Nucleophilic Addition of 2-Acetylindole Enolates to Pyridinium Salts. Acylation of the Intermediate Dihydropyridines†

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Pyridinium salts undergo the addition of nucleophiles to give dihydropyridines,[1] which are not only valuable intermediates in organic synthesis[2] but also interesting compounds in medicinal[3] and bioorganic chemistry.[4] The reaction of stabilized carbon nucleophiles (enolate ions) and *N*-alkylpyridinium salts bearing an electron-withdrawing substituent at the β-position constitutes a good method of forming carbon–carbon bonds, leading to the thermodynamically more stable 1,4-dihydropyridines. However, the intermolecular dihydropyridine adducts are not usually stable enough to be isolated, and consequently, they are directly transformed into more stable products, either by rearomatization or by conversion into the corresponding dihydropyridinium ions by acid treatment, with further cyclization. Both transformations have been successfully used in the synthesis of structurally complex alkaloids.[5] In this context, the addition of indole-containing enolates to *N*-alkylpyridinium salts followed by acid-induced cyclization of the resultant 1,4-dihydropyridines[6] has proved to be a powerful tool for the synthesis of bridged indole alkaloids belonging to a variety of structural types.[7]

In connection with our synthetic studies[8] on the 2-acylindole alkaloid ervitsine,[9] we have been involved in the above nucleophilic addition–acid cyclization sequence starting from 2-acetylindoles. In the course of these studies and in previous work operating with different carbon nucleophiles (indoleacetic ester enolates,[7a,c] 2-indolylacyl anion equivalents[10]), some questions arose concerning the regioselectivity of the nucleophilic attack on the pyridinium ring.

Table 1. Reactions of Dihydropyridines Derived from 2-Acetylindoles 1 and 2 and Pyridinium Salts 3 with Electrophiles

entry	dihydropyridines derived from	electrophile	products (ratio, overall yield (%))
1	**1** + **3a**	HCl, TFAA, or TCAA	*a*
2	**1** + **3b**	HCl	**4** + **5b** (1:4, 15)
3	**1** + **3c**	HCl	**5c** (10)
4	**1** + **3d**	HCl	**5d** (20)
5	**2** + **3d**	HCl	**6d** (< 5)
6	**1** + **3b**	TFAA	**13b** + **19b** (2:1, 15)
7	**1** + **3b**	TCAA	**14b** + **20b** (1:2, 20)
8	**1** + **3c**	TFAA	**13c** + **19c** (5:4, 45)
9	**1** + **3c**	TCAA	**14c**[b] + **17c**[b] + **20c** (2:1:1, 60)
10	**1** + **3d**	TFAA	**13d** + **19d** (1:5, 30)
11	**1** + **3d**	TCAA	**14d** + **20d** (3:2, 40)
12	**1** + **3e**	TFAA	**13e**[b] + **16e**[b] + **19e** (1:1:3, 35)
13	**1** + **3e**	TCAA	**14e**[b] + **17e**[b] + **20e** (1:1:1, 60)
14	**1** + **3f**	TFAA	**13e**[c] + **19e** (3:2, 35)
15	**1** + **3f**	TCAA	**17e**[c] + **20e** (2:1, 30)
16	**1** + **3g**	TCAA	**20g** (20)
17	**2** + **3b**	TCAA	*a*
18	**2** + **3c**	TCAA	**15c**[b] + **18c**[b] + **21c** (2:1:1, 40)
19	**2** + **3d**	TCAA	**15d** + **21d** (1:2, 45)

[a] Complex mixture. [b] Inseparable mixture of 1,2-dihydropyridines. [c] Trace amounts of the regioisomeric 1,2-dihydropyridine were also detected.

In order to better understand the regioselectivity observed in the above nucleophilic addition–acid cyclization processes, we undertook a study using the enolates derived from 2-acetylindoles **1** and **2** and a variety of pyridinium salts **3** (Scheme 1). The results are shown in Table 1 (entries 1–5) and seem to be dependent on the nature of the electron-withdrawing substituent at the β-position of the pyridinium ring. Surprisingly, no tetracyclic compounds were detected when 3-formylpyridinium salt **3a** was exposed to the enolate derived from 2-acetylindole **1** and then to acid. However, starting from 3-acetylpyridinium salt **3b**, along with the expected tetracycle **5b**, minor amounts of the "unnatural" tetracycle **4**, coming from acid cyclization of 1,2-dihydropyridine **7b**, were also isolated. In contrast, the "natural" tetracycles **5c** and **5d** were the only isolable products, although in low yields, when operating from the respective pyridinium salts **3c** and **3d**. As expected, no reaction was observed with 3-ethylpyridinium salt **3g**, thus indicating that the success of the intermolecular nucleophilic addition–cyclization sequence is associated with the presence of a β-acyl function in the starting pyridinium salt.[11] Poorer results were obtained with the *N*-unsubstituted 2-acetylindole (**2**): reaction was only observed with pyridinium salt **3d**, although the corresponding tetracycle **6d** was isolated in very low yield.

On the other hand, when the acid treatment was omitted, the starting products **1** or **2** were the only identifiable products from the complex reaction mixtures, thus indicating that the intermediate dihydropyridines **7**–**12** were not stable enough to be isolated.

† Dedicated to the memory of Prof. Felix Serratosa, 1925–1995.

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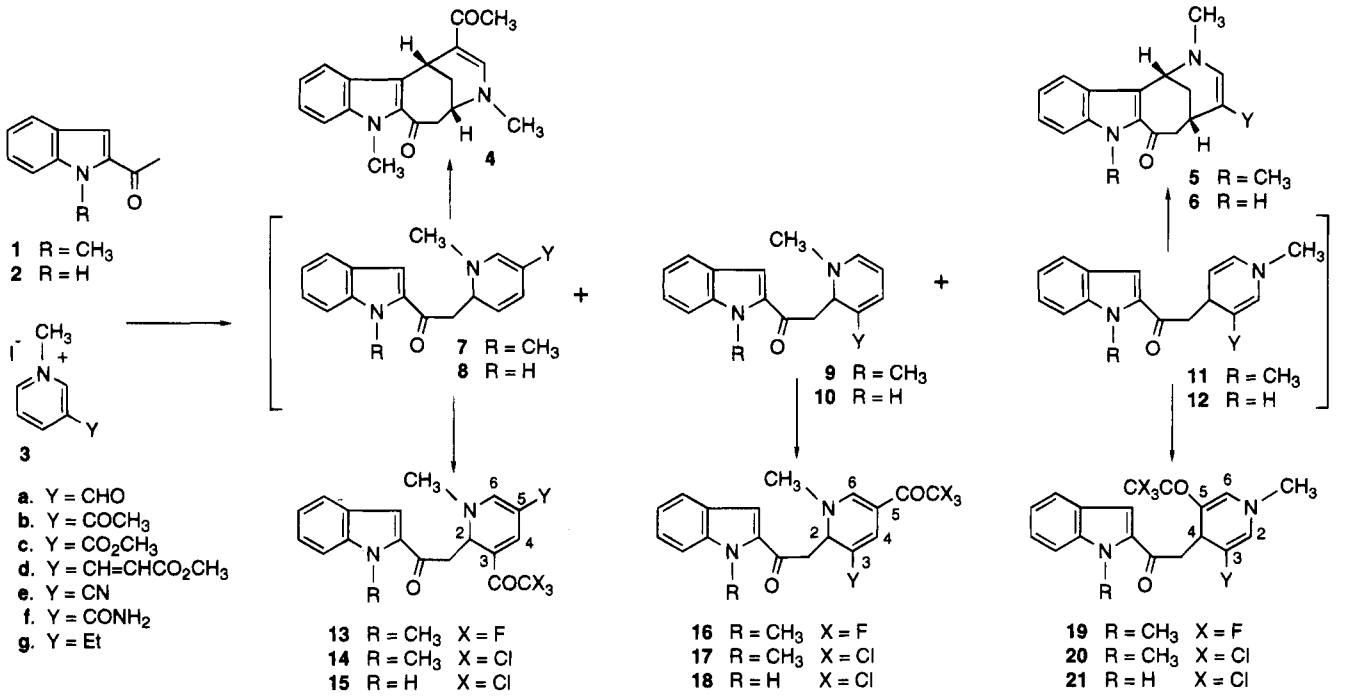
Scheme 1



Quenching the reactions between esters **1** or **2** and pyridinium salts **3** with an electrophilic acylating agent instead of acid was then investigated. There are few examples[8b,c] about further functionalization of dihydropyridines resulting from the addition of stabilized carbon nucleophiles to pyridinium salts.[1,12] The presence of a second electron-withdrawing substituent would stabilize the resultant dihydropyridines, thus allowing their isolation. Whereas no reaction was observed with methyl chloroformate, methyl cyanoformate, acetyl chloride, acetic anhydride, or chloroacetyl chloride, mixtures of the corresponding acylated dihydropyridines **13**–**21** were obtained with the more powerful acylating agents trifluoroacetic acid anhydride (TFAA) or trichloroacetic acid anhydride (TCAA) (Scheme 1).

The constitution of these dihydropyridines (**13**–**21**) was unambiguously established from their NMR data. Thus, diagnostic signals for the assignment of 1,2- and 1,4-dihydropyridines were those corresponding to the sp^3 methine carbon at C-2 or C-4, respectively, in the ^{13}C NMR spectra (Table 2) and to 2-H and 4-H in the ^1H NMR spectra.

The results of the acylation reaction are summarized in Table 1 (entries 6–19). Several points are worthy of mention:

In the *N*-methylindole series, no reaction was observed starting from 3-formylpyridinium salt **3a**. However, operating with pyridinium salts **3b** (entries 6 and 7), **3c** (entries 8 and 9), and **3d** (entries 10 and 11), yields were clearly higher than those obtained in the above acidic cyclizations. The reaction was satisfactorily extended to 3-cyanopyridinium salt **3e** (entries 12 and 13) and 3-carbamoylpyridinium salt **3f** (entries 14 and 15). In the latter case, the acylating agent promotes a concomitant dehydration of the amide group to give a mixture of cyanodihydropyridines. In most cases, the use of TCAA gives better results than TFAA.

In contrast with the results observed when the initially formed dihydropyridines were subjected to acid cyclizations, the presence of an electron-withdrawing substituent at the β-position of the starting pyridinium salt is not a necessary requisite for the success of the addition–acylation sequence: the unstable 1,4-dihydropyridine **20g** could be isolated starting from 3-ethylpyridinium salt **3g** (entry 16).

Also in sharp contrast with the results observed from the *N*-unsubstituted indole **2** in the above addition–acid cyclization sequence, acceptable yields of acylated dihydropyridines were obtained when the dianion derived from 2-acetylindole (**2**) was allowed to react with pyridinium salts **3c** and **3d**, and the initially formed mixtures of dihydropyridines were treated with TCAA (entries 18 and 19). However, complex mixtures were formed from 3-acetylpyridinium salt **3b** (entry 17).

The nucleophilic addition to the pyridinium ring is not a regioselective process since mixtures of acylated 1,2- and 1,4-dihydropyridines, **13**–**15** and **19**–**21**, respectively, were obtained. Surprisingly, in most cases 1,2-dihydropyridines were the major products. Furthermore, starting from pyridinium salts **3c** and **3e**, in which the β-substituents are smaller groups, the corresponding regioisomeric 1,2-dihydropyridines **16**–**18** were also isolated. These results make evident that the pyridinium ring undergoes not only the addition of the nucleophile at the 6- and 4-positions to initially give the intermediate dihydropyridines **7**–**8** and **11**–**12**, respectively, but also in some cases at the 2-position to give dihydropyridines **9** and **10**.

For a particular pyridinium salt, the ratio of products coming from the initially formed α- or γ-dihydropyridine adducts in the above TCAA or TFAA acylations is different from that previously observed in the acid cyclizations. These ratios must reflect not only the preference of the nucleophilic attack for a specific position of the pyridinium ring but also the ability of the initially formed dihydropyridines to react with the acylating agent or to undergo acid cyclization. Dihydropyridines which

(12) For a review on reactions of 1,4-dihydropyridines, see: Sausins, A.; Duburs, G. *Heterocycles* **1988**, *27*, 291.

Table 2. Significant ^{13}C NMR Data of Dihydropyridines 13–26

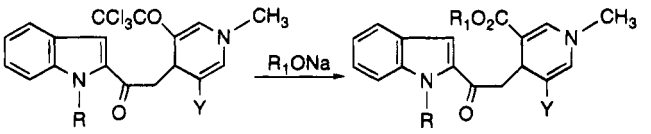
	C-2	C-3	C-4	C-5	C-6	CH_2CO	β-COR	NCH_3	Y
13b	56.4	120.3	132.0	102.8	153.9	43.7 190.2	*a*	32.0 44.4	24.8 195.4
19b	139.3	109.9	28.5	119.6	145.4	45.7 191.9	117.0 177.0	31.9 42.3	24.8 194.7
14b	56.3	120.0	134.6	98.8	155.3	43.2 190.3	96.2 175.8	32.0 44.2	24.7 195.1
20b	139.2	105.5	30.0	119.2	145.0	45.9 192.1	96.0 178.8	31.9 42.5	24.9 194.6
13c	55.4	110.6	139.8	100.4	152.5	43.2 190.0	117.0 176.0	32.0 44.1	51.3 165.0
19c	138.0	109.1	29.6	*a*	145.7	46.3 191.5	116.8 170.0	31.8 42.1	51.5 166.0
14c	56.5	106.1	139.5	99.5	151.6	44.0 190.2	95.5 177.9	31.9 42.8	51.3 165.2
17c	56.5	99.1	133.1	106.1	154.9	44.0 190.0	96.2 175.8	31.9 42.8	51.7 165.4
20c	138.0	104.1	31.0	109.3	145.4	46.0 191.7	95.7 178.8	31.8 42.2	51.4 166.2
13d	55.6	114.7	128.5	104.0	152.0	44.0 189.5	*a*	32.1 44.2	51.5 113.8 142.5 167.2
19d[b]	135.0	108.0	29.3	118.5	145.6	45.2 191.0	117.0 176.0	31.8 42.4	51.4 115.0 142.2 167.8
14d	55.6	118.3	131.1	100.4	153.4	43.4 189.7	96.4 175.8	32.1 44.1	51.4 112.8 143.0 167.3
20d	134.8	102.9	31.0	117.7	145.3	45.5 191.3	95.9 178.8	31.9 42.5	51.4 114.4 142.2 167.6
13e	54.7	111.2	139.5	80.9	152.9	42.7 189.4	*a*	32.0 44.1	118.0
16e	55.5	94.5	135.4	102.8	152.9	43.5 188.4	*a*	32.0 44.0	117.4
19e	140.6	92.2	30.5	107.9	145.3	45.3 190.4	116.1 177.2	32.0 42.3	117.8
14e	55.8	107.0	139.1	79.4	152.0	42.4 189.7	99.4 177.4	32.0 44.0	118.5
17e	56.4	90.9	137.5	*a*	154.5	43.2 188.6	99.4 175.3	32.1 44.0	117.9
20e[c]	142.7	89.5	31.3	101.7	146.4	46.8 190.8	95.6 178.8	32.0 42.1	118.8
20g	122.8	98.3	34.8	*a*	146.4	46.0 192.3	96.6 178.3	31.8 42.1	11.4 25.5
15c[c]	56.2	105.1	139.7	98.3	153.1	41.0 189.2	95.9 177.1	43.3	51.2 164.8
18c[c]	56.5	97.6	138.3	105.1	156.3	42.3 89.2	96.9 174.9	43.5	51.7 165.0
21c[c]	139.4	102.8	30.7	108.4	146.9	45.0 190.2	96.0 178.8	42.1	51.6 166.1
15d[c]	55.8	118.6	131.3	98.8	155.0	41.8 189.2	96.4 174.8	43.3	51.4 112.9 143.6 167.1
21d[c]	137.1	102.1	29.8	117.2	146.3	44.6 190.2	96.1 178.4	42.2	51.4 113.1 143.1 167.1
22b	141.3	116.4	29.9	107.1	139.4	47.2 192.4	51.1 166.7	31.8 41.4	24.6 194.6
22c	139.8	105.8	31.0			48.1 192.2	51.1 166.9	31.8 41.3	
22d[d]	137.0	114.7	30.8	104.4	139.8	46.8 191.8	51.1 167.2[e]	31.9 41.3	51.1 111.8 143.5 167.9[e]
22e	141.9	87.5	31.7	104.6	139.4	47.5 191.1	51.4 166.5	32.1 41.4	119.1
23c	139.7[e]	105.9[f]	31.1	106.4[f]	139.9[e]	48.2 192.3	14.1 60.0 167.0[g]	31.9 41.4	51.1 167.1[g]
24c	140.2	105.8	31.1			46.5 191.6	51.3 167.2	41.4	

Table 2 (Continued)

	C-2	C-3	C-4	C-5	C-6	CH_2CO	β-COR	NCH_3	Y
24d[d]	139.4	113.8	30.1	103.9	140.6	45.9	51.0[e]	41.1	51.3[e]
						190.6	167.0[f]		112.9
									144.5
									167.5[f]
25	56.3	108.8	133.1	98.7	149.8	44.0	50.0[e]	31.9	51.5[e]
						190.8	165.8[f]	43.3	165.9[f]
26	56.6	108.7	133.3	98.7	149.9	42.7	51.0[e]	43.3	51.5[e]
						190.2	166.0[f]		165.9[f]

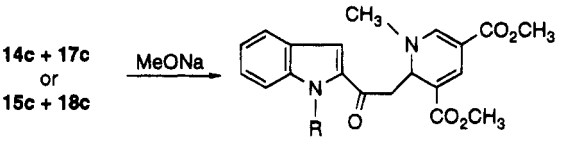
[a] Not observed. [b] Assignments were aided by HMQC. [c] In DMSO-d_6 solution. [d] Numbering of the pyridine ring as depicted in Scheme 1. [e-g] May be interchanged.

Scheme 2[a]



[a] Y according to Scheme 1.

Scheme 3



are not able to react with the electrophile undergo either decomposition or fragmentation into the starting products. Therefore, the absence of a specific cyclized product is not indicative of the absence of the corresponding dihydropyridine precursor.

Whereas the trifluoroacetyl group of 1,4-dihydropyridines **19** proved to be reluctant to undergo haloform-type reactions,[13] (trichloroacetyl)-1,4-dihydropyridines **20** and **21** were prone to react under the above conditions; the most interesting result from the synthetic standpoint was the smooth reaction occurring with MeONa–MeOH[13a,14] to give the corresponding methyl esters **22b–e** and **24c,d** in high yield (Scheme 2),[15] thus providing a general method for the preparation of 3,4,5-trisubstituted 1,4-dihydropyridines bearing two different electron-withdrawing groups at the β-positions. The reaction is compatible with a variety of substituents at the β-position of the pyridine ring, but only decomposition products were isolated from the unstable 3-alkyl-substituted dihydropyridine **20g**. The use of EtONa–EtOH allows for the preparation of 1,4-dihydropyridines with two different ester groups; for instance, dihydropyridine **23c** was obtained from **20c** in 90% yield. Similarly, the regioisomeric mixtures of 1,2-dihydropyridines **14c** and **17c**, and **15c** and **18c** were smoothly and efficiently converted into the corresponding 3,5-bis(methoxycarbonyl)-1,2-dihydropyridines **25** and **26**, respectively (Scheme 3).

Dihydropyridines **13–26** (with the exception of **20g**) are crystalline solids, stable enough to be characterized by elemental analyses. This stability, due to the presence of two electron-withdrawing substituents, deserves mention because it is in contrast to the usual instability of dihydropyridines resulting from the intermolecular addition of stabilized carbon nucleophiles.

In conclusion, the above results not only make evident the low regioselectivity in the addition of enolates to pyridinium salts but also demonstrate the dramatic influence of the method used for the trapping of the initially formed dihydropyridines on the regioselectivity observed in the process. The acylation of the intermediate dihydropyridines is reported for the first time, thus providing an efficient and versatile method for the preparation of polysubstituted 1,2- and 1,4-dihydropyridines.

Experimental Section

Melting points were determined in a capillary tube and are uncorrected. Unless otherwise noted, NMR spectra were recorded in $CDCl_3$ solution at 200, 300, or 500 MHz (^1H) and 50.3 or 75 MHz (^{13}C). Coupling constants are expressed in hertz. Only noteworthy IR absorptions (cm^{-1}) are listed. TLC was carried out on SiO_2 (silica gel 60 F_{254}, Merck, 0.063–0.200 mm), and the spots were located with iodoplatinate reagent. Column chromatography was carried out on SiO_2 (silica gel 60, SDS, 0.060–0.2 mm). Flash chromatography was carried out on SiO_2 (silica gel 60, SDS, 0.040–0.060 mm). Drying of organic extracts during the workup of reactions was performed over anhydrous Na_2SO_4. Evaporation of solvents was accomplished with a rotatory evaporator. Microanalyses were performed by Centro de Investigación y Desarrollo (CSIC), Barcelona.

General Procedure for the Synthesis of Tetracyclic Compounds 4–6. LDA (3 or 6 mmol) was slowly added to a solution of acetylindole **1** or **2** (3 mmol) in anhydrous THF (40 mL) under N_2 cooled at −70 °C, and the resulting solution was stirred at −70 °C for 30 min. Then, pyridinium iodide **3** (3 mmol) was added in portions, and the mixture was allowed to rise to a temperature of −30 °C and stirred at this temperature for 1.5 h. Enough of a saturated C_6H_6 solution of dry HCl was added dropwise to bring the pH to 3.5–4, and the mixture was permitted to rise to room temperature. After being stirred at room temperature for 2 h, the reaction mixture was poured into saturated aqueous Na_2CO_3 and extracted with Et_2O. Evaporation of the dried extracts gave a crude residue which was chromatographed (CH_2Cl_2 and 99:1 CH_2Cl_2–MeOH). The results are given in Table 1. Melting points, IR and ^1H and ^{13}C NMR spectroscopy data, and elemental analyses are provided below.

2-Acetyl-4,8-dimethyl-7-oxo-4,5,6,7-tetrahydro-1,5-methano-1*H*-azonino[5,6-*b*]indole (4): mp 198 °C (acetone–MeOH); ^1H NMR (200 MHz) 2.01 (s, 3 H), 2.30 (m, 1 H), 2.60 (dm, J = 13 , 1 H), 3.07 (dd, J = 15, 2.7, 1H), 3.20 (s, 3 H), 3.30 (ddd, J = 15, 5.4, 1.2, 1 H), 3.67 (m, 1 H), 3.79 (s, 3 H), 5.00 (m, 1 H), 7.10–7.40 (m, 4 H), 8.45 (d, J = 8, 1 H); ^{13}C NMR (50.3 MHz) 23.5, 24.3, 30.8, 31.7, 41.6, 48.2, 53.2, 109.4, 110.5, 119.8, 120.1, 124.0, 125.8, 126.2, 133.1, 139.2, 146.8, 191.8, 195.0. Anal. Calcd for $C_{19}H_{20}N_2O_2 \cdot {}^1/_2H_2O$: C, 71.90; H, 6.66; N, 8.82. Found: C, 71.97; H, 6.42; N, 8.57.

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(15) In fact **20d** could be easily converted into the corresponding 1,4-dihydropyridine-3-carboxylate salt (unstable) by alkaline hydrolysis (1 N NaOH, rt, 10 min). No reaction was observed with other hard nucleophiles (CsF, LiCl, or $NaNH_2$).

4-Acetyl-2,8-dimethyl-7-oxo-2,5,6,7-tetrahydro-1,5-methano-1*H*-azonino[4,3-*b*]indole (5b): mp 224 °C (acetone–MeOH); IR 1561, 1650; ^{1}H NMR (200 MHz) 2.12 (s, 3 H), 2.50 (m, 2 H), 2.90 (masked, 1 H), 2.93 (s, 3 H), 3.50 (m, 2 H), 3.85 (s, 3 H), 4.93 (br d, J = 3.3, 1 H), 7.09 (s, 1 H), 7.20–7.40 (m, 3 H), 7.78 (d, J = 8, 1 H); ^{13}C NMR (50.3 MHz) 23.5, 25.4, 31.2, 32.0, 42.1, 48.8, 50.4, 110.1, 110.6, 118.2, 119.9, 120.9, 125.6, 125.9, 133.9, 138.1, 146.6, 192.8, 198.2. Anal. Calcd for $C_{19}H_{20}N_2O_2 \cdot {}^1/_4H_2O$: C, 72.94; H, 6.60; N, 8.95. Found: C, 72.56; H, 6.73; N, 8.84.

Methyl 2,8-dimethyl-7-oxo-2,5,6,7-tetrahydro-1,5-methano-1*H*-azonino[4,3-*b*]indole-4-carboxylate (5c): mp 208–209 °C (acetone–MeOH); IR 1600, 1663, 1686; ^{1}H NMR (200 MHz) 2.53 (m, 2 H), 2.86 (s, 3 H), 2.93 (dd, J = 14, 2.8, 1 H), 3.15 (br s, 1 H), 3.39 (dd, J = 14, 5.7, 1 H), 3.69 (s, 3 H), 3.88 (s, 3 H), 4.90 (t, 1 H), 7.20–7.40 (m, 3 H), 7.77 (d, J = 8, 1 H); ^{13}C NMR (50.3 MHz) 26.3, 31.3, 31.8, 41.5, 49.3, 50.0, 50.3, 95.6, 110.4, 118.2, 120.0, 120.8, 125.6, 125.8, 132.0, 138.1, 145.0, 168.6, 198.3. Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.63. Found: C, 70.28; H, 6.33; N, 8.49.

Methyl 2,8-dimethyl-7-oxo-2,5,6,7-tetrahydro-1,5-methano-1*H*-azonino[4,3-*b*]indole-4(*E*)-acrylate (5d): mp 271–272 °C (acetone); IR 1560, 1640, 1670; ^{1}H NMR (200 MHz) 2.55 (m, 2 H), 2.82 (s, 3 H), 2.97 (m, 1 H), 3.30 (dd, J = 14.7, 6.2, 1 H), 3.40 (br s, 1 H), 3.71 (s, 3 H), 3.88 (s, 3 H), 4.94 (t, 1 H), 5.40 (d, J = 15, 1 H), 6.35 (s, 1 H), 7.20–7.50 (m, 4 H), 7.80 (d, J = 8, 1 H); ^{13}C NMR (50.3 MHz) 26.5, 31.2, 31.8, 41.4, 47.6, 50.4, 50.6, 102.0, 106.1, 110.5, 118.2, 120.0, 120.8, 125.7, 125.9, 132.5, 138.2, 144.2, 147.0, 169.8, 196.7. Anal. Calcd for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.32; N, 7.99. Found: C, 71.99; H, 6.34; N, 7.99.

Methyl 2-methyl-7-oxo-2,5,6,7-tetrahydro-1,5-methano-1*H*-azonino[4,3-*b*]indole-4(*E*)-acrylate (6d): mp 288–289 °C (acetone); IR 1570, 1610, 1670, 3300; ^{1}H NMR ($CDCl_3$–CD_3OD, 200 MHz) 2.56 (m, 2 H), 2.85 (dd, J = 15, 2.5, 1 H), 2.96 (s, 3 H), 3.35 (m, 1 H), 3.40 (dm, J = 15, 1 H), 3.71 (s, 3 H), 5.00 (t, 1 H), 5.40 (d, J = 15, 1 H), 6.40 (s, 1 H), 7.20–7.50 (m, 4 H), 7.81 (d, J = 8, 1 H), 10.47 (br s, 1 H); ^{13}C NMR (50.3 MHz) 25.3, 30.5, 41.5, 44.8, 50.4, 50.5, 102.0, 106.3, 112.2, 117.9, 120.5, 120.6, 126.2, 127.0, 132.0, 136.6, 144.4, 147.5, 170.0, 194.6. Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99; N, 8.32. Found: C, 71.13; H, 6.00; N, 8.17.

General Procedure for the Preparation of Dihydropyridines 13–21. Acetylindole **1** or **2** (3 mmol) in anhydrous THF (40 mL) was allowed to react as above with LDA (3 or 6 mmol) and then with pyridinium iodides **3** (3 mmol) at −30 °C for 1.5 h. TCAA or TFAA (9 mmol) was slowly added, and the mixture was stirred at 0 °C for 3 h. Workup as above gave a crude residue which was chromatographed (hexane–AcOEt, increasing polarity). The product ratio and yields are given in Table 1. ^{13}C NMR assignments are listed in Table 2. Melting points, IR, ^{1}H NMR, and elemental analyses are provided below. The dihydropyridines are reported in the same order as in Table 1.

5-Acetyl-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trifluoroacetyl)-1,2-dihydropyridine (13b): mp 80–82 °C (cyclohexane); IR 1561, 1615, 1651; ^{1}H NMR (200 MHz) 2.30 (s, 3 H), 2.98 (dd, J = 14.6, 3.8, 1 H), 3.28 (dd, J = 14.6, 7, 1 H), 3.37 (s, 3 H), 4.02 (s, 3 H), 5.34 (m, 1 H), 7.12–7.40 (m, 4 H), 7.58 (br s, 1 H), 7.69 (dm, J = 8, 1 H), 7.70 (br s, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_3F_3$: C, 62.37; H, 4.74; N, 6.93. Found: C, 62.22; H, 4.89; N, 6.67.

3-Acetyl-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trifluoroacetyl)-1,4-dihydropyridine (19b): mp 150 °C (acetone–Et_2O); IR 1613, 1645, 1652; ^{1}H NMR (300 MHz) 2.26 (s, 3 H), 2.94 (d, J = 6, 2 H), 3.35 (s, 3 H), 3.97 (s, 3 H), 4.53 (t, J = 6, 1 H), 6.95 (s, 1 H), 7.13 (m, 1 H), 7.23 (s, 1 H), 7.35 (m, 2 H), 7.42 (s, 1 H), 7.72 (dt, J = 8, 0.9, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_3F_3$: C, 62.37; H, 4.74; N, 6.93. Found: C, 62.34; H, 4.75; N, 6.85.

5-Acetyl-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trichloroacetyl)-1,2-dihydropyridine (14b): mp 146–148 °C (Et_2O); IR 1596, 1630, 1667; ^{1}H NMR (300 MHz) 2.27 (s, 3 H), 2.95 (dd, J = 14, 4, 1 H), 3.26 (dd, J = 14, 6.6, 1 H), 3.37 (s, 3 H), 3.99 (s, 3 H), 5.31 (m, 1 H), 7.10–7.42 (m, 4 H), 7.65 (dd, J = 8, 0.8, 1 H), 7.76 (s, 1 H), 8.06 (s, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_3Cl_3$: C, 55.59; H, 4.22; N, 6.17. Found: C, 55.33; H, 4.27; N, 5.93.

3-Acetyl-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,4-dihydropyridine (20b): mp 163–165 °C (acetone–Et_2O); IR 1557, 1614, 1657; ^{1}H NMR (300 MHz) 2.27 (s, 3 H), 2.87 (dd, J = 12.5, 6.2, 1 H), 2.97 (dd, J = 12.5, 6, 1 H), 3.33 (s, 3 H), 3.97 (s, 3 H), 4.57 (t, J = 6, 1 H), 6.98 (s, 1 H), 7.13 (m, 1 H), 7.35 (m, 2 H), 7.47 (s, 1 H), 7.73 (s, 1 H), 7.74 (d, J = 8, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_3Cl_3 \cdot 1H_2O$: C, 53.46; H, 4.48; N, 5.93. Found: C, 53.52; H, 4.33; N, 5.87.

5-(Methoxycarbonyl)-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trifluoroacetyl)-1,2-dihydropyridine (13c): mp 164 °C (Et_2O); IR 1616, 1659, 1696; ^{1}H NMR (300 MHz) 2.88 (dd, J = 14.8, 3.6, 1 H), 3.30 (masked, 1 H), 3.32 (s, 3 H), 3.78 (s, 3 H), 4.03 (s, 3 H), 5.36 (dd, J = 7.6, 3.6, 1 H), 7.10–7.40 (m, 4 H), 7.70 (d, J =8, 1 H), 7.75 (s, 1 H), 7.89 (s, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_4F_3$: C, 60.00; H, 4.56; N, 6.66. Found: C, 60.02; H, 4.62; N, 6.58.

3-(Methoxycarbonyl)-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trifluoroacetyl)-1,4-dihydropyridine (19c): mp 73 °C (Et_2O); IR 1557, 1652, 1705; ^{1}H NMR (300 MHz) 3.00 (d, J = 6, 2 H), 3.30 (s, 3 H), 3.69 (s, 3 H), 3.99 (s, 3 H), 4.45 (t, J = 6, 1 H), 7.11 (s, 1 H), 7.15 (m, 1 H), 7.22 (s, 1 H), 7.35 (m, 2 H), 7.43 (s, 1 H), 7.72 (dm, J = 8, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_4F_3$: C, 60.00; H, 4.56; N, 6.66. Found: C, 60.01; H, 4.53; N, 6.59.

5-(Methoxycarbonyl)-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trichloroacetyl)-1,2-dihydropyridine (14c): ^{1}H NMR (200 MHz, from the mixture of **14c** + **17c**) 2.93 (dd, J = 14.6, 3.6, 1 H), 3.30 (masked, 1 H), 3.32 (s, 3 H), 3.78 (s, 3 H), 4.04 (s, 3 H), 5.36 (m, 1 H), 7.10–7.40 (m, 4 H), 7.69 (m, 1 H), 7.99 (s, 1 H), 8.27 (s, 1 H).

3-(Methoxycarbonyl)-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,2-dihydropyridine (17c): ^{1}H NMR (200 MHz, from the mixture of **14c** + **17c**) 3.04 (dd, J = 14.8, 3.8, 1 H), 3.30 (masked, 1 H), 3.35 (s, 3 H), 3.75 (s, 3 H), 4.03 (s, 3 H), 5.23 (m, 1 H), 7.10–7.40 (m, 4 H), 7.68 (m, 1 H), 7.91 (s, 1 H), 8.27 (s, 1 H).

3-(Methoxycarbonyl)-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,4-dihydropyridine (20c): mp 158–160 °C (Et_2O); IR 1560, 1615, 1639, 1702; ^{1}H NMR (200 MHz) 2.93 and 3.03 (2 dd, J = 12.5, 6, 2 H), 3.30 (s, 3 H), 3.69 (s, 3 H), 4.00 (s, 3 H), 4.47 (t, J = 6, 1 H), 7.13 (m, 1 H), 7.13 (s, 1 H), 7.37 (m, 2 H), 7.46 (s, 1 H), 7.73 (s, 1 H), 7.74 (dm, J = 8, 1 H). Anal. Calcd for $C_{21}H_{19}N_2O_4Cl_3$: C, 53.69; H, 4.08; N, 5.96. Found: C, 53.70; H, 4.10; N, 5.93.

5-[(*E*)-2-(Methoxycarbonyl)vinyl]-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trifluoroacetyl)-1,2-dihydropyridine (13d): mp 152–153 °C (acetone–Et_2O); IR 1568, 1620, 1656, 1700; ^{1}H NMR (200 MHz) 2.90 (dd, J = 16.6, 2.8, 1 H), 3.27 (s, 3 H), 3.55 (dd, J = 16.6, 7.8, 1 H), 3.72 (s, 3 H), 4.06 (s, 3 H), 5.17 (dd, J = 7.8, 2.8, 1 H), 5.80 (d, J = 15.8, 1 H), 6.97 (br s, 1 H), 7.10–7.41 (m, 5 H), 7.63 (br s, 1 H), 7.66 (d, J = 8, 1 H). Anal. Calcd for $C_{23}H_{21}N_2O_4F_3$: C, 61.88; H, 4.74; N, 6.28. Found: C, 61.89; H, 4.69; N, 6.24.

3-[(*E*)-2-(Methoxycarbonyl)vinyl]-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trifluoroacetyl)-1,4-dihydropyridine (19d): mp 174 °C (acetone–iPr_2O); IR 1553, 1615, 1639, 1715; ^{1}H NMR (500 MHz) 2.83 (dd, J = 13, 6, 1 H), 2.99 (dd, J = 13, 6, 1 H), 3.34 (s, 3 H), 3.69 (s, 3 H), 3.95 (s, 3 H), 4.33 (t, J = 6, 1 H), 5.89 (d, J = 16, 1 H), 6.71 (s, 1 H), 7.12 (ddd, J = 8, 7, 1, 1 H), 7.31 (d, J = 16, 1 H), 7.34 (s, 1 H), 7.37 (dd, J = 7, 1.5, 1 H), 7.44 (m, 1 H), 7.48 (s, 1 H), 7.68 (dm, J = 8, 1 H). Anal. Calcd for $C_{23}H_{21}N_2O_4F_3$: C, 61.88; H, 4.74; N, 6.27; Found: C, 61.92; H, 4.77; N, 6.21.

5-[(*E*)-2-(Methoxycarbonyl)vinyl]-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trichloroacetyl)-1,2-dihydropyridine (14d): mp 173–175 °C (acetone–Et_2O); IR 1558, 1593, 1652, 1707; ^{1}H NMR (200 MHz) 2.93 (dd, J = 16, 3.2, 1 H), 3.30 (s, 3 H), 3.53 (dd, J = 16, 7.2, 1 H), 3.75 (s, 3 H), 4.06 (s, 3 H), 5.13 (dd, J = 7.2, 3.2, 1 H), 5.77 (d, J = 15.8, 1 H), 7.10–7.42 (m, 6 H), 7.65 (d, J = 8, 1 H), 7.94 (s, 1 H). Anal. Calcd for $C_{23}H_{21}N_2O_4Cl_3$: C, 55.72; H, 4.27; N, 5.65. Found: C, 55.79; H, 4.30; N, 5.68.

3-[(*E*)-2-(Methoxycarbonyl)vinyl]-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,4-dihydropyridine (20d): mp 171–172 °C (acetone–Et_2O); IR 1554, 1615, 1635, 1650, 1702; ^{1}H NMR (200 MHz) 2.98 (d, J = 6, 2 H), 3.30 (s, 3 H), 3.70 (s, 3 H), 3.96 (s, 3 H), 4.39 (t, J = 6, 1 H), 5.88 (d, J = 15.6, 1 H), 6.36 (s, 1 H), 7.10–7.40 (m, 5 H), 7.72 (d, J = 8, 1 H), 7.74 (s, 1 H). Anal. Calcd for $C_{23}H_{21}N_2O_4Cl_3$: C, 55.72; H, 4.27; N, 5.65. Found: C, 55.60; H, 4.18; N, 5.77.

5-Cyano-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trifluoroacetyl)-1,2-dihydropyridine (13e): ^{1}H NMR (300 MHz) 2.87 (dd, J = 15, 3.6, 1 H), 3.33 (s, 3 H), 3.38 (dd, J = 15, 7.8, 1 H), 4.06 (s, 3 H), 5.36 (dd, J = 7.8, 3.6, 1 H), 7.18–7.45 (m, 6 H), 7.70 (d, J = 8, 1 H).

3-Cyano-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trifluoroacetyl)-1,2-dihydropyridine (16e): ^{1}H NMR (300 MHz, from the mixture of **13e** + **16e**) 3.22 (dd, J = 16, 4.4, 1 H), 3.34 (s, 3 H), 3.53 (dd, J = 16, 6.8, 1 H), 4.05 (s, 3 H), 4.96 (dd, J = 6.8, 4.4, 1 H), 7.15–7.50 (m, 6 H), 7.70 (d, J = 8, 1 H).

3-Cyano-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trifluoroacetyl)-1,4-dihydropyridine (19e): mp 154 °C (Et_2O); IR 1557, 1614, 1650, 1660, 2213; ^{1}H NMR (300 MHz) 3.07 (dd, J = 14.6, 4.6, 1 H), 3.17 (dd, J = 14.6, 6.7, 1 H), 3.22 (s, 3 H), 4.01 (s, 3 H), 4.18 (m, 1 H), 6.60 (s, 1 H), 7.10–7.40 (m, 5 H), 7.72 (d, J = 8, 1 H). Anal. Calcd for $C_{20}H_{16}N_3O_2F_3$: C, 62.01; H, 4.16; N, 10.85. Found: C, 62.01; H, 4.15; N, 10.78.

5-Cyano-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-3-(trichloroacetyl)-1,2-dihydropyridine (14e): ^{1}H NMR (300 MHz, from the mixture of **14e** + **17e**) 2.90 (dd, J = 15, 3.8, 1 H), 3.33 (s, 3 H), 3.37 (dd, J = 15, 7.9, 1 H), 4.07 (s, 3 H), 5.38 (m, 1 H), 7.10–7.40 (m, 5 H), 7.70 (m, 1 H), 7.76 (s, 1 H).

3-Cyano-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,2-dihydropyridine (17e): mp 109 °C (Et_2O); ^{1}H NMR (200 MHz) 3.19 (dd, J = 15.6, 4.7, 1 H), 3.50 (dd, J = 15.6, 6.5, 1 H), 3.36 (s, 3 H), 4.04 (s, 3 H), 4.94 (m, 1 H), 7.10–7.50 (m, 4 H), 7.54 (s, 1 H), 7.70 (d, J = 8, 1 H), 7.96 (s, 1 H). Anal. Calcd for $C_{20}H_{16}N_3O_2Cl_3$: C, 55.00; H, 3.69; N, 9.62. Found: C, 54.99; H, 3.69; N, 9.42.

3-Cyano-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,4-dihydropyridine (20e): mp 184–185 °C (CH_2Cl_2); IR 1550, 1618, 1651, 2206; ^{1}H NMR (DMSO-d_6, 200 MHz) 2.86 (dd, J = 14, 4.8, 1 H), 3.13 (dd, J = 14, 7, 1 H), 3.32 (s, 3 H), 3.96 (s, 3 H), 4.06 (dd, J = 7, 4.8, 1 H), 7.12 (dd, J = 7.9, 7, 1 H), 7.31 (s, 1 H), 7.37 (m, 1 H), 7.45 (s, 1 H), 7.56 (d, J = 8.5, 1 H), 7.70 (d, J = 7.9, 1 H), 7.83 (s, 1 H). Anal. Calcd for $C_{20}H_{16}N_3O_2Cl_3 \cdot 1/2H_2O$: C, 53.89; H, 3.84; N, 9.42. Found: C, 53.95; H, 3.71; N, 9.23.

3-Ethyl-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-5-(trichloroacetyl)-1,4-dihydropyridine (20g): ^{1}H NMR (200 MHz) 1.06 (t, J = 7.3, 3 H), 2.10 (m, 2 H), 2.90 (dd, J = 12.5, 4.5, 1 H), 3.10 (dd, J = 12.5, 6, 1 H), 3.19 (s, 3H), 4.04 (s, 3 H), 4.06 (masked, 1 H), 5.76 (br s, 1 H), 7.15 (m, 1 H), 7.39 (m, 3 H), 7.74 (d, J = 8, 1 H), 7.76 (s, 1 H).

2-[(2-Indolylcarbonyl)methyl]-5-(methoxycarbonyl)-1-methyl-3-(trichloroacetyl)-1,2-dihydropyridine (15c): ^{1}H NMR (DMSO-d_6, 300 MHz, from the mixture of **15c** + **18c**) 2.90 (dd, J = 13, 3.5, 1 H), 3.37 (masked, 1 H), 3.37 (s, 3 H), 3.67 (s, 3 H), 5.30 (t, J = 3.5, 1 H), 7.00–7.50 (m, 4 H), 7.70 (d, J = 8, 1 H), 8.02 (s, 1 H), 8.19 (s, 1 H), 11.90 (s, 1 H).

2-[(2-Indolylcarbonyl)methyl]-3-(methoxycarbonyl)-1-methyl-5-(trichloroacetyl)-1,2-dihydropyridine (18c): ^{1}H NMR (DMSO-d_6, 300 MHz, from the mixture of **15c** + **18c**) 3.15 (dd, J = 13, 3, 1 H), 3.37 (masked, 1 H), 3.42 (s, 3 H), 3.63 (s, 3 H), 5.20 (t, J = 3 Hz, 1 H), 7.00–7.50 (m, 4 H), 7.70 (d, J = 8, 1 H), 7.80 (s, 1 H), 8.19 (s, 1 H), 11.90 (s, 1 H).

4-[(2-Indolylcarbonyl)methyl]-3-(methoxycarbonyl)-1-methyl-5-(trichloroacetyl)-1,4-dihydropyridine (21c): mp 158 °C (acetone–MeOH); IR 1561, 1638, 1652, 1708, 3299; ^{1}H NMR (DMSO-d_6, 300 MHz) 2.78 (m, 2 H), 3.37 (s, 3 H), 3.57 (s, 3 H), 4.28 (t, J = 5.8, 1 H), 7.05 (dd, J = 8, 7, 1 H), 7.30 (m, 2 H), 7.32 (s, 1 H), 7.40 (d, J = 8, 1 H), 7.69 (d, J = 8, 1 H), 7.86 (s, 1 H), 11.70 (s, 1 H). Anal. Calcd for $C_{20}H_{17}N_2O_4Cl_3$: C, 52.71; H, 3.76; N, 6.15. Found: C, 52.49; H, 3.76; N, 5.92.

2-[(2-Indolylcarbonyl)methyl]-5-[(*E*)-2-(methoxycarbonyl)vinyl]-1-methyl-3-(trichloroacetyl)-1,2-dihydropyridine (15d): mp 179 °C (acetone–MeOH); IR 1556, 1592, 1638, 1705, 3376; ^{1}H NMR (DMSO-d_6, 300 MHz) 3.04 (dd, J = 15.6, 4.3, 1 H), 3.34 (s, 3 H), 3.46 (dd, J = 15.6, 5.7, 1 H), 3.60 (s, 3 H), 5.22 (dd, J = 5.7, 4.3, 1 H), 5.79 (d, J = 16, 1 H), 7.05 (m, 1 H), 7.12 (s, 1 H), 7.22–7.40 (m, 4 H), 7.64 (d, J = 8 Hz, 1 H), 8.12 (s, 1 H), 11.80 (s, 1 H). Anal. Calcd for $C_{22}H_{19}N_2O_4Cl_3$: C, 54.85; H, 3.96; N, 5.81. Found: C, 54.78; H, 4.02; N, 5.72.

4-[(2-Indolylcarbonyl)methyl]-3-[(*E*)-2-(methoxycarbonyl)vinyl]-1-methyl-5-(trichloroacetyl)-1,4-dihydropyridine (21d): mp 170 °C; IR 1557, 1609, 1642, 1705; ^{1}H NMR (DMSO-d_6, 200 MHz) 2.77 (dd, J = 13.5, 5.5, 1 H), 2.90 (dd, J = 13.5, 5.5, 1 H), 3.37 (s, 3 H), 3.64 (s, 3 H), 4.23 (t, J = 5.5, 1 H), 5.94 (d, J = 15.6, 1 H), 6.99 (s, 1 H), 7.04 (m, 1 H), 7.15–7.40 (m, 4 H), 7.64 (d, J = 8, 1 H), 7.91 (s, 1 H), 11.70 (s, 1 H). Anal. Calcd for $C_{22}H_{19}N_2O_4Cl_3 \cdot 1/4H_2O$: C, 54.34; H, 4.03; N, 5.75. Found: C, 54.31; H, 4.10; N, 5.60.

General Procedure for the Preparation of Dihydropyridines 22–24. (Trichloroacetyl)dihydropyridine **20** or **21** (0.4 mmol) in a MeOH (or EtOH)–THF solution (1:1, 20 mL) was slowly added to a solution of MeONa (or EtONa) (1.7 mmol) in MeOH (or EtOH) (20 mL), and the resulting mixture was stirred at room temperature for 3 min. The solvents were removed, and the residue was partitioned between H_2O and Et_2O and extracted with Et_2O. Evaporation of the dried extracts gave a crude residue which was chromatographed (flash, 8:2 hexane–AcOEt and AcOEt). Yields, melting points, IR, ^{1}H NMR, and elemental analyses are given below. ^{13}C NMR assignments are listed in Table 2.

3-Acetyl-5-(methoxycarbonyl)-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-1,4-dihydropyridine (22b): 84%; mp 116–118 °C (Et_2O); IR 1563, 1624, 1648, 1699; ^{1}H NMR (200 MHz) 2.21 (s, 3 H), 2.92 (d, J = 6, 2 H), 3.21 (s, 3 H), 3.65 (s, 3 H), 4.00 (s, 3 H), 4.50 (t, J = 6, 1 H), 6.95 (s, 1 H), 7.12 (s, 1 H), 7.13 (m, 1 H), 7.35 (m, 2 H), 7.47 (s, 1 H), 7.65 (d, J = 8, 1 H). Anal. Calcd for $C_{21}H_{22}N_2O_4 \cdot 1/4\ H_2O$: C, 68.00; H, 6.11; N, 7.55. Found: C, 68.05; H, 6.02; N, 7.45.

3,5-Bis(methoxycarbonyl)-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-1,4-dihydropyridine (22c): 88%; mp 113–115 °C (Et_2O); IR 1572,1651,1698; ^{1}H NMR (300 MHz) 2.98 (d, J = 6.1, 2 H), 3.17 (s, 3 H), 3.66 (s, 6 H), 4.03 (s, 3 H), 4.37 (t, J = 6.1, 1 H), 7.10 (s, 2 H), 7.13 (m, 1 H), 7.35 (m., 2 H), 7.44 (s, 1 H), 7.71 (d, J = 8, 1 H). Anal. Calcd for $C_{21}H_{22}N_2O_5$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.90; H, 5.80; N, 7.29.

3-(Methoxycarbonyl)-5-[(*E*)-2-(methoxycarbonyl)vinyl]-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-1,4-dihydropyridine (22d): 85%; mp 124–126 °C (Et_2O–MeOH); IR 1561, 1607, 1651, 1690, 1708; ^{1}H NMR (200 MHz) 2.85 (dd, J = 13.1, 5.8, 1 H), 3.10 (dd, J = 13.1, 5.6, 1 H), 3.14 (s, 3 H), 3.59 (s, 3 H), 3.68 (s, 3 H), 3.99 (s, 3 H), 4.28 (dd, J = 5.8, 5.6, 1 H), 5.81 (d, J = 15.5, 1 H), 6.31 (s, 1 H), 7.10 (s, 1 H), 7.11–7.40 (m, 5 H), 7.69 (d, J = 8, 1 H). Anal. Calcd for $C_{23}H_{24}N_2O_5 \cdot 1/2H_2O$: C, 66.17; H, 6.03; N, 6.71. Found: C, 66.28; H, 5.88; N, 6.65.

3-Cyano-5-(methoxycarbonyl)-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-1,4-dihydropyridine (22e): 90%; mp 127 °C (Et_2O–acetone); IR 1576, 1655, 1682, 2198; ^{1}H NMR (300 MHz) 3.14 (d, J = 5.7, 2 H), 3.14 (s, 3 H), 3.70 (s, 3 H), 4.06 (s, 3 H), 4.15 (t, J = 5.7, 1 H), 6.56 (s, 1 H), 7.06 (s, 1 H), 7.15 (m, 1 H), 7.36 (m, 3 H), 7.70 (d, J = 8, 1 H). Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.75; H, 5.48; N, 11.99.

3-(Ethoxycarbonyl)-5-(methoxycarbonyl)-1-methyl-4-[((1-methyl-2-indolyl)carbonyl)methyl]-1,4-dihydropyridine (23c): 90%; mp 107–108 °C (cyclohexane); IR 1568, 1651, 1694; ^{1}H NMR (300 MHz) 1.20 (t, J = 7.1, 3 H), 2.96 (d, J = 6, 2 H), 3.18 (s, 3 H), 3.65 (s, 3 H), 4.02 (s, 3 H), 4.14 (m, 2 H), 4.38 (t, J = 6, 1 H), 7.11 (m, 3 H), 7.35 (m, 2 H), 7.45 (s, 1 H), 7.70 (d, J = 8, 1 H). Anal. Calcd for $C_{22}H_{24}N_2O_5$: C, 66.75; H, 6.10; N, 7.07. Found: C, 66.54; H, 6.16; N, 7.00.

3,5-Bis(methoxycarbonyl)-4-[(2-indolylcarbonyl)methyl]-1-methyl-1,4-dihydropyridine (24c): 90%; mp 135 °C (MeOH-Et_2O); IR 1570, 1638, 1656, 1714; ^{1}H NMR (300 MHz) 3.00 (d, J = 5.7, 2 H), 3.08 (s, 3 H), 3.63 (s, 6 H), 4.40 (t, J = 5.7, 1 H), 7.09 (s, 2 H), 7.13 (m, 1 H), 7.33 (m, 2 H), 7.45 (d, J = 7.6, 1 H), 7.73 (d, J = 8, 1 H), 9.70 (br s, 1 H). Anal. Calcd for C_{20} H_{20} N_2O_5: C, 65.21; H, 5.47; N, 7.60. Found: C, 64.90; H, 5.69; N, 7.17.

4-[((2-Indolylmethyl)carbonyl)methyl]-3-(methoxycarbonyl)-5-[(*E*)-2-(methoxycarbonyl)vinyl]-1-methyl-1,4-dihydropyridine (24d): 95%; mp 189 °C (acetonitrile); IR 1559, 1604, 1635, 1692, 1702; ^{1}H NMR (DMSO-d_6, 300 MHz) 2.69 (dd, J = 13.8, 5, 1 H), 2.96 (dd, J = 13.8, 5.8, 1 H), 3.19 (s, 3 H), 3.41 (s, 3 H), 3.59 (s, 3 H), 4.11 (dd, J = 5.8, 5.1, 1 H), 5.80 (d, J = 15.6, 1 H), 6.90 (s, 1 H), 7.07 (m, 1 H), 7.15 (m, 1 H), 7.24 (m, 2 H), 7.40 (d, J = 7.5, 1 H), 7.65 (d, J = 8, 1 H), 11.70 (s, 1 H). Anal. Calcd for $C_{22}H_{22}N_2O_5$: C, 66.99; H, 5.62; N, 7.10. Found: C, 66.62; H, 5.61; N, 7.41.

3,5-Bis(methoxycarbonyl)-1-methyl-2-[((1-methyl-2-indolyl)carbonyl)methyl]-1,2-dihydropyridine (25). This compound was prepared as described in the above general procedure, starting from a mixture of dihydropyridines **14c** and **17c** (0.1 g,

0.21 mmol) and MeONa (0.8 mmol): 73 mg (90%); mp 104–106 °C (*i*-Pr_2O); IR 1630, 1673; ^1H NMR (200 MHz) 2.93 (dd, J = 14.7, 3.7, 1 H), 3.19 (s, 3 H), 3.34 (dd, J = 14.7, 7.8, 1 H), 3.70 (s, 3 H), 3.74 (s, 3 H), 4.05 (s, 3 H), 5.19 (m, 1 H), 7.16 (m, 1 H), 7.33 (s, 1 H), 7.38 (m, 2 H), 7.51 (br s, 1 H), 7.66 (br s, 1 H), 7.72 (d, J = 8, 1 H); ^{13}C NMR, Table 2. Anal. Calcd for $C_{21}H_{22}N_2O_5$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.99; H, 5.93; N, 7.27.

3,5-Bis(methoxycarbonyl)-2-[(2-indolylcarbonyl)methyl]-1-methyl-1,2-dihydropyridine (26). This compound was prepared as described in the above general procedure, starting from a mixture of dihydropyridines **15c** and **18 c** (0.1 g, 0.22 mmol) and MeONa (0.9 mmol): 74 mg (92%); mp 148 °C (Et_2O); IR 1627, 1639, 1673; ^1H NMR (300 MHz) 2.92 (dd, J = 14.4, 3.5, 1 H), 3.13 (s, 3 H), 3.30 (dd, J = 14.4, 8.2, 1 H), 3.71 (s, 3 H), 3.75 (s, 3 H), 5.21 (m, 1 H), 7.16 (m, 1 H), 7.28 (s, 1 H), 7.37 (m, 1 H), 7.45 (d, J = 7.5, 1 H), 7.54 (s, 1 H), 7.69 (s, 1 H), 7.71 (d, J = 8, 1 H); ^{13}C NMR, Table 2. Anal. Calcd for $C_{20}H_{20}N_2O_5 \cdot {}^1/_2H_2O$: C, 63.65; H, 5.60; N, 7.42. Found: C, 63.73; H, 5.45; N, 7.27.

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