208(2)	2255(2)	48(1)
O(2)	2193(3)	5698(2)	1312(2)	65(1)
O(3)	4470(2)	6871(2)	6747(2)	49(1)
O(4)	4018(3)	5277(2)	7361(2)	65(1)
N(1)	3365(3)	4025(2)	4210(3)	40(1)
C(1)	4294(3)	4398(3)	5092(3)	34(1)
C(2)	4319(3)	5583(2)	5282(3)	33(1)
C(3)	3412(3)	6240(3)	4457(3)	33(1)
C(4)	3004(3)	5677(3)	3310(3)	34(1)
C(5)	2949(3)	4634(3)	3284(4)	35(1)
C(6)	2552(3)	6273(3)	2282(3)	39(1)
C(7)	4249(3)	5865(3)	6591(4)	41(1)
C(8)	2287(3)	6592(3)	5078(3)	43(1)
C(9)	1481(4)	5876(4)	5510(4)	58(1)
C(10)	493(4)	6185(6)	6110(5)	84(2)
C(11)	275(6)	7182(7)	6266(5)	94(2)
C(12)	1016(7)	7921(7)	5853(6)	94(2)
C(13)	2050(4)	7618(4)	5235(4)	61(1)
C(61)	1743(6)	6249(4)	230(4)	86(2)
C(62)	1529(7)	5521(5)	-708(5)	127(2)
C(71)	4414(5)	7275(4)	7955(4)	82(2)
C(72)	4043(9)	8276(6)	7961(6)	181(5)
H(61A)	985(6)	6610(4)	361(4)	129
H(61B)	2347(6)	6753(4)	20(4)	129
H(62A)	2300(8)	5237(30)	-907(33)	191
H(62B)	1129(46)	5855(11)	-1400(17)	191
H(62C)	1012(40)	4977(22)	-452(18)	191
H(71A)	3847(5)	6858(4)	8375(4)	122
H(71B)	5222(5)	7218(4)	8385(4)	122
H(72A)	4345(62)	8594(18)	8702(30)	272
H(72B)	3159(9)	8305(6)	7881(67)	272
H(72C)	4362(56)	8635(14)	7304(42)	272
H(1N)	3309(37)	3275(37)	4039(37)	81(15)
H(1)	4258(25)	4054(22)	5819(28)	26(8)
H(3)	3837(27)	6866(26)	4258(26)	33(9)
H(5)	2559(29)	4303(25)	2564(31)	40(9)
H(9)	1619(39)	5128(35)	5380(37)	76(14)
H(10)	-123(40)	5558(32)	6344(37)	78(14)
H(11)	-424(48)	7443(38)	6648(46)	105(18)
H(12)	939(64)	8520(53)	5836(58)	134(31)
H(13)	2565(32)	8054(27)	4926(30)	35(11)

[a] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor. Hydrogen atoms of the ethoxy group are in calculated positions, while all other hydrogen atoms were located in a difference fourier map and refined isotropically.

The six-membered rings of **4a** have a boat-like conformation as was reported for the related 2,6-dimethyl-1,4-dihydropyridines [7], their pseudoaxial 4-aryl-substituents bisecting the dihydropyridine plane of **1a**.

An *anti*-head-to-tail dimer was previously reported as the photoadduct of diethyl 1,4-dihydropyridine-3,5-dicarboxylate on irradiation as a film, while a cage dimer was produced in solution in a comparable low yield of about 30% in addition to other products such as diethyl 1,2-dihydro-pyridine-3,5-dicarboxylate and diethyl pyridine-3,5-dicarboxylate as

Table 3
Crystal Data for **4a**

Formula	$C_{34}H_{38}N_2O_8$
Crystal dimensions (mm)	0.42 x 0.19 x 0.11
Formula weight	602.66
Monoclinic space group	$P2_1/n$
a (\AA)	10.8940(10)
b (\AA)	12.964(2)
c (\AA)	11.194(2)
β (degree)	94.730(10)
V (\AA^3)	1575.5(4)
Z	2
Dc (g cm^{-3})	1.270
μ (mm^{-1})	0.091
F (000)	640
Radiation MoK α , graphite monochromatized	$\lambda = 0.71073 \text{ \AA}$
Diffractionmeter	Stoe-STADI4
T(K)	293
Scan method	$\omega/2\theta$
Data collection range [θ]	$2.41^\circ < 2\theta < 45^\circ$
No. unique reflections	2052
No. of observed reflections	1157
No. of parameters	238
wR2 for unique reflections [b]	0.140
R1 for observed reflections [c]	0.050
Largest positive peak ($e\text{\AA}^{-3}$)	0.324
Largest negative peak ($e\text{\AA}^{-3}$)	-0.259

[a] Due to the very weak diffracting power of the crystals of **4a** data were collected only up to $2\theta = 45^\circ$. [b] $wR1 = [\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]]^{1/2}$. [c] $R1 = [\sum||F_o| - |F_c|| / \sum|F_o|]$. Weighting scheme: $w = 1 / [\sigma^2(F_o^2) + (0.0603 \times P)^2 + 0.0 \times P]$, $P = (F_o^2 + 2 \times F_c^2) / 3$.

photooxidation product [8]. Only in the case of **1a** was a pyridine found as an additional product, even though all irradiations were carried out in air. In general, the crystal structure of the monomers leading to dimers **2** and **3**, which are currently under investigation, are probably the same and must be favourable for the dimerization reaction that photooxidation to pyridines does not take place and thus cage dimers **3** are formed *via syn*-dimers **2** in nearly quantitative yields.

Experimental

Commercial reagents were used as received without additional purification. The ^1H nmr spectra were recorded on a Bruker AC-200 F or a Varian Gemini 200 spectrometer at 200 or 500 MHz using tetramethylsilane as the internal standard. Melting points were determined with a Linström apparatus and are uncorrected. The tlc analysis were performed on silica gel 60 plates F₂₅₄. The ir spectra were recorded as potassium bromide disks. The uv spectra were measured on a Diode Array spectrophotometer 8452A in chloroform. The mass spectra were recorded on a Varian Mat 311 A or an AMD 402 (Fa. AMD INTECRA) mass spectrometer.

Dialkyl-1-Benzyl-1,4-dihydro-4-(4-methoxyphenyl)pyridine-3,5-dicarboxylates **1e,f**.

Ethyl propiolate, 1.96 g (20 mmoles) or 1.68 g (20 mmoles) of methyl propiolate, were heated in 1 ml of glacial acetic acid on a steam-bath for 15 minutes with 1.36 g (10 mmoles) 4-methoxy-

benzaldehyde and 1.07 g (10 mmoles) benzylamine. While **1f** crystallized on cooling, the reaction mixture of **1e** was poured into 10 ml of ice-water, the precipitate was filtered and recrystallized from ethanol.

Diethyl 1-Benzyl-1,4-dihydro-4-(4-methoxyphenyl)pyridine-3,5-dicarboxylate (**1e**).

This compound was obtained in a yield of 70% (2.95 g) as yellow crystals, mp 104-106°; ir: ν 1705, 1664 cm^{-1} ; uv: λ_{max} 254 (ϵ 12965), 292 sh, 368 (ϵ 8625) nm; ^1H nmr (deuteriochloroform): δ 1.17 (t, $J = 7$ Hz, 6H, CH_2CH_3), 3.75 (s, 3H, 4- $\text{H}_3\text{CO-Ph}$), 4.06 (q, $J = 7$ Hz, 4H, CH_2CH_3), 4.57 (s, 2H, NCH_2), 4.84 (s, 1H, 4-H), 6.68-7.34 (m, 11H, aromatic H, 2-, 6-H); ms: m/z 421 (M^+ , 1), 392 ($\text{M}^+ - \text{C}_2\text{H}_5$, 1).

Anal. Calcd. for $\text{C}_{25}\text{H}_{27}\text{NO}_5$: C, 71.24; H, 6.46; N, 3.32. Found: C, 71.30; H, 6.49; N, 3.53.

Dimethyl 1-Benzyl-1,4-dihydro-4-(4-methoxyphenyl)pyridine-3,5-dicarboxylate (**1f**).

This compound was obtained in a yield of 65% (2.55 g) of yellow crystals, mp 120-122°; ir: ν 1703, 1604 cm^{-1} ; uv: λ_{max} 254 (ϵ 11685), 292 sh, 368 (ϵ 7883) nm; ^1H nmr (deuteriochloroform): δ 3.59 (s, 6H, COOCH_3), 3.73 (s, 3H, 4- $\text{H}_3\text{CO-Ph}$), 4.55 (s, 2H, NCH_2), 4.83 (s, 1H, 4-H), 6.71-7.43 (m, 11H, aromatic H, 2-, 6-H); ms: m/z 393 (M^+ , 21), 378 ($\text{M}^+ - \text{CH}_3$, 5).

Anal. Calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_5$: C, 70.23; H, 5.85; N, 3.56. Found: C, 69.93; H, 5.88; N, 3.50.

Dialkyl 1,4-Dihydro-4-(4-methoxyphenyl)-1-methyl-pyridine-3,5-dicarboxylate **1g,h**.

One g (3.02 mmoles) of **1c** [6] or 1 g (3.3 mmoles) of **1d** [5] dissolved in a minimum volume of dimethylpropyleneurea were treated with the 7-fold excess of a sodium hydride suspension in oil (80%). After stirring for 1 hour at 50°, a 3-fold excess of methyl iodide was added over a period of 30 minutes.

After having stirred for an additional hour at room temperature, the solution was hydrolysed with portions of water. Upon standing overnight, the semisolid product was filtered and recrystallized from alcohol.

Diethyl 1,4-Dihydro-4-(4-methoxyphenyl)-1-methylpyridine-3,5-dicarboxylate (**1g**).

This compound was obtained in 91% yield (0.95 g) as yellow crystals, mp 90-91° (ethanol, ref [6] 94°).

Dimethyl 1,4-Dihydro-4-(4-methoxyphenyl)-1-methylpyridine-3,5-dicarboxylate (**1h**).

This compound was obtained in 89% yield (0.93 g) as yellow crystals, mp 200-202° (methanol); ir: ν 1708, 1608 cm^{-1} ; uv: λ_{max} 252 (ϵ 6607), 283 (ϵ 1549), 368 (ϵ 4786) nm; ^1H nmr (deuteriochloroform): δ 3.23 (s, 3H, NCH_3), 3.62 (s, 6H, COOCH_3), 3.75 (s, 3H, 4- $\text{H}_3\text{CO-Ph}$), 4.82 (s, 1H, 4-H), 6.71-7.26 (m, 6H, aromatic H, 2-, 6-H); ms: m/z 317 (M^+ , 13), 302 ($\text{M}^+ - \text{CH}_3$, 7).

Anal. Calcd. for $\text{C}_{17}\text{H}_{19}\text{NO}_5$: C, 64.34; H, 6.03; N, 4.41. Found: C, 64.34; H, 6.01; N, 4.45.

Dimerization Reactions.

One g of crystalline 1,4-dihydropyridine **1** with a thickness of 1 mm was irradiated with Ultra-Vitalux^R lamps from a distance of 60 cm at a temperature of 25°. After dimerization had occurred

as indicated by tlc of the mixed solid substances during a reaction time of 3-4 days, products **2**, **3** and **4a** were dissolved in boiling toluene or ethanol, from which they crystallized. The following yields are based on 1 g of **1** corresponding to 100% with those of **3** obtained by direct irradiation of **1**.

Tetramethyl 1,5,8,8b β -Tetrahydro-4,8-diphenyl-cyclobuta[1,2-*b*:3,4-*b'*]dipyridine-3,4a β ,7,8a β (4H,4b β H)tetracarboxylate (**2b**).

This compound was obtained in a yield of 50% (0.5 g) as a white powder, mp 238-240° (toluene); ir: ν 3374, 1731, 1670, 1628 cm^{-1} ; uv: λ_{max} 242 (ϵ 4166), 278 (ϵ 6603) nm; ^1H nmr (dimethyl- d_6 sulfoxide): δ 3.15 (s, 6H, C-4a,8a- COOCH_3), 3.37 (s, 6H, C-3,7- COOCH_3), 3.90 (s, 2H, 4-,8-H), 4.43 (s, 2H, 4b-,8b-H), 6.92-7.20 (m, 10H, aromatic H), 7.29 (d, after deuterium oxide addition s, $J = 7$ Hz, 2H, 2-,6-H), 7.68 (d, $J = 7$ Hz, 2H, exchangable, NH); ms: (ESI) m/z 585 ($\text{M}+\text{K}^+$, 100), 569 ($\text{M}+\text{Na}^+$, 23), 547 ($\text{M}+\text{H}^+$, 10).

Anal. Calcd. for $\text{C}_{30}\text{H}_{30}\text{N}_2\text{O}_8$: C, 65.93; H, 5.49; N, 5.13. Found: C, 65.87; H, 5.62; N, 5.04.

Tetraethyl 1,5,8,8b β -Tetrahydro-4,8-bis(4-methoxyphenyl)-cyclobuta[1,2-*b*:3,4-*b'*]dipyridine-3,4a β ,7,8a β (4H,4b β H)-tetracarboxylate (**2c**).

This compound was obtained in a yield of 40% (0.4g) as white needles, mp 273-276° (ethanol); ir: ν 3289, 1731, 1660, 1620 cm^{-1} ; uv: λ_{max} 240 (ϵ 5613), 283 (ϵ 10458) nm; ^1H nmr (deuteriochloroform): δ 0.90 (t, $J = 7$ Hz, 6H, C-4a,8a- $\text{COOCH}_2\text{CH}_3$), 1.10 (t, $J = 7$ Hz, 6H, C-3,7- $\text{COOCH}_2\text{CH}_3$), 3.55 (AMX_3 , $J = 11$ Hz, 7 Hz, 2H, C-4a,8a- $\text{COOCH}_M\text{CH}_3$), 3.65 (s, 6H, 4- $\text{H}_3\text{CO-Ph}$), 3.67 (AMX_3 , $J = 11$ Hz, 7 Hz, 2H, C-4a,8a- $\text{COOCH}_A\text{CH}_3$), 3.82 (AMX_3 , $J = 11$ Hz, 7 Hz, 2H, C-3,7- $\text{COOCH}_M\text{CH}_3$), 3.86 (s, 2H, 4-,8-H), 3.99 (AMX_3 , $J = 11$ Hz, 7 Hz, 2H, C-3,7- $\text{COOCH}_A\text{CH}_3$), 4.45 (s, 2H, 4b-,8b-H), 6.66-6.88 (m, 8H, aromatic H), 7.23 (d, after deuterium oxide addition s, $J = 6$ Hz, 2H, 2-,6-H), 7.63 (d, $J = 6$ Hz, 2H, exchangable, NH); ms: (FD) m/z 662 (M^+ , 100).

Anal. Calcd. for $\text{C}_{36}\text{H}_{42}\text{N}_2\text{O}_{10}$: C, 65.26; H, 6.34; N, 4.23. Found: C, 65.24; H, 6.29; N, 4.04.

Tetramethyl 1,5,8,8b β -Tetrahydro-4,8-bis(4-methoxyphenyl)-cyclobuta[1,2-*b*:3,4-*b'*]dipyridine-3,4a β ,7,8a β (4H,4b β H)-tetracarboxylate (**2d**).

This compound was obtained in a yield of 65% (0.65 g) as white scales, mp 273-275° (toluene); ir: ν 3330, 1731, 1662, 1631 cm^{-1} ; uv: λ_{max} 242 (ϵ 8167), 280 (ϵ 14571) nm; ^1H nmr (dimethyl- d_6 sulfoxide): δ 3.21 (s, 6H, C-4a,8a- COOCH_3), 3.44 (s, 6H, C-3,7- COOCH_3), 3.65 (s, 6H, 4- $\text{H}_3\text{CO-Ph}$), 3.86 (s, 2H, 4-,8-H), 4.43 (s, 2H, 4b-,8b-H), 6.66-6.86 (m, 8H, aromatic H), 7.27 (d, after deuterium oxide addition s, $J = 6$ Hz, 2H, 2-,6-H), 7.67 (d, $J = 6$ Hz, 2H, exchangable, NH); ms: (FD) m/z 606 (M^+ , 100).

Anal. Calcd. for $\text{C}_{32}\text{H}_{34}\text{N}_2\text{O}_{10}$: C, 63.37; H, 5.61; N, 4.62. Found: C, 63.21; H, 5.65; N, 4.54.

Tetraethyl 1,5-Dibenzyl-1,5,8,8b β -tetrahydro-4,8-bis(4-methoxyphenyl)-cyclobuta[1,2-*b*:3,4-*b'*]dipyridine-3,4a β ,7,8a β (4H,4b β H)tetracarboxylate (**2e**).

This compound was obtained in a yield of 60% (0.6 g) as white prisms, mp 195-197° (ethanol); ir: ν 1739, 1672, 1626 cm^{-1} ; uv: λ_{max} 240 (ϵ 13473), 293 (ϵ 24795) nm; ^1H nmr (deuteriochloroform): δ 0.92 (t, $J = 7$ Hz, 6H, C-4a,8a- $\text{COOCH}_2\text{CH}_3$), 1.17 (t, $J = 7$ Hz, 6H, C-3,7- $\text{COOCH}_2\text{CH}_3$), 3.57 (AMX_3 , $J = 11$

H_z, 7 Hz, 2H, C-4a,8a-COOCH_MCH₃), 3.68 (s, 6H, 4-H₃CO-Ph), 3.69 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-4a,8a-COOCH_ACH₃), 3.99 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-3,7-COOCH_MCH₃), 4.02 (s, 2H, 4-,8-H), 4.08 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-3,7-COOCH_ACH₃), 4.45 (s, 2H, 4b-8b-H), 4.59, 4.67 (AB, J = 15 Hz, 4H, NCH₂), 6.50-7.41 (m, 18H, aromatic H), 7.57 (s, 2H, 2-,6-H); ms: (ESI) m/z 881 (M+K⁺, 100), 865 (M+Na⁺, 17).

Anal. Calcd. for C₅₀H₅₄N₂O₁₀: C, 71.26; H, 6.41; N, 3.33. Found: C, 71.11; H, 6.57; N, 3.14.

Tetraethyl 1,5,8,8bβ-Tetrahydro-4,8-bis(4-methoxyphenyl)-1,5-dimethyl-cyclobuta[1,2-b:3,4-b']dipyridine-3,4aβ,7,8aβ-(4H,4bβH)tetracarboxylate (2g).

This compound was obtained in 52% yield (0.52 g) as a white powder, mp 197-199° (ethanol); ir: ν 1728, 1684, 1611 cm⁻¹; uv: λ_{max} 241 (ε 9872), 291 (ε 19513) nm; ¹H nmr (deuteriochloroform): δ 0.98 (t, J = 7 Hz, 6H, C-4a,8a-COOCH₂CH₃), 1.17 (t, J = 7 Hz, 6H, C-3,7-COOCH₂CH₃), 3.70 (s, 12H, NCH₃, 4-H₃CO-Ph), 3.99 (q, J = 7 Hz, 4H, C-4a,8a-COOCH₂CH₃), 4.09 (q, J = 7 Hz, 4H, C-3,7-COOCH₂CH₃), 4.90, 4.85 (2s, 2H, 4-,8-H), 5.85, 5.81 (2s, 2H, 4b-,8b-H), 6.68-6.83 (m, 8H, aromatic H), 8.30 (s, 2H, 2-,6-H); ms: (ESI) m/z 729 (M+K⁺, 100), 713 (M+Na⁺, 50), 691 (M+H⁺, 36).

Anal. Calcd. for C₃₈H₄₆N₂O₁₀: C, 66.09; H, 6.67; N, 4.06. Found: C, 65.86; H, 6.65; N, 3.96.

Tetramethyl 1,5,8,8bβ-Tetrahydro-4,8-bis(4-methoxyphenyl)-1,5-dimethyl-cyclobuta[1,2-b:3,4-b']pyridine-3,4aβ,7,8aβ-(4H,4bβH)tetracarboxylate (2h).

This compound was obtained in 60% yield (0.6 g) as a white powder, mp 247-249° (toluene); ir: ν 1732, 1689, 1635 cm⁻¹; uv: λ_{max} 242 (ε 10233), 294 (ε 20529) nm; ¹H nmr (dimethyl-d₆ sulfoxide): δ 3.20 (s, 6H, C-4a,8a-COOCH₃), 3.26 (s, 6H, C-3,7-COOCH₃), 3.44 (s, 6H, NCH₃), 3.67 (s, 6H, 4-H₃CO-Ph), 3.78 (s, 2H, 4-,8-H), 4.23 (s, 2H, 4b-,8b-H), 6.68-6.87 (m, 8H, aromatic H), 7.44 (s, 2H, 2-,6-H); ms: (FD) m/z 634 (M⁺, 100).

Anal. Calcd. for C₃₄H₃₈N₂O₁₀: C, 64.35; H, 5.99; N, 4.42. Found: C, 64.63; H, 6.10; N, 4.25.

Tetramethyl 6,12-Diphenyl-3,9-diazahexacyclo[6.4.0.0.2⁷.0.4.11.0.5.10]dodecane-1,5,7,11-tetracarboxylate (3b).

This compound was obtained in 97% yield (0.97 g) as white scales, mp 265-267° (toluene); ir: ν 3329, 1728 cm⁻¹; ¹H nmr (dimethyl-d₆ sulfoxide): δ 3.40 (s, 12H, COOCH₃), 3.86 (s, 2H, 6-,12-H), 4.04 (d, after deuterium oxide addition s, J = 3 Hz, 4H, 2-,4-,8-,10-H), 4.64 (t, J = 3 Hz, 2H, exchangable, NH), 7.13-7.41 (m, 10H, aromatic H); ms: (ESI) m/z 569 (M+Na⁺, 100), 547 (M+H⁺, 83).

Anal. Calcd. for C₃₀H₃₀N₂O₈: C, 65.93; H, 5.49; N, 5.13. Found: C, 65.65; H, 5.63; N, 5.07.

Tetraethyl 6,12-Bis(4-methoxyphenyl)-3,9-diazahexacyclo[6.4.0.0.2⁷.0.4.11.0.5.10]dodecane-1,5,7,11-tetracarboxylate (3c).

This compound was obtained in 92% yield (0.92 g) as white scales, mp 241-243° (toluene); ir: ν 3227, 1724 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.0 (t, J = 7 Hz, 12H, COOCH₂CH₃), 3.70 (s, 6H, 4-H₃CO-Ph), 3.80 (s, 2H, 6-,12-H), 3.91 (q, J = 7 Hz, 8H, COOCH₂CH₃), 4.24 (s, 4H, 2-,4-,8-,10-H), 4.70 (s, br, 2H, exchangable, NH), 6.66-7.43 (m, 8H, aromatic H); ms: (ESI) m/z 701 (M+K⁺, 100), 685 (M+Na⁺, 41), 663 (M+H⁺, 63).

Anal. Calcd. for C₃₆H₄₂N₂O₁₀: C, 65.26; H, 6.34; N, 4.23. Found: C, 65.07; H, 6.32; N, 4.12.

Tetramethyl 6,12-Bis(4-methoxyphenyl)-3,9-diazahexacyclo[6.4.0.0.2⁷.0.4.11.0.5.10]dodecane-1,5,7,11-tetracarboxylate (3d).

This compound was obtained in 91% yield (0.91 g) as a white powder, mp 272-275° (toluene); ir: ν 3330, 1731 cm⁻¹; ¹H nmr (dimethyl-d₆ sulfoxide): δ 3.41 (s, 12H, COOCH₃), 3.69 (s, 6H, 4-H₃CO-Ph), 3.79 (s, 2H, 6-,12-H), 4.01 (d, after deuterium oxide addition s, J = 3 Hz, 4H, 2-,4-,8-,10-H), 4.57 (t, J = 3 Hz, 2H, exchangable, NH), 6.72-7.34 (m, 8H); ms: (ESI) m/z 645 (M+K⁺, 100), 629 (M+Na⁺, 67), 607 (M+H⁺, 13).

Anal. Calcd. for C₃₂H₃₄N₂O₁₀: C, 63.37; H, 5.61; N, 4.62. Found: C, 63.30; H, 5.61; N, 4.54.

Tetraethyl 3,9-Dibenzyl-6,12-bis(4-methoxyphenyl)-3,9-diazahexacyclo[6.4.0.0.2⁷.0.4.11.0.5.10]dodecane-1,5,7,11-tetracarboxylate (3e).

This compound was obtained in 96% yield of (0.96 g) as a white powder, mp 170-173° (ethanol); ir: ν 1725 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.02 (t, J = 7 Hz, 12H, COOCH₂CH₃), 3.75 (s, 6H, 4-H₃CO-Ph), 3.99 (q, J = 7 Hz, 8H, COOCH₂CH₃), 4.24 (s, 2H, 6-,12-H), 4.26 (s, 4H, 2-,4-,8-,10-H), 4.48 (s, 4H, NCH₂), 6.59-7.34 (m, 18H, aromatic H); ms: (FD) m/z 842 (M⁺, 100).

Anal. Calcd. for C₅₀H₅₄N₂O₁₀: C, 71.26; H, 6.41; N, 3.33. Found: C, 71.05; H, 6.29; N, 3.20.

Tetraethyl 6,12-Bis(4-methoxyphenyl)-3,9-dimethyl-3,9-diazahexacyclo[6.4.0.0.2⁷.0.4.11.0.5.10]dodecane-1,5,7,11-tetracarboxylate (3g).

This compound was obtained in 90% yield (0.90 g) as a white powder, mp 210-213° (ethanol); ir: ν 1723 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.17 (t, J = 7 Hz, 12H, COOCH₂CH₃), 3.10 (s, 6H, NCH₃), 3.71 (s, 6H, 4-H₃CO-Ph), 3.98 (q, J = 7 Hz, 8H, COOCH₂CH₃), 4.06 (s, 4H, 2-,4-,8-,10-H), 4.11 (s, 2H, 6-,12-H), 6.64-7.21 (m, 8H, aromatic H); ms: (ESI) m/z 729 (M+K⁺, 100), 713 (M+Na⁺, 8).

Anal. Calcd. for C₃₈H₄₆N₂O₁₀: C, 66.09; H, 6.67; N, 4.06. Found: C, 66.05; H, 6.72; N, 3.99.

Tetramethyl 6,12-Bis(4-methoxyphenyl)-3,9-dimethyl-3,9-diazahexacyclo[6.4.0.0.2⁷.0.4.11.0.5.10]dodecane-1,5,7,11-tetracarboxylate (3h).

This compound was obtained in 96% yield (0.96 g) as white scales, mp 252-254° (toluene); ir: ν 1721 cm⁻¹; ¹H nmr (dimethyl-d₆ sulfoxide): δ 3.00 (s, 6H, NCH₃), 3.50 (s, 12H, COOCH₃), 3.69 (s, 6H, 4-H₃CO-Ph), 3.95 (s, 4H, 2-,4-,8-,10-H), 4.05 (s, 2H, 6-,12-H), 6.71-7.08 (m, 8H, aromatic H); ms: (FD) m/z 634 (M⁺, 100).

Anal. Calcd. for C₃₄H₃₈N₂O₁₀: C, 64.35; H, 5.99; N, 4.42. Found: C, 64.56; H, 6.0; N, 4.24.

Tetraethyl 1,5,8,8bα-Tetrahydro-4,8-diphenyl-cyclobuta[1,2-b:3,4-b']dipyridine-3,4aα,7,8aβ(4H,4bβH)tetracarboxylate (4a).

This compound was obtained in 70% yield of (0.7 g) as white crystals, mp 235-237° (ethanol); ir: ν 3352, 1733, 1662, 1628 cm⁻¹; uv: λ_{max} 240 (ε 2344), 280 (ε 21878) nm; ¹H nmr (deuteriochloroform): δ 0.81 (t, J = 7 Hz, 6H, C-4a,8a-COOCH₂CH₃), 1.08 (t, J = 7 Hz, 6H, C-3,7-COOCH₂CH₃), 3.43 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-4a,8a-COOCH_MCH₃), 3.58 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-4a,8a-COOCH_ACH₃), 3.80 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-3,7-COOCH_MCH₃), 3.90 (AMX₃, J = 11 Hz, 7 Hz, 2H, C-3,7-COOCH_ACH₃), 3.95 (s, 2H, 4-, 8-H), 4.31 (d, after deuterium oxide addition s, J = 3 Hz, 2H, 4b-,8b-H), 7.18-7.01 (m, 10H, aromatic H), 7.31 (dd, J = 7 Hz, 3 Hz, 2H, exchangable, NH), 7.39 (d, after deuterium

oxide addition s, $J = 7$ Hz, 2H, 2-,6-H); ms: (FD) m/z 602 (M^+ , 100).

Anal. Calcd. for $C_{34}H_{38}N_2O_8$: C, 67.77; H, 6.31; N, 4.65. Found: C, 67.61; H, 6.34; N, 4.61.

Diethyl 4-Phenylpyridine-3,5-dicarboxylate (**5a**).

After the separation of **4a**, the ethanolic mother liquid was evaporated to dryness *in vacuo*. The residual oil was separated by preparative tlc (chloroform/ethyl acetate 75:25, 2 mm thickness, silica gel 60_{F254}). The fraction with $R_f = 0.8$ was worked up by washing the silica gel with acetone, which was removed *in vacuo* leaving a greenish oil, that crystallized on cooling, 25% yield (0.25 g) as greenish plates, mp 60-63°; ν 1720 cm^{-1} ; 1H nmr (deuteriochloroform): δ 0.95 (t, $J = 7$ Hz, 6H, $COOCH_2CH_3$), 4.05 (q, $J = 7$ Hz, 4H, $COOCH_2CH_3$), 7.39-7.15 (m, 5H, aromatic H), 9.06 (s, 2H, 2-,6-H); EI-ms: m/z 299 (M^+ , 86), 254 ($M^+ - OC_2H_5$, 48).

Anal. Calcd. for $C_{17}H_{17}NO_4$: C, 68.23; H, 5.69; N, 4.68. Found: 68.27; H, 5.94; N, 4.49.

Crystal Structure Determination.

A summary of the crystal data and structure refinement details are given in Table 3. The structure was solved by direct methods [9], and refined by full matrix least squares using SHELXL-93 [10]. The atoms other than hydrogen were refined anisotropically. The atomic scattering factors for all atoms and the anomalous dispersion correction factors for atoms other than hydrogen were taken from the literature [11].

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