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Synthetic Studies on Indoles and Related Compounds. XXV.[1] The Friedel–Crafts Acylation of Ethyl 1*H*-Indole-2-carboxylate. (2)[2]

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The Friedel–Crafts acylation of ethyl 1*H*-indole-2-carboxylate (1) with various acylating reagents having a functional group or hetero atom and the acylation of some derivatives (6, 7, 8, and 9) of ethyl 1*H*-indole-2-carboxylate (1) with simple acylating reagents are described. Acylation occurred at the C_3-position or on the benzene moiety (mainly at the C_5-position) of the indole nucleus. The regioselectivity of the above acylation of indoles (1, 6, 7, 8, and 9) is discussed.

Keywords Friedel–Crafts reaction; ethyl 1*H*-indole-2-carboxylate; acylation; regioselectivity; aluminum chloride; *N*-benzylindole

We have reported[2] that the Friedel–Crafts acylation of ethyl 1*H*-indole-2-carboxylate (**1**) occurred not only at the most reactive C_3-position, but also on the benzene moiety. The ratio of products depended on the kinds of acylating reagents, Lewis acids, and solvents, and other reaction conditions. It was especially characteristic that a reagent with an electron-donating group (R) tended to afford the 3-acyl product whereas one with an electron-attracting R afforded the product acylated on the benzene moiety (mainly at C-5). On the basis of the above result, we studied the scope and limitations, especially the regioselectivity for C-3, of the Friedel–Crafts acylation of ethyl 1*H*-indole-2-carboxylate (**1**) and its derivatives. We report here the regioselectivity of the Friedel–Crafts acylation of ethyl 1*H*-indole-2-carboxylate (**1**) and its derivatives with various acylating reagents having a functional group or hetero atom.

The reaction was carried out under the same conditions as used in our previous paper[2] (the molar ratio of indole : acylating reagent : aluminum chloride was 1 : 2 : 2 in 1,2-dichloroethane, the standard conditions) in order to investigate the effect of functional groups in the acylating reagents, and the results are summarized in Table I. From run 1 to run 6, it seems that the acid chlorides afforded mainly 3-acyl products whereas the acid anhydrides tended to afford 5-acyl ones more, but the total yields were not related to the acylating reagents used.

We next investigated other reaction conditions in order to obtain the 3-acyl products more effectively, in the case of the four reagents (**2b**—**e**) of runs 2, 3, 4, and 5. We know from the previous paper[2] that the kind and the amount of Lewis acid, and the solvent affected the yield and the regioselectivity of the acylation. The results are shown in Table II (runs 11—16). In the case of the acid chloride (**2b**), titanium tetrachloride in place of aluminum chloride greatly improved the yield of 3-acyl product (run 11 in Table II) leaving the high regioselectivity intact. On the other hand, in the case of the acid chloride (**2c**), aluminum chloride seems to be the best Lewis acid with respect to both the yield of acylated product and the regioselectivity for C_3-acylation. In the reaction using succinic anhydride (**2d**), it was found that the use of more aluminum chloride increased the amount of 5-acyl product (see run 4 in Table I and run 14 in Table II) as described in the previous paper,[2] and the regioselectivity was greatly affected by the kind of solvent used; nitrobenzene made C_3-acylation much more favorable as reported previously,[2] although the yield was not satisfied. The reaction with phthalic anhydride (**2e**) resulted in recovery of most of the starting material under the standard conditions, but the yield was improved by using 4 mol eq of aluminum chloride, although the main product was the 5-acyl one (run 16 in Table II).

As to mesitoyl chloride and pivaloyl chloride, the former under the standard conditions and the latter using boron trifluoride exclusively afforded the 3-acyl product in good yield, respectively. This result coincides with the previous finding[2] that a reagent having an electron-donating R group tended to substitute at the C_3-position of ethyl 1*H*-indole-2-carboxylate (**1**).

Dichloromethyl methyl ether, which is a different type of acylating reagent from acid chloride and anhydride, gave unsatisfactory yield and regioselectivity when aluminum chloride was used (run 8 in Table I). Although the use of a larger amount of aluminum chloride did not improve them (runs 18 and 19 in Table II), tin tetrachloride gave the 3-formylindole (**3h**) exclusively (run 20 in Table II).

The oxazolone derivative (**2i**), which is a kind of cyclic acid anhydride, and the acid chloride (**2j**) derived from glycine gave the 5- or 7-acyl products in low yields, but no 3-acylindole (runs 9 and 10). All attempts to obtain 3-acylindole with glycine derivatives were unsuccessful.

The results in Tables I and II suggest that it is difficult to find regularity of regioselectivity in the Friedel–Crafts acylation of ethyl 1*H*-indole-2-carboxylate (**1**) with acylating reagents having a functional group or hetero atom with some reagents, the regioselectivity can be controlled by changing the reactions conditions but some of the glycine

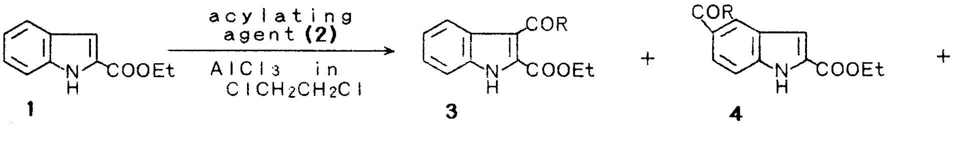

Chart 1

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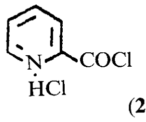
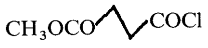
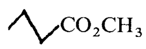
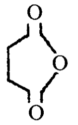
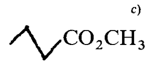
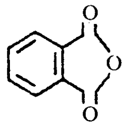
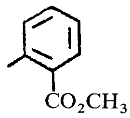
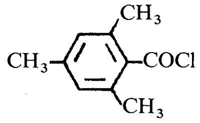
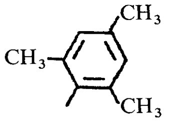
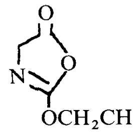
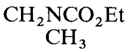
Table I. The Friedel–Crafts Acylation of Ethyl 1*H*-Indole-2-carboxylate (**1**) with Various Acylating Agents

Run	Acylating agent (**2**)	Temp.[a]	Time (h)	Products (**3**, **4**, **5**)			Recovery of **1** (%)
				R	Total yield (%)	Ratio of **3**:**4**:**5**	
1	 (**2a**)	r.t.[b]	0.8		75.7	100: 0:0	Trace
2	 (**2b**)	Reflux	2.5		30.3	100: 0:0	13.7
3	 (**2c**)	60 °C	1.5		84.2	94: 5:1	9.3
4	 (**2d**)	Reflux	3.7	 [c]	44.0[d]	46:46:8	27.3
5	 (**2e**)	Reflux	1.5	 [c]	15.9	79:21:0	79.8
6	 (**2f**)	70 °C	2.5		69.9	100: 0:0	11.1
7	$(CH_3)_3CCOCl$ (**2g**)	Reflux	1.0	$C(CH_3)_3$	0	—	84.7
8	Cl_2CHOCH_3 (**2h**)	r.t.	2.2	H	45.7	53:25:22	Trace
9	 (**2i**)	r.t.	24.0	 $CH_2\underset{H}{N}CO_2Et$	29.4	0:73:27	0
10	 $EtOCO\underset{CH_3}{N}CH_2COCl$ (**2j**)	r.t.	4.0	 $CH_2\underset{CH_3}{N}CO_2Et$	26.7	0:75:25	8.8

[a] Temp., temperature. [b] r.t., room temperature. [c] Yield after methylation using CH_2N_2. [d] The *N*-acylated product was also isolated in 4.4% yield.

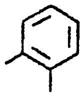
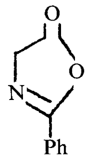
derivatives could not provide selective C_3-acylation of ethyl 1*H*-indole-2-carboxylate (**1**).

So, we next focused our attention on the derivatives of ethyl 1*H*-indole-2-carboxylate (**1**) as substrates for regioselective C_3-acylation and the results are summarized in Table III. At first, we carried out acylation of the *N*-benzylindole (**6**), because an *N*-alkyl substituent is expected to make the C_3-position more nucleophilic than the corresponding NH one, and the benzyl group could be removed by our novel debenzylation method.[3] The results obtained by using the *N*-benzylindole (**6**) are shown in runs 23 and 24 in Table III. Apparently, the *N*-benzyl substituent did make C_3-acylation more advantageous (see runs 22 and 23) under the same conditions.

Use of acetic anhydride made the C_3-acylation more favorable (run 24 in Table III). These results revealed that *N*-benzylindole (**6**) is a better substrate for C_3-acylation. It is also noteworthy that debenzylation did not occur under the Friedel–Crafts acylation conditions, although the debenzylation conditions (aluminum chloride–benzene)[3] closely resemble the Friedel–Crafts acylation conditions.

As it was reported that indole-2-carboxamide is superior to the indole-2-ester compound (**1**) in C_3-formylation by means of the Vilsmeier reaction,[4] we next investigated the Friedel–Crafts acylation of the indole-2-carboxamide (**7**). The acetylation, contrary to our expectation, gave the 3-acetylindole (**13l**) with low selectivity, and the yield of the 7-acetyl compound (**15l**) was higher than that of the 5-acetyl one (**14l**) (run 25 in Table III). This result is the first such case in the course of our investigation, but the reason is not clear. In the chloroacetylation of the indole-2-amide (**7**) the 5-acyl compound (**14m**) was obtained as the main

TABLE II. The Friedel–Crafts Acylation under Different Conditions from Table I

Run	Acylating agent (**2**)	Lewis acid	Solvent[a)]	Temp.	Time (h)	Products (**3**, **4**, **5**) R	Products (**3**, **4**, **5**) Total yield (%)	Products (**3**, **4**, **5**) Ratio of **3**:**4**:**5**	Recovery of **1** (%)
11	**2b**	$TiCl_4$	A	60 °C	3.0		71	100: 0: 0	13.3
12	**2c**	$BF_3 \cdot OEt_2$	B	60 °C	1.0	 CO_2CH_3	34	78:22: 0	45.9
13	**2c**	$AlCl_3$	B	r.t.	1.5	 CO_2CH_3	95	95: 5: 0	0
14	**2d**	$AlCl_3$[b)]	A	r.t.	1.5	 CO_2CH_3[c)]	81	4:73:23	7.8
15	**2d**	$AlCl_3$	B	110 °C	1.5	 CO_2CH_3[c)]	31	83:17: 0	38.4
16	**2e**	$AlCl_3$[b)]	A	Reflux	1.5	 CO_2CH_3[c)]	75	10:90: 0	8.7
17	**2g**	$BF_3 \cdot OEt_2$	A	Reflux	8.0	$C(CH_3)_3$	61	100: 0: 0	Trace
18	**2h**	$AlCl_3$[d)]	A	r.t.	1.5	H	40	31:40:29	Trace
19	**2h**[e)]	$AlCl_3$	C	−46 °C	0.7	H	30	25:38:37	Trace
20	**2h**	$SnCl_4$	A	0 °C	0.3	H	66[f)]	100: 0: 0	Trace
21	 **2k**	$AlCl_3$[g)]	A	r.t.	1.0	$CH_2NHCOPh$	84	0:78:22	0

a) A, $ClCH_2CH_2Cl$; B, $PhNO_2$; C, CH_2Cl_2. b) Four eq with respect to **1** was used. c) Isolated after methylation. d) Five eq with respect to **1** was used. e) Five eq with respect to **1** was used. f) The *N*-CHO derivative was also isolated in 21% yield. g) Six eq with respect to **1** was used.

product (run 26 in Table III). The indole-2-ester (**1**) had also provided the 5-chloroacetyl derivative in our previous experiment.[2)] Thus, we must conclude that the indole-2-amide (**7**) is not superior to the indole-2-ester (**1**) for C_3-acylation by means of the Friedel–Crafts reaction.

The Friedel–Crafts acylation of 1*H*-indole-2-carboxylic acid (**8**) afforded almost the same result as for the indole-2-ester (**1**) in terms of regioselectivity, with the formation of an appreciable amount of the 3,5-diacetyl indole (**12l**). The products were converted to the corresponding ethyl esters for isolation and identification.

Finally, we investigated the Friedel–Crafts acylation of the 3-methylindole (**9**) which should give exclusively the product substituted on the benzene moiety. As expected, the acetylation of the 3-methylindole (**9**) afforded the 5-acetyl product (**16l**) as the major product and the 7-acetyl derivative (**17l**) as a minor product (run 28 in Table III).

On the other hand, the formylation of the 3-methylindole (**9**) using tin tetrachloride afforded the *N*-formyl product (**18h**) (run 29 in Table III). It is interesting that Friedel–Crafts acylation could occur even on indolic NH.

The structures of the products, especially the substitution position of the acyl group, were determined by the method described in our previous paper[2)] [mainly from the ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectra], and the physical and analytical data are summarized in Table IV.

In conclusion, it is difficult to anticipate the substitution position in the case of the acylation with a functionalized acylating reagent, although the electronic effect of acylating reagents could be straightforwardly explained for the previous Friedel–Crafts acylation[2)] with simple acylating reagents. This may be a consequence of complex coordination of the Lewis acid with the functional groups of the acylating reagent. Therefore, it is worth trying to change the reaction conditions in order to improve the yield and to get a desired regioisomer.

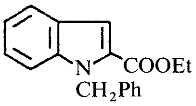
In the reactions of derivatives of the indole-2-ester (**1**) (Table III), the *N*-benzylindole (**6**) afforded more of the 3-acyl product than the corresponding NH compound did, while the indole-2-amide (**7**) was not useful for improvement of regioselective C_3-acylation. But the latter (**7**) was found to be effective for C_7-acylation. It is interested that the 3-methylindole (**9**) gave the *N*-formyl derivative (**18h**) exclusively.

The results presented above suggest that it would be interesting to investigate the Friedel–Crafts acylation of ethyl 1*H*-indole-2-carboxylate (**1**) in more detail to establish the mechanism and possible synthetic utility.

Experimental

All melting points were measured on a micro melting point hot stage apparatus (Yanagimoto) and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu IR-400 spectrometer (in Nujol, unless otherwise stated). ^{1}H-NMR spectra were measured on Hitachi R-24B (60 MHz) and JEOL GX-400 (400 MHz) spectrometers in deuteriochloroform, unless otherwise stated, with tetramethylsilane as an internal reference. ^{1}H-NMR spectra were recorded at 60 MHz, unless otherwise stated. The assignments of NH signals of indoles were confirmed by disappearance of the signals after addition of deuterium oxide, and the protons of the 3-position were identified at the same time, by observing that the broad singlet or doublet signal changed to sharp singlet signal. Mass spectra (MS) were measured on JEOL JMS-01-SG-2 and JEOL JMS-D 300 spectrometers with a direct

TABLE III. The Friedel–Crafts Acylation of Various Indoles (**6**, **7**, **8** and **9**)



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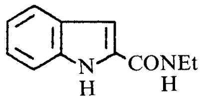

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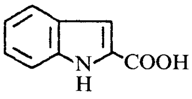

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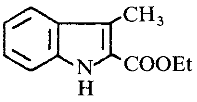

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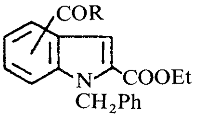
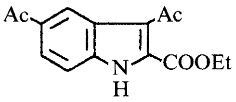
Run	Indole	Acylating agent	Lewis acid	Temp.	Time (h)	Products			Recovery of S.M. (%)
						R	Total yield (%)	Ratio of 3-acyl : 5-acyl : 7-acyl : *N*-acyl	
22	**1**	CH_3COCl **(2l)**	$AlCl_3$	r.t.	1.0	CH_3	73.2	55:31:14: 0	0
23	**6**	CH_3COCl **(2l)**	$AlCl_3$	0 °C	1.0	CH_3	77.3	83:17: 0: 0	Trace
24	**6**	$(CH_3CO)_2O$ **(2l′)**	$AlCl_3$	0 °C	3.5	CH_3	50.2	100: 0: 0: 0	41.9
25	**7**	CH_3COCl **(2l)**	$AlCl_3$	40 °C	1.0	CH_3	89.8	46:12:42: 0	0
26	**7**	$ClCH_2COCl$ **(2m)**	$AlCl_3$	Reflux	1.7	CH_2Cl	26.1	10:90: 0: 0	49.7
27	**8**	CH_3COCl[a] **(2l)**	$AlCl_3$[b]	Reflux	1.8	CH_3	53.4[c]	55:41: 4: 0	0
28	**9**	CH_3COCl **(2l)**	$AlCl_3$	0 °C	0.5	CH_3	72.0	0:90:10: 0	17.0
29	**9**	Cl_2CHOCH_3 **(2h)**	$SnCl_4$	0 °C	1.0	H	91.6	0: 0: 0:100	Trace

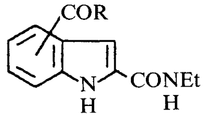
a) Three eq with respect to **8** was used. *b*) Five eq with respect to **8** was used. *c*) The 3,5-diacetyl derivative (**12l**) was also isolated in 19.5% yield.



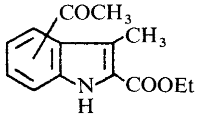
10l: C_3-COR ($R=CH_3$)
11l: C_5-COR ($R=CH_3$)



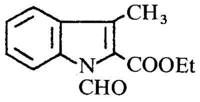
12l



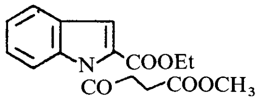
13l: C_3-COR ($R=CH_3$)
14l: C_5-COR ($R=CH_3$)
15l: C_7-COR ($R=CH_3$)
13m: C_3-COR ($R=CH_2Cl$)
14m: C_5-COR ($R=CH_2Cl$)



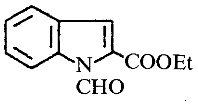
16l: C_5-$COCH_3$
17l: C_7-$COCH_3$



18h



19c



20h

inlet system. For column chromatography, Silica gel 60 (70—230 mesh ASTM, Merck, unless otherwise stated), and for thin layer chromatography (TLC), Silica gel 60 F_{254} (Merck) were used. All identification of products was done by comparisons of melting points, IR spectra, ^{1}H-NMR spectra, and *Rf* values in TLC with those of authentic samples, when available. The ratios of the yields of the 3- and 5-acylindoles (**3** and **4**) were measured on a Hitachi 635A liquid chromatograph (high performance liquid chromatography, HPLC) (column, Waters Radial Pack Silica (5 mm) (8 × 100 mm); wavelength, 295 nm; solvent, methylene chloride : ethyl acetate = 50 : 1). The abbreviations used are as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet; br, broad; dif, diffused; arom, aromatic; BP, base peak.

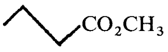
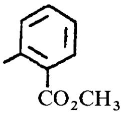
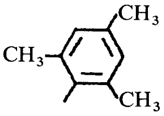
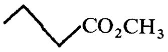
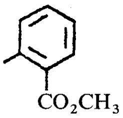
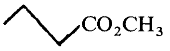
General Procedure of the Friedel–Crafts Acylation of Ethyl 1*H*-Indole-2-carboxylate (1) A solution of ethyl 1*H*-indole-2-carboxylate (**1**) (2 mmol) in 1,2-dichloroethane or nitrobenzene (10 ml) was added dropwise to the ice-cooled acylating agent (4 mmol)–Lewis acid (4 mmol) complex solution under an argon atmosphere, and the reaction mixture was stirred under the conditions given in the tables, until the formation of products was found to have ceased by TLC monitoring. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give the residue. When the acylindoles were carboxylic acids, the residue was subjected to esterification using diazomethane or diazoethane. Then the residue was subjected to column chromatography on silica gel; gradient elution with benzene–ethyl acetate or ethyl acetate–hexane gave the 7-acylindole (**5**), the starting material (**1**), and a mixture of the 3- and 5-acylindoles (**3** and **4**) in order of elution. The mixture of **3** and **4** was further subjected to careful column chromatography on silica gel with a gradient of ethyl acetate–hexane or methylene chloride–ethyl acetate in order to obtain pure products. The ratio of the yields of the 3- and 5-acylindole (**3** and **4**) was estimated by measuring the areas of the peaks on the HPLC chart, with reference to those of authentic samples, isolated by the above method of previously. The ratio of the yields of the three acylindoles (**3**, **4**, and **5**) was estimated from the combination of the isolated yields of **5** and HPLC determination of **3** and **4**.

Spectral Data for Ethyl Acylindole-2-carboxylates (3, 4, and 5) Ethyl 3-Cinnamoyl-1*H*-indole-2-carboxylate (**3a**): IR ν_{max} cm^{-1}: 3280 (NH), 1700 (C=O). ^{1}H-NMR δ: 1.25 (3H, t, $J=8$ Hz, $CH_2C\underline{H}_3$), 4.37 (2H, q, $J=8$ Hz, $OC\underline{H}_2CH_3$), 7.00—8.10, (11H, m, arom-H, olefinic H), 9.77 (1H, br s, NH). MS *m*/*z*: 319 (M^+, 63%), 246 (BP).

Ethyl 3-Picolynoyl-1*H*-indole-2-carboxylate (**3b**): IR ν_{max} cm^{-1}: 3280 (NH), 1700 (C=O). ^{1}H-NMR δ: 0.82 (3H, t, $J=8$ Hz, $CH_2C\underline{H}_3$), 3.92 (2H, q, $J=8$ Hz, $OC\underline{H}_2CH_3$), 7.03—8.40 (7H, m, arom-H), 8.59 (1H, m, arom-H), 10.00 (1H, br s, NH). MS *m*/*z*: 294 (M^+, BP).

Ethyl 3-[3-(Methoxycarbonyl)propionyl]-1*H*-indole-2-carboxylate (**3c**): IR ν_{max} cm^{-1}: 3300 (NH), 1740, 1715 (C=O). ^{1}H-NMR δ: 1.40 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 2.80 (2H, t, $J=7$ Hz, $CH_2C\underline{H}_2COOMe$), 3.47 (2H,

TABLE IV. Physical and Analytical Data for Ethyl 3-, 5-, and 7-Acylindole-2-carboxylate Derivatives

Compound		Melting point (°C)	Recrystallization solvent (Crystal form)	Formula	Analysis (%) Calcd (Found)		
No.	R				C	H	N
3a		131.5—133.5	Benzene–hexane (Pale yellow needles)	$C_{20}H_{17}NO_4$	75.22 (75.30	5.36 5.30	4.39 4.45)
3b		175—177	Benzene–hexane (Colorless needles)	$C_{17}H_{14}N_2O_3$	69.38 (69.21	4.79 4.71	9.52 9.50)
3c		81.5—84	Benzene–hexane (Colorless prisms)	$C_{16}H_{17}NO_5$	63.36 (63.23	5.65 5.66	4.62 4.51)
3e		152—153	Cyclohexane (Colorless needles)	$C_{20}H_{17}NO_5$	68.37 (68.33	4.88 4.86	3.98 4.03)
3f		168—171	Ethyl acetate–hexane (Colorless needles)	$C_{21}H_{21}NO_3$	75.20 (75.40	6.31 6.42	4.18 4.23)
3g	$C(CH_3)_3$	107—110	Benzene–hexane (Colorless prisms)	$C_{16}H_{19}NO_3$	70.31 (70.57	7.01 7.15	5.12 5.20)
3h	H	187—189[a]	Ethyl acetate–hexane (Colorless needles)	$C_{12}H_{11}NO_3$	66.35 (66.43	5.10 5.16	6.45 6.40)
4c		158—162	Ethyl acetate–hexane (Colorless needles)	$C_{16}H_{17}NO_5$	63.36 (63.59	5.65 5.71	4.62 4.53)
4e		172—175	Ether–cyclohexane (Colorless needles)	$C_{20}H_{17}NO_5$	68.37 (68.09	4.88 4.89	3.98 4.05)
4h	H	144.5—146.5	CH_2Cl_2–hexane (Colorless needles)	$C_{12}H_{11}NO_3$	66.35 (66.33	5.10 5.10	6.45 6.49)
4i	CH_2NCO_2Et H	189—191	EtOH–ethyl acetate (Colorless needles)	$C_{16}H_{18}N_2O_5$	60.37 (60.14	5.70 5.77	8.80 8.68)
4j	CH_2NCO_2Et CH_3	201—203	Ethyl acetate–benzene (Colorless needles)	$C_{17}H_{20}N_2O_5$	61.43 (61.69	6.07 6.03	8.43 8.33)
5d		65.5—67	CH_2Cl_2–hexane (Colorless needles)	$C_{16}H_{17}NO_5$	63.36 (63.85	5.65 5.66	4.62 4.77)
5h	H	48.5—50	Benzene–hexane (Colorless needles)	$C_{12}H_{11}NO_3$	66.35 (66.34	5.10 5.11	6.45 6.47)
5i	CH_2NCO_2Et H	117—121	Benzene–hexane (Colorless needles)	$C_{16}H_{18}N_2O_5$	60.37 (60.07	5.70 5.54	8.80 8.71)
5j	CH_2NCO_2Et CH_3	88—91	Benzene–hexane (Pale yellow needles)	$C_{17}H_{20}N_2O_5$	61.43 (61.25	6.07 6.00	8.43 8.26)
4k	CH_2NCOPh H	214–217	EtOH–ethyl acetate (Colorless prisms)	$C_{20}H_{18}N_2O_4$	68.56 (68.45	5.18 5.16	8.00 8.01)
5k	CH_2NCOPh H	195—197	CH_2Cl_2 (Colorless needles)	$C_{20}H_{18}N_2O_4$	68.56 (68.48	5.18 5.19	8.00 7.92)
10l	CH_3	58—59[b]	Hexane (Colorless needles)	$C_{20}H_{19}NO_3$	74.74 (74.72	5.96 5.97	4.36 4.49)
11l	CH_3	128—129.5	Hexane–ethyl acetate (Colorless prisms)	$C_{20}H_{19}NO_3$	74.74 (74.99	5.96 5.87	4.36 4.28)
16l	CH_3	183—184.5	Ethyl acetate (Colorless needles)	$C_{14}H_{15}NO_3$	68.56 (68.50	6.16 6.16	5.71 5.51)
17l	CH_3	114—115.5	Hexane–benzene (Pale yellow needles)	$C_{14}H_{15}NO_3$	68.56 (68.65	6.16 6.23	5.71 5.65)

a) Ref. 5, mp 190.5—192 °C. *b*) Ref. 6, mp 55—57 °C.

t, $J=7$ Hz, COC$\underline{H}_2$CH$_2$), 3.69 (3H, s, OC$\underline{H}_3$), 4.41 (2-H, q, $J=7.5$ Hz, OC$\underline{H}_2$CH$_3$), 7.00—7.55 (3H, m, 5, 6, 7-H), 8.00 (1H, m, 4-H), 9.42 (1H, br s, NH). MS *m*/*z*: 303 (M$^+$, 33%), 216 (BP).

Ethyl 3-[*o*-(Methoxycarbonyl)benzoyl]-1*H*-indole-2-carboxylate (**3e**): IR ν_{max} cm^{-1}: 3310 (NH), 1740, 1680 (C=O). ^{1}H-NMR δ: 1.03 (3H, t, $J=8$ Hz, CH$_2$C$\underline{H}_3$), 3.50 (3H, s, OC$\underline{H}_3$), 3.97 (2H, q, $J=8$ Hz, OC$\underline{H}_2$CH$_3$), 7.10—8.20 (8H, m, arom-H), 9.92 (1H, br s, NH). MS *m*/*z*: 351 (M$^+$, BP).

Ethyl 3-Mesitoyl-1*H*-indole-2-carboxylate (**3f**): IR ν_{max} cm^{-1}: 3160 (NH), 1735 (C=O). ^{1}H-NMR δ: 1.17 (3H, t, $J=8$ Hz, CH$_2$C$\underline{H}_3$), 2.14 (6H, s, arom-C$\underline{H}_3$ × 2), 2.30 (3H, s, arom-C$\underline{H}_3$), 4.11 (2H, q, $J=8$ Hz, OC$\underline{H}_2$CH$_3$), 6.84 (2H, s, 3′- and 5′-H), 7.00—7.50 (3H, m, 5, 6, 7-H), 7.68 (1H, m, 4-H), 9.75 (1H, br s, NH). MS *m*/*z*: 335 (M$^+$, 31%), 262 (BP).

Ethyl 5-[3-(Methoxycarbonyl)propionyl]-1*H*-indole-2-carboxylate (**4c**): IR ν_{max} cm^{-1}: 3340 (NH), 1730, 1705 (C=O). ^{1}H-NMR δ: 1.42 (3H, t, $J=7.5$ Hz, CH$_2$C$\underline{H}_3$), 2.80 (2H, t, $J=6.5$ Hz, CH$_2$C$\underline{H}_2$COOMe), 3.40 (2H, t, $J=6.5$ Hz, COC$\underline{H}_2$CH$_2$), 3.70 (3H, s, OC$\underline{H}_3$), 4.44 (2H, q, $J=7.5$ Hz, OC$\underline{H}_2$CH$_3$), 7.30 (1H, dif s, 3-H), 7.43 (1H, d, $J=9$ Hz, 7-H), 7.98 (1H, dd, $J=9$, 2Hz, 6-H), 8.38 (1H, dif s, 4-H), 9.55 (1H, br s, NH). MS *m*/*z*: 303 (M$^+$, 33%), 216 (BP).

Ethyl 5-[*o*-(Methoxycarbonyl)benzoyl]-1*H*-indole-2-carboxylate (**4e**): IR ν_{max} cm^{-1}: 3315 (NH), 1720, 1695 (C=O). ^{1}H-NMR δ: 1.40 (3-H, t, $J=7.5$ Hz, CH$_2$C$\underline{H}_3$), 3.60 (3H, s, OC$\underline{H}_3$), 4.42 (2H, q, $J=7.5$Hz,

$OC\underline{H}_2CH_3$), 7.17—8.16 (8H, m, arom-H), 9.30 (1H, br s, NH). MS *m/z*: 351 (M^+, 75%), 216 (BP).

Ethyl 5-Formyl-1*H*-indole-2-carboxylate (**4h**): IR ν_{max} cm^{-1}: 3305 (NH), 1685 (C=O). ^1H-NMR δ: 1.42 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 4.45 (2H, q, $J=7.5$ Hz, $OC\underline{H}_2CH_3$), 7.34 (1H, d, $J=2.5$ Hz, 3-H), 7.51 (1H, d, $J=9$ Hz, 7-H), 7.88 (1H, dd, $J=9$, 2 Hz, 6-H), 8.21 (1H, difs, 4-H), 9.80 (1H, br s, NH), 10.02 (1H, s, CHO). MS *m/z*: 217 (M^+, 88%), 171 (BP).

Ethyl 5-[*N*-(Ethoxycarbonyl)glycyl]-1*H*-indole-2-carboxylate (**4i**): IR ν_{max} cm^{-1}: 3340, 3270 (NH), 1718, 1690, 1680 (C=O). ^1H-NMR δ: 1.25 and 1.40 (each 3H, t, $J=7$ Hz, $CH_2C\underline{H}_3\times 2$), 4.18 and 4.42 (each 2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3\times 2$), 4.75 (2H, d, $J=5$ Hz, $COC\underline{H}_2NH$), 5.78 (1H, br s, $CH_2N\underline{H}CO$), 7.28 (1H, dif s, 3-H), 7.46 (1H, d, $J=8$ Hz, 7-H), 7.93 (1H, dd, $J=8$, 1.5 Hz, 6-H), 8.35 (1H, dif s, 4-H), 9.58 (1H, br s, NH). MS *m/z*: 318 (M^+, 7%), 216 (BP).

Ethyl 5-[*N*-(Ethoxycarbonyl)sarcosyl]-1*H*-indole-2-carboxylate (**4j**): IR ν_{max} cm^{-1}: 3300 (NH), 1710 and 1680 (C=O). ^1H-NMR δ: 1.30 and 1.42 (each 3H, t, $J=7$ Hz, $CH_2C\underline{H}_3\times 2$), 3.02 (3H, s, $NC\underline{H}_3$), 4.32 and 4.45 (each 2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3\times 2$), 4.78 (2H, s, $COC\underline{H}_2N$), 7.30 (1H, difs, 3-H), 7.45 (1H, difd, $J=9$ Hz, 7-H), 7.91 (1H, difd, $J=9$ Hz, 6-H), 8.31 (1H, difs, 4-H), 9.78 (1H, br s, NH). MS *m/z*: 332 (M^+, 12%), 216 (BP).

Ethyl 5-[*N*-(Benzoyl)glycyl]-1*H*-indole-2-carboxylate (**4k**): IR ν_{max} cm^{-1}: 3400, 3240 (NH), 1680, 1645 (C=O). ^1H-NMR (DMSO-d_6) δ: 1.35 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 4.37 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 4.85 (2H, d, $J=6$ Hz, $COC\underline{H}_2NH$), 7.20—7.72 (5H, m, arom-H), 7.72—8.10 (3H, m, arom-H), 8.53 (1H, difs, 4-H), 8.78 (1H, br t, $J=6$ Hz, $CH_2N\underline{H}CO$), 12.15 (1H, br s, NH). MS *m/z*: 350 (M^+, 5%), 216 (BP).

Ethyl 7-[3-(Methoxycarbonyl)propionyl]-1*H*-indole-2-carboxylate (**5c**): IR ν_{max} cm^{-1}: 3430 (NH), 1730, 1715 (C=O). ^1H-NMR δ: 1.40 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 2.79 (2H, t, $J=6.5$ Hz, $CH_2C\underline{H}_2COOMe$), 3.43 (2H, t, $J=6.5$ Hz, $COC\underline{H}_2CH_2$), 4.22 (3H, s, $OC\underline{H}_3$), 4.42 (2H, q, $J=7.5$ Hz, $OC\underline{H}_2CH_3$), 7.18 (1H, t, $J=8$ Hz, 5-H), 7.22 (1H, d, $J=2.5$ Hz, 3-H), 7.92 (2H, d, $J=8$ Hz, 4- and 6-H), 10.65 (1H, br s, NH). MS *m/z*: 303 (M^+, 57%), 170 (BP).

Ethyl 7-Formyl-1*H*-indole-2-carboxylate (**5h**): IR ν_{max} cm^{-1}: 3330 (NH), 1720 (C=O). ^1H-NMR δ: 1.40 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 4.42 (2H, q, $J=7.5$ Hz, $OC\underline{H}_2CH_3$), 7.25 (1H, t, $J=8$ Hz, 5-H), 7.25 (1H, d, $J=2.5$ Hz, 3-H), 7.74 (1H, dd, $J=8$, 1.5 Hz, 4- or 6-H), 7.95 (1H, dd, $J=8$, 1 Hz, 6- or 4-H), 10.90 (1H, s, CHO), 10.35 (1H, br s, NH). MS *m/z*: 217 (M^+, 80%), 143 (BP).

Ethyl 7-[*N*-(Ethoxycarbonyl)glycyl]-1*H*-indole-2-carboxylate (**5i**): IR ν_{max} cm^{-1}: 3450, 3320 (NH), 1730, 1680, 1670 (C=O). ^1H-NMR δ: 1.32 and 1.40 (each 3H, t, $J=7$ Hz, $CH_2C\underline{H}_3\times 2$), 4.18 and 4.41 (each 2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3\times 2$), 4.78 (2H, d, $J=5$ Hz, $COC\underline{H}_2NH$), 5.62 (1H, br s, $CH_2N\underline{H}CO$), 7.09—7.45 (2H, m, arom-H), 7.65—8.05 (2H, m, arom-H), 10.56 (1H, br s, NH). MS *m/z*: 318 (M^+, 41%), 170 (BP).

Ethyl 7-[*N*-(Ethoxycarbonyl)sarcosyl]-1*H*-indole-2-carboxylate (**5j**): IR ν_{max} cm^{-1}: 3440 (NH), 1720, 1698 (C=O). ^1H-NMR δ: 1.41 (6H, t, $J=7$ Hz, $CH_2C\underline{H}_3\times 2$), 3.04 (3H, s, $NC\underline{H}_3$), 4.31 and 4.41 (each 2H, dif q, $J=7$ Hz, $OC\underline{H}_2CH_3\times 2$), 4.82 (2H, s, $COC\underline{H}_2N$), 7.15—7.37 (2H, m, arom-H), 7.75—8.05 (2H, m, arom-H), 10.65 (1H, br s, NH). MS *m/z*: 332 (M^+, 43%), 116 (BP).

Ethyl 7-[*N*-(Benzoyl)glycyl]-1*H*-indole-2-carboxylate (**5k**): IR ν_{max} cm^{-1}: 3440, 3320 (NH), 1719, 1669 (C=O). ^1H-NMR δ: 1.40 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 4.41 (2H, q, $J=7$ Hz, $OC\underline{H}_2CH_3$), 5.05 (2H, d, $J=4$ Hz, $COC\underline{H}_2NH$), 7.00—7.70 (6H, m, arom-H), 7.70—8.15 (4H, m, arom-H and $CH_2N\underline{H}CO$), 10.55 (1H, br s, NH). MS *m/z*: 350 (M^+, 31%), 105 (BP).

Other ethyl acylindole-2-carboxylates (**3**, **4**, and **5**) were identified by comparison with the samples reported in the previous paper.[2]

General Procedure of the Friedel–Crafts Acetylation of Ethyl 1-Benzyl-1*H*-indole-2-carboxylate (6) Acetyl chloride or acetic anhydride (4 mmol) was added to an ice-cooled suspension of aluminum chloride (4 mmol) in 1,2-dichloroethane (10 ml), and the whole was stirred for 5 min under an argon atmosphere. A solution of ethyl 1-benzyl-1*H*-indole-2-carboxylate (**6**) (2 mmol) in 1,2-dichloroethane (4 ml) was added dropwise, and the whole mixture was stirred under the conditions given in Table III, until the formation of products was found to have ceased by TLC monitoring. The reaction mixture was poured into ice-water (120 ml) and extracted with methylene chloride. The organic layer was washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give the residue. The residue was subjected to column chromatography on silica gel with mixed solvent (benzene : AcOEt = 30 : 1 or 50 : 1) to give the starting material (**6**), and a mixture of the 3- and 5-acetylindoles (**10l** and **11l**). The ratio of the yields of the 3- and 5-acetylindoles (**10l** and **11l**) was estimated by HPLC.

General Procedure of the Friedel–Crafts Acylation of *N*-Ethyl-1*H*-Indole-2-carboxamide (7) Acetyl chloride or chloroacetyl chloride (2 mmol) was added to an ice-cooled suspension of *N*-ethyl-1*H*-indole-2-carboxamide (**7**) (1 mmol) and aluminum chloride (2 mmol) in 1,2-dichloroethane (8 ml), and the reaction mixture was stirred under the conditions shown in Table III, then poured into ice-water (70 ml) and extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give the residue. The residue was subjected to column chromatography on silica gel; gradient elution with benzene–ethyl acetate gave the 3-acylindole-2-(*N*-ethyl)carboxamide (**13**), 7-acetylindole-2-(*N*-ethyl)carboxamide (**15l**), and the 5-acylindole-2-(*N*-ethyl)carboxamide (**14**) in order of elution.

3-Acetyl-*N*-ethyl-1*H*-indole-2-carboxamide (**13l**): Colorless needles, mp 194—196 °C (AcOEt–hexane). *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.52; H, 6.14; N, 12.09. IR ν_{max} cm^{-1}: 3225 (NH), 1640 (C=O). ^1H-NMR (400 MHz, DMSO-d_6) δ: 1.20 (3H, t, $J=7.2$ Hz, $CH_2C\underline{H}_3$), 2.69 (3H, s, $COC\underline{H}_3$), 3.39 (2H, dq, $J=1.8$, 7.2 Hz, $NHC\underline{H}_2CH_3$), 7.28 (1H, dt, $J=7.0$, 1.3 Hz, 5- or 6-H), 7.32 (1H, dt, $J=7.0$, 1.3 Hz, 6- or 5-H), 7.58 (1H, dd, $J=7.0$, 1.3 Hz, 7-H), 8.08 (1H, dd, $J=7.0$, 1.3 Hz, 4-H), 10.41 (1H, dif t, $CON\underline{H}Et$), 12.62 (1H, br s, NH). MS *m/z*: 230 (M^+, BP).

7-Acetyl-*N*-ethyl-1*H*-indole-2-carboxamide (**15l**): Colorless prisms, mp 276—278 °C (EtOH). IR ν_{max} cm^{-1}: 3440, 3325 (NH), 1662, 1630 (C=O). ^1H-NMR (400 MHz, DMSO-d_6) δ: 1.16 (3H, t, $J=7.2$ Hz, $CH_2C\underline{H}_3$), 2.70 (3H, s, $COC\underline{H}_3$), 3.34 (2H, dq, $J=7.2$, 1.7 Hz, $NHC\underline{H}_2CH_3$), 7.25 (1H, d, $J=1.7$ Hz, 3-H), 7.26 (1H, t, $J=7.5$ Hz, 5-H), 8.02 (2H, d, $J=7.5$ Hz, 4- and 6-H), 8.84 (1H, dif t, $CON\underline{H}Et$), 10.88 (1H, br s, NH). MS *m/z*: 230 (M^+, BP). High resolution MS: Calcd for $C_{13}H_{14}N_2O_2$: 230.1052. Found: 230.1063.

5-Acetyl-*N*-ethyl-1*H*-indole-2-carboxamide (**14l**): Colorless prisms, mp 261—262 °C (EtOH). *Anal.* Calcd for $C_{13}H_{12}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.73; H, 6.18; N, 11.98. IR ν_{max} cm^{-1}: 3370, 3220 (NH), 1660, 1640 (C=O). ^1H-NMR (400 MHz, DMSO-d_6) δ: 1.16 (3H, t, $J=7.1$ Hz, $CH_2C\underline{H}_3$), 2.61 (3H, s, $COC\underline{H}_3$), 3.33 (2H, dq, $J=1.7$, 7.1 Hz, $NHC\underline{H}_2CH_3$), 7.27 (1H, d, $J=1.6$ Hz, 3-H), 7.48 (1H, d, $J=8.6$ Hz, 7-H), 7.80 (1H, dd, $J=8.6$, 1.7 Hz, 6-H), 8.37 (1H, d, $J=1.7$ Hz, 4-H), 8.62 (1H, dif t, $CON\underline{H}Et$), 11.95 (1H, br s, NH). MS *m/z*: 230 (M^+, BP).

3-Chloroacetyl-*N*-ethyl-1*H*-indole-2-carboxamide (**13m**): Colorless prisms, mp 220—222 °C (EtOH). *Anal.* Calcd for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; N, 10.58. Found: C, 60.22; H, 5.28; N, 10.44. IR ν_{max} cm^{-1}: 3175 (NH), 1644, 1635 (C=O). ^1H-NMR (400 MHz, DMSO-d_6) δ: 1.21 (3H, t, $J=7.2$ Hz, $CH_2C\underline{H}_3$), 3.40 (2H, dq, $J=7.2$, 1.8 Hz, $NHC\underline{H}_2CH_3$), 5.04 (2H, s, $COC\underline{H}_2Cl$), 7.29 (1H, dt, $J=5.9$, 1.7 Hz, 5- or 6-H), 7.33 (1H, dt, $J=7.0$, 1.7 Hz, 6- or 5-H), 7.56 (1H, dd, $J=7.1$, 1.0 Hz, 7-H), 8.06 (1H, d, $J=7.5$ Hz, 4-H), 9.82 (1H, dif t, $CON\underline{H}Et$), 12.73 (1H, dif s, NH). MS *m/z*: 266 ($M^+ + 2$, 34% of M^+), 264 (M^+, 64% of BP), 215 (BP).

5-Chloroacetyl-*N*-ethyl-1*H*-indole-2-carboxamide (**14m**): Pale yellow prisms, mp 277—280 °C (EtOH). *Anal.* Calcd for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; N, 10.58. Found: C, 58.83; H, 4.94; N, 10.46. IR ν_{max} cm^{-1}: 3380, 3220 (NH), 1695 (C=O). ^1H-NMR (DMSO-d_6) δ: 1.18 (3H, t, $J=7$ Hz, $CH_2C\underline{H}_3$), 3.35 (2H, m, $NHC\underline{H}_2CH_3$), 5.17 (2H, s, $COC\underline{H}_2Cl$), 7.25 (1H, d, $J=3$ Hz, 3-H), 7.48 (1H, d, $J=9$ Hz, 7-H), 7.81 (1H, dd, $J=9$, 2 Hz, 6-H), 8.38 (1H, d, $J=2$ Hz, 4-H), 8.55 (1H, br s, $CON\underline{H}Et$), 11.85 (1H, br s, NH). MS *m/z*: 266 ($M^+ + 2$, 29% of M^+), 264 (M^+, 35% of BP), 215 (BP).

The Friedel–Crafts Acetylation of 1*H*-Indole-2-carboxylic Acid (8) Acetyl chloride (5.9 mmol) was added dropwise to an ice-cooled suspension of 1*H*-indole-2-carboxylic acid (**8**) (2.0 mmol) and aluminum chloride (9.6 mmol) in 1,2-dichloroethane (20 ml) under argon atmosphere, and the whole was stirred at reflux temperature for 1.8 h, then worked up according to the general procedure. The crude product was then subjected to esterification with an ether solution of diazoethane [prepared from nitrosoethylurea (15 mmol)] at room temperature. The mixture was evaporated to dryness *in vacuo*. The residue was then subjected to column chromatography on silica gel; gradient elution with benzene–ethyl acetate gave the ethyl 7-acetylindole-2-carboxylate (2.3%), a mixture of ethyl 3- and 5-acetylindole-2-carboxylate (51.1%), and ethyl 3,5-diacetyl-1*H*-indole-2-carboxylate (**12l**, 19.5%) in order of elution. The ratio of the yields of the 3- and 5-acetylindoles was estimated by measuring the areas of the peaks on the HPLC chart, with reference to those of authentic samples prepared previously.

Ethyl 3,5-Diacetyl-1*H*-indole-2-carboxylate (**12l**): Colorless needles, mp 178.5—179.5 °C (benzene–AcOEt). IR ν_{max} cm^{-1}: 3150 (NH), 1708, 1675, 1645 (C=O). ^1H-NMR δ: 1.45 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 2.68 and 2.78 (each 3H, s, $COC\underline{H}_3\times 2$), 4.50 (2H, q, $J=7.5$ Hz, $OC\underline{H}_2CH_3$), 7.45

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(1H, d, $J=8$ Hz, 7-H), 8.04 (1H, dd, $J=8$, 2 Hz, 6-H), 8.71 (1H, d, $J=2$ Hz, 4-H), 9.68 (1H, br s, NH). MS *m/z*: 273 (M^+, 81%), 212 (BP).

The Friedel–Crafts Formylation of Ethyl 3-Methyl-1*H*-indole-2-carboxylate (9) 1,1-Dichloromethyl methyl ether (1.6 mmol), $SnCl_4$ (1.6 mmol), and a solution of ethyl 3-methyl-1*H*-indole-2-carboxylate (**9**) (0.8 mmol) in 1,2-dichloroethane (3 ml) were successively added to ice-cooled 1,2-dichloroethane (3 ml) under an argon atmosphere. The whole mixture was stirred for 1 h at 0 °C. After work-up according to the general procedure, the crude product was subjected to column chromatography on silica gel; gradient elution with hexane–ethyl acetate gave ethyl 1-formyl-3-methyl-1*H*-indole-2-carboxylate (**18h**, 91.6%), and a trace amount of starting material (**9**).

Ethyl 1-Formyl-3-methyl-1*H*-indole-2-carboxylate (**18h**): Colorless needles, mp 127—130 °C (AcOEt–hexane). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.46; H, 5.67; N, 6.02. IR ν_{max} cm^{-1}: 1669, 1680 (C=O). ^{1}H-NMR δ: 1.43 (3H, t, $J=8$ Hz, $CH_2C\underline{H}_3$), 2.55 (3H, s, arom-$C\underline{H}_3$), 4.42 (2H, q, $J=8$ Hz, $OC\underline{H}_2CH_3$), 7.12—7.78 (3H, m, arom-H), 8.49 (1H, m, arom-H), 10.01 (1H, s, CHO). MS *m/z*: 231 (M^+, 30%), 157 (BP).

Ethyl 1-[3-(Methoxycarbonyl)propionyl]-1*H*-indole-2-carboxylate (**19c**): Colorless oil. IR ν_{max} cm^{-1} (neat): 1720 (C=O). ^{1}H-NMR δ: 1.42 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 2.85 (2H, t, $J=6$ Hz, $CH_2C\underline{H}_2COOMe$), 3.24 (2H, t, $J=6$ Hz, $COC\underline{H}_2CH_2$), 3.65 (3H, s, $OC\underline{H}_3$), 4.42 (2H, q, $J=7.5$ Hz, $OC\underline{H}_2CH_3$), 7.05—7.85 (3H, m, arom-H), 7.85—9.22 (1H, m, arom-H). MS *m/z*: 303 (M^+, 38%), 189 (BP).

Ethyl 1-Formyl-1*H*-indole-2-carboxylate (**20h**): Colorless needles, mp 90—92 °C (hexane–AcOEt). *Anal.* Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.27; H, 5.10; N, 6.44. IR ν_{max} cm^{-1}: 1730 (C=O). ^{1}H-NMR δ: 1.40 (3H, t, $J=7.5$ Hz, $CH_2C\underline{H}_3$), 4.37 (2H, q, $J=7.5$ Hz, $OC\underline{H}_2CH_3$), 7.10—7.77 (4H, m, arom-H), 8.49 (1H, m, arom-H), 10.08 (1H, s, CHO). MS *m/z*: 217 (M^+, 47%), 143 (BP).

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