Reaction of Ethyl Acylindole-2-carboxylates with Thallium Trinitrate (Synthetic Studies on Indoles and Related Compounds. XXXIII[1])

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Received July 23, 1993; accepted October 25, 1993

Ethyl acylindole-2-carboxylates were treated with thallium trinitrate (TTN) in methanol, methyl orthoformate, methyl orthoformate/sulfuric acid, and acetic acid. The reactions in the former three methanolic solvents gave methyl indoleacetate derivatives *via* the Favorskii-type rearrangement reaction at the acyl group, whereas the reaction in acetic acid gave oxindole derivative with rearrangement of the C_2-ethoxycarbonyl group. The TTN reaction was applied to a model compound leading to the synthesis of lysergic acid.

Keywords acylindole; thallium trinitrate, Favorskii-type rearrangement; methyl orthoformate; oxindole; mechanism

Thallium trinitrate (TTN) reacts with a double bond or an enolic double bond to cause a rearrangement reaction *via* initial oxidative addition to it.[2] A cyclic ketone reacts with TTN to give a carboxylic acid (or ester) with ring-contraction[2c] and an acyclic aryl alkyl ketone gives arylacetic acid (or ester) *via* Favorskii-type rearrangement.[3] These reactions should have synthetic utility, because preparation of the resulting functional group by another method would require a longer route. If indolic ketones undergo this reaction with TTN, they should be converted to useful compounds. However, the electron-rich indole ring itself might react with TTN in place of the ketone group, since TTN is potentially an oxidative reagent. Ban *et al.*[4] reported only one example of the reaction with TTN in the indole field, in which indole-3-propionic acid reacted with TTN in 5% aqueous acetonitrile to give an oxindole derivative having spirolactone at C_3-position; that is, the indole nucleus was oxidized. We have reported acylation of ethyl indole-2-carboxylate.[5] Ethyl indole-2-carboxylates are stabilized with respect to oxidation due to their C_2-ethoxycarbonyl group, so that ethyl acylindole-2-carboxylates (**1**) are expected to undergo the desired TTN reaction at the acyl group without affecting the indole nucleus. Here, we report in detail the results of the reaction of **1** with TTN and the feasibility of a synthetic application.

Reaction of Ethyl Acylindole-2-carboxylate (1) with TTN As a preliminary experiment, the reaction of ethyl 3-acetylindole-2-carboxylate (**1a**) with TTN was successfully carried out to give the expected indole acetate (**2a**). Then the reaction of several ethyl 3- and 5-acylindole-2-carboxylates (**1**) with TTN was carried out in methanol,[2a] in methyl orthoformate,[2b] in methyl orthoformate/sulfuric acid, and in acetic acid[2c] in order to examine the effects of these conditions in detail. We had thought that 3-acylindole and 5-acylindole would show different reactivity, because 3-acylindole has a vinylogous amide character in part, whereas 5-acylindole is a usual aromatic ketone. The acylindoles (**1**) were treated with 1.0—3.0 eq of TTN in the four kinds of solvents, and the results are shown in Charts 1 and 2, and in Table I.

The reactions described in Chart 1 and Table I were carried out in methanol, methyl orthoformate, and methyl orthoformate containing sulfuric acid (methanolic solvents). All reactions in runs 1 to 18 gave the expected rearrangement product (**2**) and the further methoxylated product (**3**) together. The only clear tendency is that the acyl group having a longer alkyl substituent (propionyl) showed a better yield in orthoformate (runs 4—6, 10—12, and 16—18), while the one having a shorter alkyl

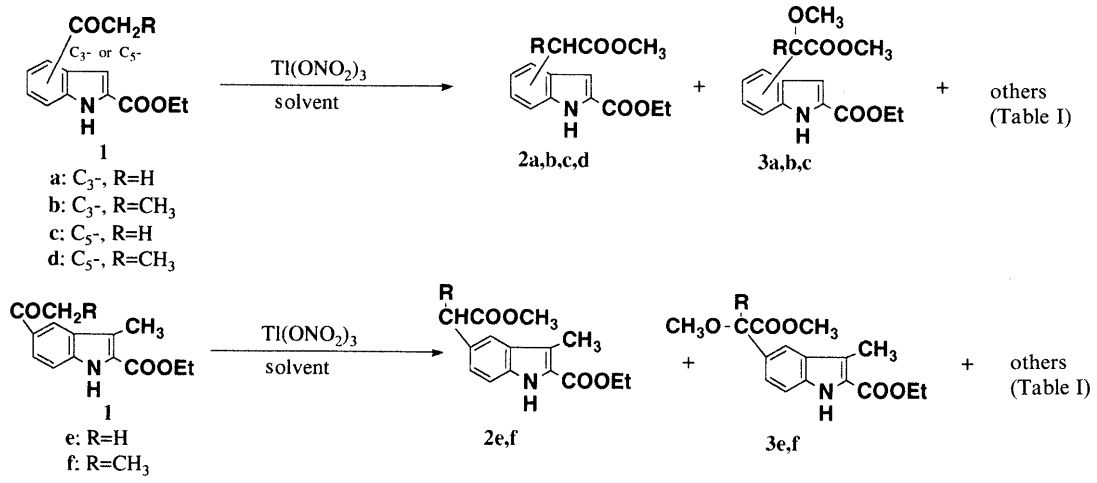
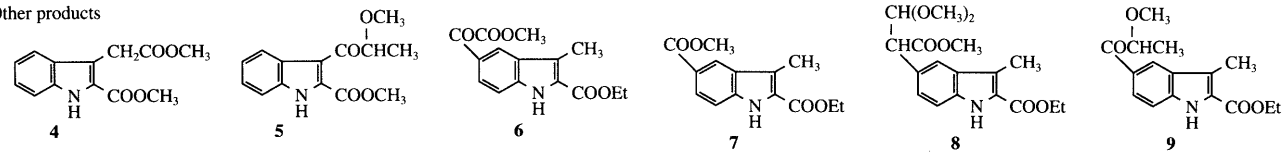


Chart 1

TABLE I. Reaction of Acylindoles with TTN in Methanolic Solvents

Run	Substrate 1	TTN (eq)	Solvent	R. conditions		Products (yield: %)		
				Temp. (°C)	Time	2	3	Others
1	**1a**	1.4	MeOH	r.t.	Overnight	61	—	**4**; 25
2	**1a**	1.8	$HC(OCH_3)_3$	r.t.	Overnight	21	48	
3	**1a**	1.5	$HC(OCH_3)_3/H_2SO_4$	0	1 h	14	56	
4	**1b**	3.0	MeOH	r.t.	2 d	—	—	**5**; 13
5	**1b**	1.5	$HC(OCH_3)_3$	0	2.4 h	78	14	
6	**1b**	1.5	$HC(OCH_3)_3/H_2SO_4$	0	2 h	Complex mixture		
7	**1c**	1.3	MeOH	r.t.	Overnight	84	—	
8	**1c**	1.8	$HC(OCH_3)_3$	r.t.	Overnight	18	20	
9	**1c**	1.5	$HC(OCH_3)_3/H_2SO_4$	0	1 h	29	25	
10	**1d**	1.5	MeOH	r.t.	2 h	Complex mixture		
11	**1d**	1.5	$HC(OCH_3)_3$	r.t.	3.5 h	52	—	
12	**1d**	1.5	$HC(OCH_3)_3/H_2SO_4$	0	2.3 h	89	—	
13	**1e**	1.5	MeOH	r.t.	2 d	63	—	
14	**1e**	1.5	$HC(OCH_3)_3$	r.t.	2 d	—	34	**6**; 22, **7**; 9
15	**1e**	1.5	$HC(OCH_3)_3/H_2SO_4$	0	1.5 h	6	36	**8**; 11
16	**1f**	1.5	MeOH	r.t.	3 d	—	—	**9**; 23
17	**1f**	1.5	$HC(OCH_3)_3$	r.t.	4.5 h	52	24	
18	**1f**	1.6	$HC(OCH_3)_3/H_2SO_4$	0	2.3 d	85	—	

Other products



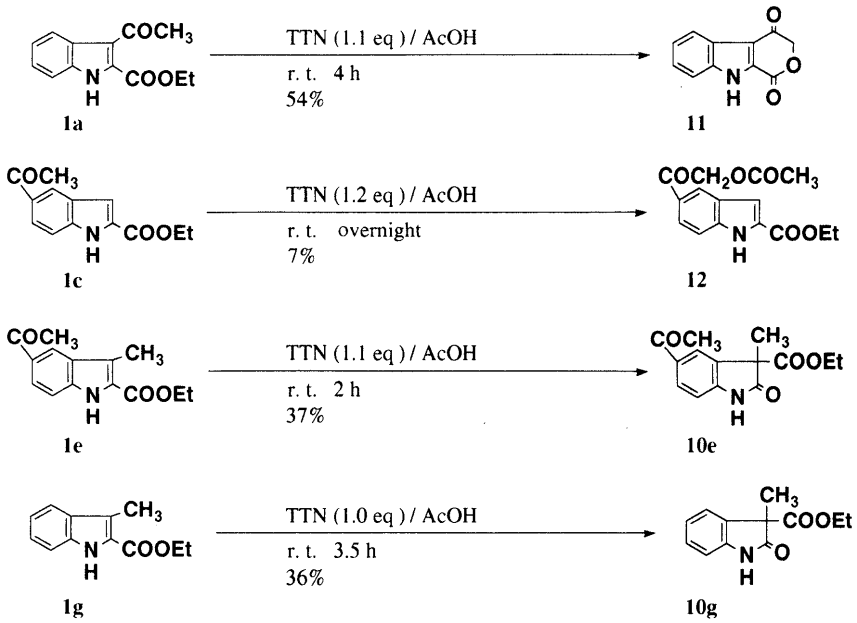


Chart 2

substituent (acetyl) did so in MeOH (runs 1—3, 7—9, and 13—15). The difference of reactivity between 3-acylindoles (**1a**, **b**) and 5-acylindoles (**1c**, **d**) is apparently very small (runs 1—3 and 4—6 *vs.* runs 7—9 and 10—12). The further methoxylated compound (**3**) and abnormally oxidized products (**6**, **7**, **8**, and **9**) were obtained as minor products. In order to obtain the desired product (**2**) in high yield, it is necessary to suppress further methoxylation of **2**. However, we could not find conditions that would prevent further methoxylation. Generally speaking, a high reaction temperature (50 °C or above, for example) accelerated the reaction but simultaneously tended to transform the products into a tar. Lower temperature (0 °C to room temperature) and consequent longer reaction time give more favorable results, as shown in Table I. A methyl group at the 3-position showed no particular effect (runs

5 and 6).

The by-product (**4**) from **1a** is essentially the desired product formed by *trans*-esterification at the C_2-ester during the rearrangement reaction. The by-product (**5**) from **1b** is a product derived from α-methoxylation at the acyl group of **1**, followed by *trans*-esterification.

Next, the reaction was carried out in AcOH. The reactions in AcOH gave different products from the reactions in methanolic solvents, as shown in Chart 2.

The acylindoles (**1a, c**) carrying no methyl group at the 3-position gave the products (**11, 12**) formed by acetoxylation at the α-position of the acyl group of the starting ketone, and **11** was formed through intramolecular cyclization of the α-acetoxylated compound. The 5-acylindole (**1e**) having a methyl group at the 3-position produced the oxindole (**10e**) with rearrangement of the ethoxycarbonyl group from the 2- to the 3-position. The same result was obtained with the 3-methylindole (**1g**) carrying no acyl group. These results (Table I and Chart 2) revealed that TTN reaction in methanolic solvents gave the desired **2**, whereas the reaction in AcOH proceeded on a different course to give the oxindole (**10**).

The rearranged products (**2**) should belong to a group of arylacetic acids, many compounds of which are known to have anti-inflammatory effect.[6] So we converted **2b** and **2d** into the corresponding carboxylic acids (**13** and **14**), respectively. These compounds were examined for anti-inflammatory action in the carrageenin induced edema model in rats. The indole-3-acetic acid (**13**) showed no effect and the indole-5-acetic acid (**14**) showed only a weak effect (*ca.* one-tenth or less of that of indomethacin).

Various other results are shown in Chart 4. When the 5- and 7-acetylindoles (**1c**, **16**) were treated with TTN in trifluoroacetic acid (much more acidic than acetic acid), the C_3-nitrated compounds (**15**, **17**) were obtained as sole products, in place of the rearranged product or the oxindole. When the 3-acetylindole (**18**) which carried no 2-ethoxycarbonyl group was allowed to react with TTN in methanol, the reaction afforded a complex mixture and no product could be characterized.

Finally, we examined $PhI(OAc)_2$[7] and $Pb(OAc)_4$[8] for the same purpose. Both reagents have been reported to

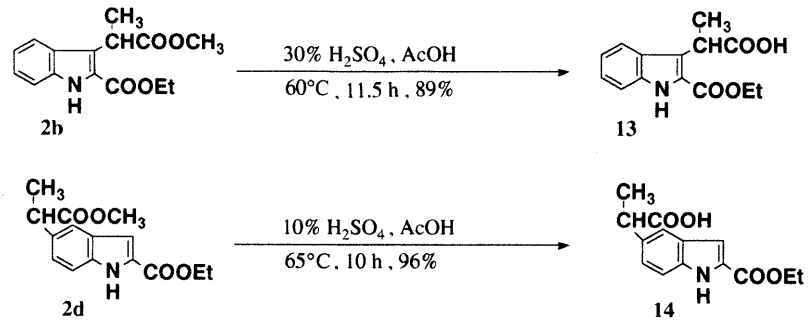


Chart 3

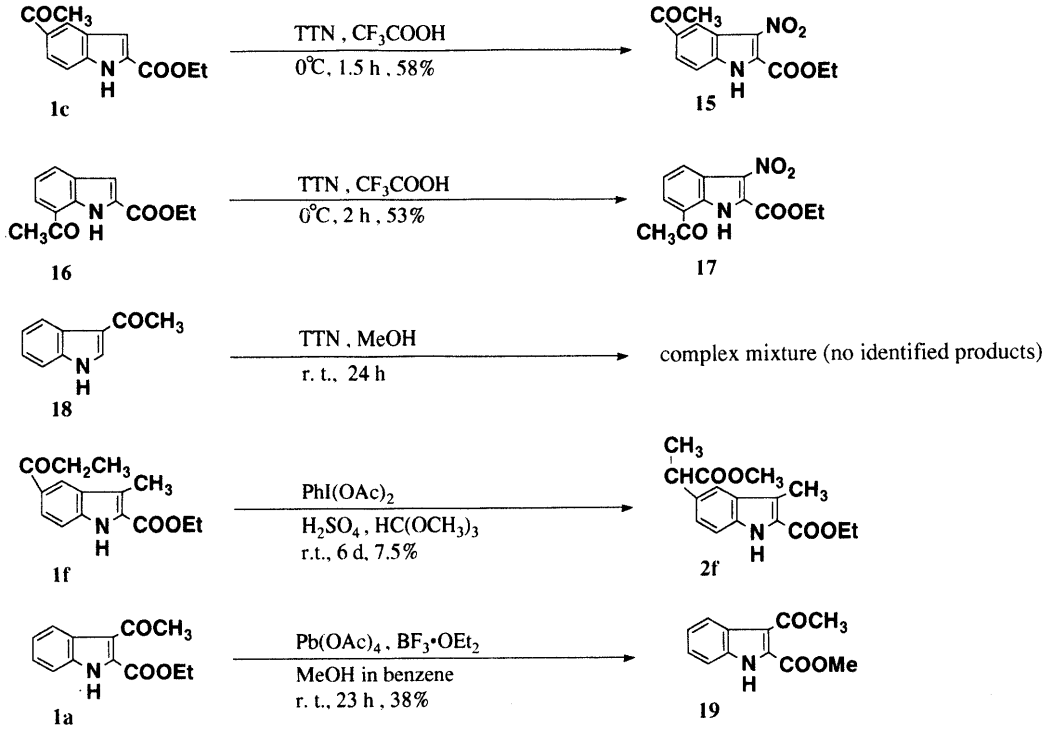


Chart 4

react with an acyl group in the same manner as TTN. The reaction of **1f** with $PhI(OAc)_2$ gave **2f** in only 7.5% yield. The reaction of **1a** with $Pb(OAc)_4$ gave no rearranged product and no oxindole.

Thus, Favorskii-type rearrangement on acylindoles requires a 2-ethoxycarbonylindole as the substrate and TTN as the reagent.

Structures of the rearranged products (**2**) were determined chiefly by ^{1}H-NMR. For example, the ^{1}H-NMR spectrum of **1a** shows[5a] C_4-H at δ 8.10 (shifted downfield by anisotropy due to the 3-acetyl group) and acetyl methyl at δ 2.86, whereas the ^{1}H-NMR spectrum of **2a** shows C_4-H at δ 7.57 and ester methyl at δ 3.65. The ^{1}H-NMR spectrum of **1c** shows[5b] C_4-H at δ 8.37 and C_6-H at 7.99, whereas that of **2c** shows C_4-H at δ 7.46 and C_6-H at 7.01—7.30 among other aromatic protons. These upfield shifts demonstrate clearly the transformation of the acyl group to acetate.

Structure determination of the oxindoles by means of ^{1}H-NMR is exemplified with **10e** as follows; the ^{1}H-NMR spectrum of **1e** [two methyl groups at δ 2.63 and 2.66 (s), three aromatic protons at δ 7.34 (C_7-H), 7.92 (C_6-H), and 8.27 (C_4-H)] was compared with that of **10e** [aliphatic C_3-methyl at δ 1.71, aromatic acetyl methyl at 2.56, and three aromatic protons at δ 7.00 (C_7-H), δ 7.81 (C_4-H), and δ 7.90 (C_6-H)]. One methyl group shows a large upfield shift, while the other shows no appreciable change in chemical shift. Three aromatic protons of **1e** show upfield shifts to some extent, while their relative features are broadly unchanged. These data demonstrate the formation of the oxindole moiety with the acetyl group unchanged. The ^{13}C-NMR spectrum of **10e** also shows a new C_2-carbonyl group at δ 177.95 (s). Hydrolysis of **10e** under acidic conditions readily gave **20**, with decarboxylation. This also supports the existence of the β-keto ester group in **10e**.

The Reaction Mechanism The mechanism of the present reaction with TTN is proposed to be as shown in Chart 6 on the basis of Taylor's suggestions.[2] The reaction in methanolic solvents can be described as follows in the case of the 3-acylindole (**A**) (route 1). The enol form (**B**) of **A** is attacked by TTN to yield the addition product (**C**), from which thallium is eliminated to generate the carbocation (**D**). The carbocation (**D**) gives the rearranged product (**E**) by migration of the indole part (a-direction), or gives the α-methoxy compound (**F**) by rearrangement of the methoxy group or addition of MeOH from outside (b-direction). In route 2, TTN and AcOH add to the C_2–C_3 double bond of the indole (**G**) to give the intermediate (**H**). Reductive elimination of the thallium gives the tertiary carbocation (**I**), which accepts the ethoxycarbonyl group to give the oxindole (**J**). The latter reaction (route 2) does not occur when the indole has no C_3-alkyl substituent, probably because **I** would have a less stable secondary carbocation in the absence of the C_3-alkyl substituent. The same oxindole (**10g**) was obtained[9] in the reaction of **1g** with sulfuryl chloride. The mechanism of the formation of **10g** by the reaction with TTN should be similar to that with the above reagent. A concerted mechanism might operate in the two routes. At present, we have no idea why TTN attacks at different positions, depending on the kind of solvent.

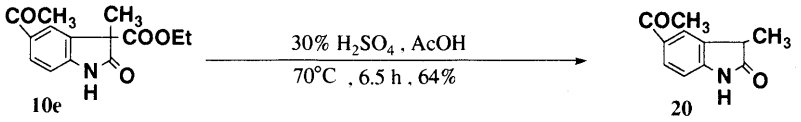


Chart 5

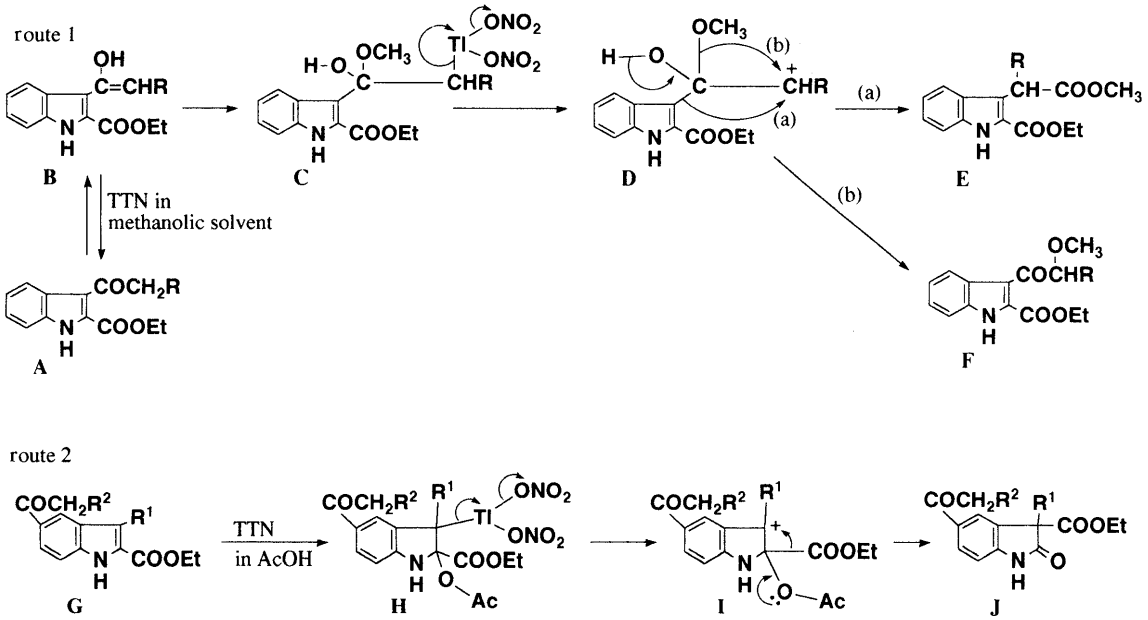


Chart 6. Mechanism for the Reaction of Acylindole with TTN

Trial for Synthetic Application As an application of the present reaction, we intended to synthesize optically active lysergic acid (**23**). Although many reports on synthesis of **23** have appeared, no synthesis of the optically active product has been reported.[10] Prior to the present experiment we had tried a synthesis of optically active lysergic acid (**23**). In that case, we had examined cyclization of the optically active 2-ethoxycarbonyltryptophan derivative (**21**) toward the 4-position for construction of the tricyclic ketone (**22**). In this reaction the 2-ethoxycarbonyl group of **21** should serve as a blocking group against cyclization toward the 2-position. However, the expected cyclization did not occur, but only a tarry product resulted. Nagasaka and Ohki reported[11] that the indole-3-propionic acid (**24a**) carrying no nitrogen functionality at the side chain cyclized to **25a** in 24% yield, whereas the indole-3-butyric acid (**24b**) which is a homo-congener of **24a**, cyclized more easily to give the tricyclic compound (**25b**) with a seven-membered ring in 73% yield. This result showed that a seven-membered ring can be formed more easily than a six-membered ring in this system. This fact suggested that the C-homo-congener (**29**) of **21** would cyclize more easily than **21** to give the seven-membered ketone (**30**). This ketone could be

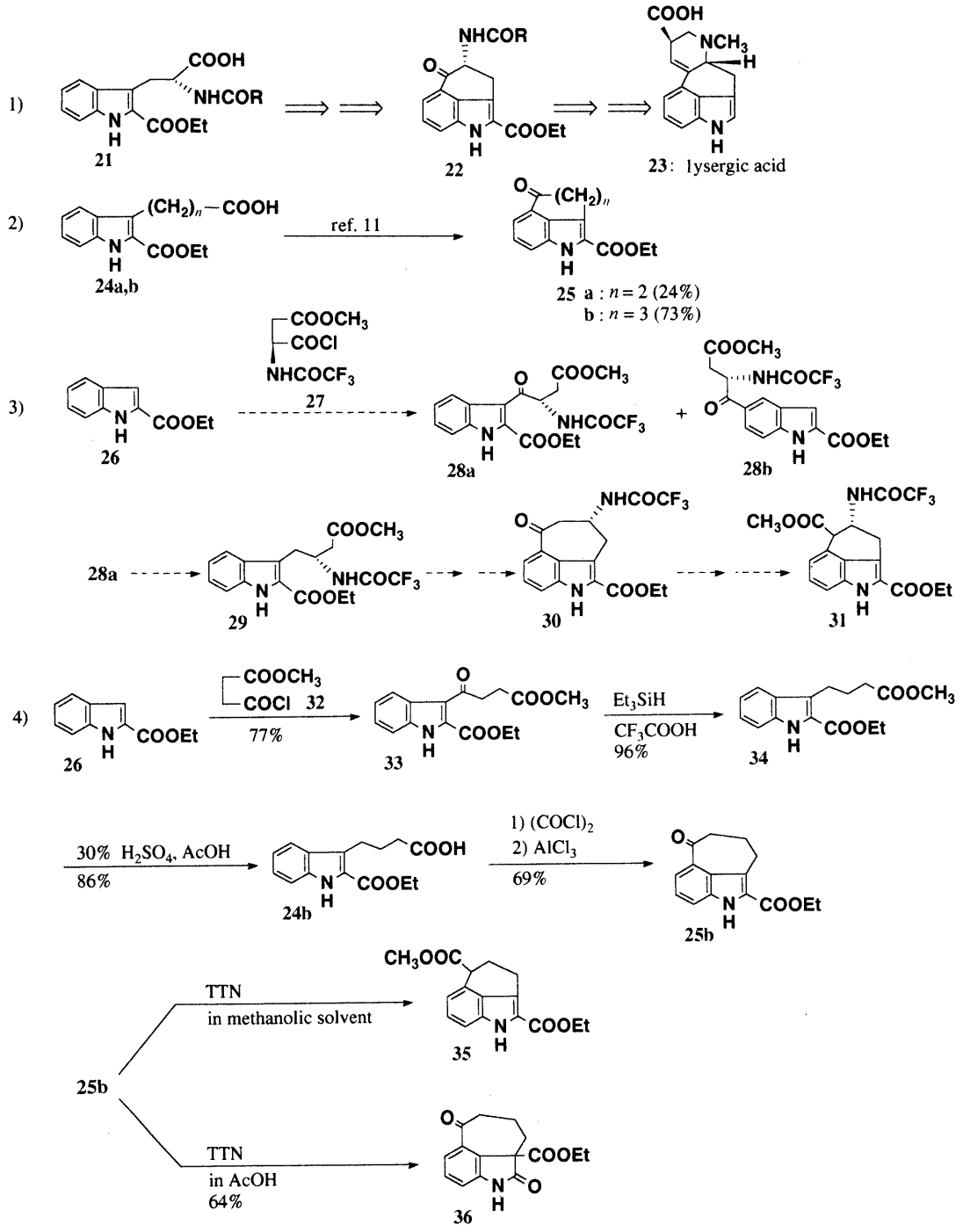


Chart 7

converted to the tricyclic 6-5-6 ring system **31** suitably substituted for synthesis of lysergic acid by means of the present TTN reaction. In order to develop this route we examined the reaction of **25b**[11] with TTN as a model. The 3-acyl compound[5c] (**33**) prepared from ethyl indole-2-carboxylate (**26**) was reduced with triethylsilane in trifluoroacetic acid to afford the 3-alkyl compound (**34**), whose aliphatic ester was hydrolyzed under acidic conditions to give **24b**.[11] Cyclization of **24b** according to the known method[11] gave a known tricyclic ketone (**25b**). The reaction of **25b** with TTN was carried out in the same way (Table I and Chart 2).

The reactions in methanolic solvents gave the desired ring-contracted product (**35**) as shown in Table II. Among them, the reaction in methyl orthoformate/H_2SO_4 gave the best result. The dependence of the product yields on the solvent was the same as in the case of **1f** (runs 16—18 in Table I), which resembles **25b** structurally in having the C_3-alkyl group and a longer alkyl chain in the acyl group. The reaction of the ketone(**25b**) in AcOH gave the oxindole (**36**), as did that of the 3-methylindole (**1e, g**).

On the basis of the successful result in the model reaction, we started to synthesize optically active lysergic acid. The Friedel–Crafts acylation of ethyl indole-2-carboxylate (**26**) with the acyl chloride (**27**) prepared from L-aspartic acid β-methyl ester hydrochloride[12] gave two acyl products. At this stage, it seemed that all spectral data and elemental analysis of the major product could be well explained in terms of the structure **28a**, and the minor product was considered to be the C-5 isomer (**28b**). Thus, **28a** was converted to the tricyclic ketone (**30**), whose structure was provisional at that time. The TTN reaction of **30** in methanol, however, did not give the corresponding ring-contracted product (desired structure **31**). The actual product had the molecular formula $C_{18}H_{17}F_3N_2O_5$ which was the same as that of **31**, but the NMR spectrum did not accord with the structure of **31**: the ^{13}C-NMR spectrum showed three signals due to carbonyl groups at δ 194.88, 161.17, and 156.38. The signal at δ 194.88 corresponded to a ketone moiety and others to the C_2-ester and trifluoroacetylamide carbonyls, suggesting that ring contraction had not occurred, and the seven-membered ring remained. The ^{1}H-NMR spectrum showed that this compound possessed a methoxy (δ 3.77), a methylene (δ 2.19 and δ 3.00), and two methine (δ 5.34 and 5.50) groups on the seven-membered ring. Each methylene proton showed double double doublet signals by coupling with each other (geminal coupling, $J=15$ Hz) and with two methine protons ($J=11$ and 2 Hz, and 5 and 1 Hz, respectively). On the other hand, the two methine protons did not couple with each other. Those data imply the presence of a ketone–methine–methylene–methine chain sequence in the structure.

The above result indicated that the product from the TTN reaction was actually **43** (Chart 8), which should result from methoxylation at the benzylic position of **42**, but not **30**. The methoxylation with TTN was sometimes observed as shown in our present experiment (see Table

TABLE II. The Reaction of **25b** with TTN in Methanolic Solvents

Run	Solvent	TTN (eq)	R. conditions		Yield of **35** (%)
			Temp. (°C)	Time (h)	
1	MeOH	1.0	r.t.	24	46
2	$HC(OCH_3)_3$	4.0	0	10	55
3	$HC(OCH_3)_3/H_2SO_4$	1.5	0	1.5	93

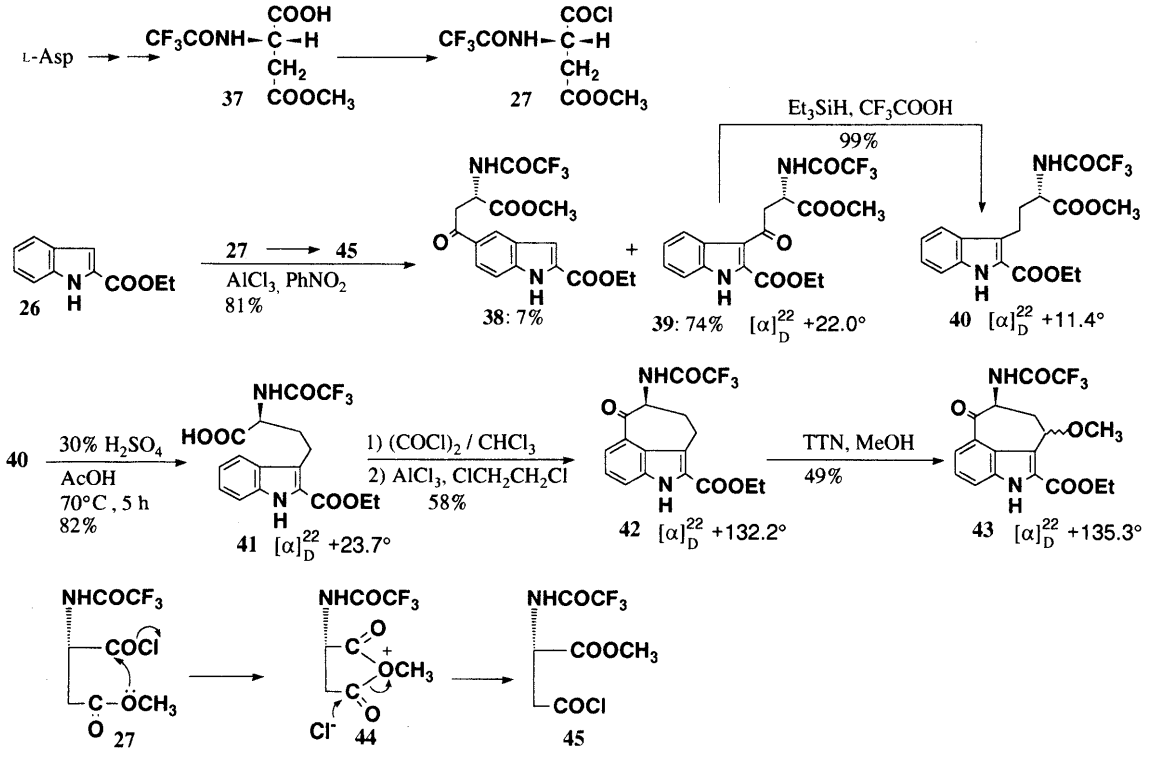


Chart 8

I).

To clarify the situation we investigated the ^{1}H-NMR spectrum of the provisional methylene compound (**29**) in detail, using a proton-proton decoupling method. When the methine proton ($CH_2C\underline{H}NHCO$) at δ 4.70 was irradiated, only the signals at δ 2.28—2.42 ($CH_2C\underline{H}_2CHNHCO$) changed. Next, when the protons at δ 2.28—2.42 ($CH_2C\underline{H}_2CHNHCO$) were irradiated, the multiplet signals at δ 3.14 and 3.30 (arom-$C\underline{H}_2CH_2$) changed to two doublets having only geminal coupling (J=15 Hz), and the signal at δ 4.70 ($CH_2C\underline{H}NHTFA$) changed to a doublet (J=7.5 Hz), derived from the coupling with the amide NH. These results imply a methylene–methylene–methine chain sequence, but not methylene–methine–methylene, so that the compound obtained from the provisional 3-acylindole (**28a**) was not the desired **29**, but **40**. Thus, **42** should be formed from the 3-acylindole **39**, which should be prepared, in turn, by acylation of the indole (**26**) with the β-carbonyl group of the aspartic reagent (**27**). Presumably, **27** was converted in the presence of $AlCl_3$ to the β-acid chloride (**45**) prior to reacting with **26** by the intervention of oxonium ion (**44**), which reacted, in turn, with **26** to give **39**. This idea is based on proposed[13] intervention of a similar oxonium intermediate in acylation. Thus, the structure of the 5-acylindole (**38**) should be as shown in Chart 8, based on acylation with the β-carbonyl of **27**. Therefore, at this stage we discontinued the original synthetic route to optically active lysergic acid.

We are still attempting to synthesize optically active lysergic acid on the basis of the above results.

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) (unless otherwise stated) and JEOL GX-400 (400 MHz) spectrometers. Deuteriochloroform was used as a solvent unless otherwise stated, with tetramethylsilane as an internal reference. The assignments of NH signals were confirmed by disappearance of the signals after addition of deuterium oxide, and the protons of the 3-position of the indole nucleus were identified at the same time, by observing that the broad singlet or doublet signal changed to sharp singlet signal. ^{13}C-NMR spectra were measured on a JEOL GX-400 (100.4 MHz) spectrometer in deuteriochloroform with tetramethylsilane as an internal reference, unless otherwise stated. Mass spectra (MS) were measured on JEOL JMS-01-SG-2 and JEOL JMS-D 300 spectrometers with a direct inlet system. Optical rotations were measured with the JASCO DIP-4 digital polarimeter. TTN was $Tl(ONO_2)_3\cdot 3H_2O$ (Merck) or $Tl(ONO_2)_3$ (Kodak). 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 were done by MS, IR, and especially NMR analyses. When the products were difficult to separate, the ratios of the products were measured by comparison of the intensity of the signals in the 400 MHz ^{1}H-NMR spectrum. The abbreviations used are as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; dt, double triplet; q, quartet; m, multiplet; br, broad; dif, diffused; arom, aromatic; BP, base peak.

General Procedure for the Favorskii-Type Rearrangement Reaction of Acylindoles (1)[5] with TTN in Methanolic Solvent Method A: Methanol or methyl orthoformate (2—4 ml) was added to a mixture of **1** (0.6 mmol) and TTN[2] (0.8—1.8 mmol) under an argon atmosphere. The whole mixture was stirred under the conditions given in Table I, until no further formation of the products was detected by TLC monitoring. The reaction mixture was poured into ice-water and acidified by adding concentrated HCl. The whole mixture was filtered on Celite, and the residue was washed with ethyl acetate. The combined filtrates were extracted with ethyl acetate. The organic layer was washed with saturated $NaHCO_3$ and NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residue was subjected to column chromatography on silica gel; gradient elution with hexane–ethyl acetate or benzene–ethyl acetate gave the products shown in Table I.

Method B (with Sulfuric Acid): Acylindole (**1**) (0.41 mmol) and TTN[2] (0.62—0.66 mmol) were added to a mixture of H_2SO_4 (97%, d=1.84, 0.82 mmol) and methyl orthoformate (2—4 ml) under an argon atmosphere. The whole mixture was stirred under the conditions given in Table I, and worked up as described in method A to give the products shown in Table I.

The Products from Ethyl 3-Acetyl-1*H*-indole-2-carboxylate (1a)[5] Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-3-yl)acetate (**2a**): Colorless prisms from ethyl acetate–hexane, mp 108—109.5 °C. *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.29; H, 5.75; N, 5.34. IR ν_{max} cm^{-1}: 3300 (NH), 1725, 1685 (CO). ^{1}H-NMR δ: 1.38 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.65 (3H, s, $OC\underline{H}_3$), 4.11 (2H, s, arom-$C\underline{H}_2CO$), 4.33 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.90—7.40 (3H, m, C_5-, C_6-, and C_7-H), 7.57 (1H, m, C_4-H), 8.90 (1H, br s, NH). MS m/z: 261 (M^+, 64% of BP), 156 (BP).

Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-3-yl)-2-methoxyacetate (**3a**): Pale orange prisms from benzene–ethyl acetate, mp 136—138 °C. *Anal.* Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.94; H, 5.94; N, 4.80. IR ν_{max} cm^{-1}: 3290 (NH), 1760, 1715 (CO). ^{1}H-NMR δ: 1.42 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.40 (3H, s, $OC\underline{H}_3$), 3.66 (3H, s, $CHOC\underline{H}_3$), 4.44 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.00 (1H, s, arom-$C\underline{H}CO$), 6.97—7.47 (3H, m, C_5-, C_6-, and C_7-H), 7.90 (1H, m, C_4-H), 8.98 (1H, br s, NH). MS m/z: 291 (M^+, 7% of BP), 232 (BP).

Methyl 2-(2-Methoxycarbonyl-1*H*-indol-3-yl)acetate (**4**): Pale yellow prisms from ethyl acetate–hexane, mp 128—129 °C. *Anal.* Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.08; H, 5.31; N, 5.67. IR ν_{max} cm^{-1}: 3325 (NH), 1735, 1677 (CO). ^{1}H-NMR δ: 3.62 (3H, s, $CH_2COOC\underline{H}_3$), 3.83 (3H, s, arom-$COOC\underline{H}_3$), 4.09 (2H, s, arom-$C\underline{H}_2CO$), 6.86—7.38 (3H, m, C_5-, C_6, and C_7-H), 7.49 (1H, m, C_4-H), 8.81 (1H, br s, NH). MS m/z: 247 (M^+, 64% of BP), 156 (BP).

The Products from Ethyl 3-Propionyl-1*H*-indole-2-carboxylate (1b)[5] Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-3-yl)-2-methylacetate (**2b**): Colorless needles from ethyl acetate, mp 104—109 °C. *Anal.* Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.33; H, 6.18; N, 4.97. IR ν_{max} cm^{-1}: 3320 (NH), 1715, 1700 (CO). ^{1}H-NMR δ: 1.39 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.58 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 3.59 (3H, s, $OC\underline{H}_3$), 4.37 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.83 [1H, q, J=7 Hz, arom-$C\underline{H}(CH_3)CO$], 6.84—7.50 (3H, m, C_5-, C_6-, and C_7-H), 7.62 (1H, dif d, J=8 Hz, C_4-H), 8.83 (1H, br s, NH). MS m/z: 275 (M^+, 42% of BP), 170 (BP).

Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-3-yl)-2-methoxy-2-methylacetate (**3b**): Colorless prisms from chloroform–hexane, mp 127—130 °C. *Anal.* Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.65; H, 6.18; N, 4.72. IR ν_{max} cm^{-1}: 3380 (NH), 1735, 1705 (CO). ^{1}H-NMR δ: 1.34 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.86 (3H, s, arom-C-$C\underline{H}_3$), 3.32 (3H, s, arom-C-$OC\underline{H}_3$), 3.69 (3H, s, arom-C-$COOC\underline{H}_3$), 4.28 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.80—7.65 (3H, m, C_5-, C_6-, and C_7-H), 8.09 (1H, m, C_4-H), 8.96 (1H, br s, NH). MS m/z: 305 (M^+, 11% of BP), 246 (BP).

Methyl 3-(2-Methoxy)propionyl-1*H*-indole-2-carboxylate (**5**): Colorless needles from ethyl acetate, mp 128—130 °C. *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.27; H, 5.85; N, 5.30. IR ν_{max} cm^{-1}: 3310 (NH), 1693 (CO). ^{1}H-NMR δ: 1.35 (3H, d, J=7 Hz, arom-$COCHC\underline{H}_3$), 3.42 (3H, s, arom-$COCHOC\underline{H}_3$), 3.90 (3H, s, arom-$COOC\underline{H}_3$), 4.82 (1H, q, J=7 Hz, arom-$COC\underline{H}CH_3$), 7.00—7.55 (3H, m, C_5-, C_6-, and C_7-H), 7.82 (1H, m, C_4-H), 9.40 (1H, br s, NH). MS m/z: 261 (M^+, 10% of BP), 202 (BP).

The Products from Ethyl 5-Acetyl-1*H*-indole-2-carboxylate (1c)[5] Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-5-yl)acetate (**2c**): Colorless needles from benzene–ethyl acetate, mp 120—121 °C. *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.26; H, 5.82; N, 5.41. IR ν_{max} cm^{-1}: 3320 (NH), 1730, 1695 (CO). ^{1}H-NMR δ: 1.39 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 3.64 (5H, s, arom-$C\underline{H}_2CO$ and $OC\underline{H}_3$), 4.37 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 7.01—7.30 (3H, m, C_3-, C_6-, and C_7-H), 7.46 (1H, dif s, C_4-H), 9.12 (1H, br s, NH). MS m/z: 261 (M^+, 81% of BP), 156 (BP).

Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-5-yl)-2-methoxyacetate (**3c**): Pale yellow prisms, mp 97—99.5 °C. *Anal.* Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 62.02; H, 5.95; N, 4.72. IR ν_{max} cm^{-1}:

3300 (NH), 1750, 1730, 1695 (CO). ^{1}H-NMR δ: 1.40 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 3.38 (3H, s, $COOC\underline{H}_3$ or $CHOC\underline{H}_3$), 3.69 (3H, s, $CHOC\underline{H}_3$ or $COOC\underline{H}_3$), 4.40 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.83 [1H, s, arom-C$\underline{H}$(OCH_3)$COOCH_3$], 7.17 (1H, d, J=2.5 Hz, C_3-H), 7.37 (2H, s, C_6- and C_7-H), 7.73 (1H, m, C_4-H), 9.05 (1H, br s, NH). MS m/z: 291 (M^+, 9% of BP), 232 (BP).

The Products from Ethyl 5-Propionyl-1*H*-indole-2-carboxylate (1d)[5] Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-5-yl)-2-methylacetate (**2d**): Colorless needles from ethyl acetate, mp 95—97 °C. *Anal.* Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.41; H, 6.18; N, 5.17. IR ν_{max} cm^{-1}: 3295 (NH), 1735, 1695 (CO). ^{1}H-NMR δ: 1.38 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.52 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 3.59 (3H, s, $OC\underline{H}_3$), 3.78 [1H, q, J=7 Hz, arom-C$\underline{H}$(CH_3)CO], 4.35 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.11 (1H, d, J=2 Hz, C_3-H), 7.23 (2H, br s, C_6- and C_7-H), 7.50 (1H, br s, C_4-H), 9.03 (1H, br s, NH). MS m/z: 275 (M^+, 41% of BP), 216 (BP).

The Products from Ethyl 5-Acetyl-3-methyl-1*H*-indole-2-carboxylate (1e)[5] Methyl 2-(2-Ethoxycarbonyl-3-methyl-1*H*-indol-5-yl)acetate (**2e**): Colorless needles from ethyl acetate–hexane, mp 115—116 °C. *Anal.* Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.37; H, 6.31; N, 5.26. IR ν_{max} cm^{-1}: 3300 (NH), 1740, 1675 (CO). ^{1}H-NMR δ: 1.38 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 2.53 (3H, s, arom-$C\underline{H}_3$), 3.63 (5H, s, arom-$C\underline{H}_2$CO and $OC\underline{H}_3$), 4.36 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 7.15 (2H, s, C_6- and C_7-H), 7.42 (1H, s, C_4-H), 8.74 (1H, br s, NH). MS m/z: 275 (M^+, BP).

Methyl 2-(2-Ethoxycarbonyl-3-methyl-1*H*-indol-5-yl)-2-methoxyacetate (**3e**): Colorless plates from ethyl acetate–hexane, mp 118.5—120 °C. *Anal.* Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.66; H, 6.29; N, 4.70. IR ν_{max} cm^{-1}: 3295 (NH), 1745, 1730, 1675 (CO). ^{1}H-NMR δ: 1.40 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.58 (3H, s, arom-$C\underline{H}_3$), 3.38 (3H, s, OCH_3), 3.68 (3H, s, $OC\underline{H}_3$), 4.39 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.83 (1H, s, arom-C$\underline{H}$$COOCH_3$), 7.30 (2H, dif s, C_6- and C_7-H), 7.68 (1H, dif s, C_4-H), 8.81 (1H, br s, NH). MS m/z: 305 (M^+, 15% of BP), 246 (BP).

Methyl (2-Ethoxycarbonyl-3-methyl-1*H*-indol-5-yl)oxalate (**6**): Colorless needles from benzene–hexane, mp 139—145 °C. High-resolution MS: Calcd for $C_{15}H_{15}NO_5$: 289.0951. Found: 289.0950. IR ν_{max} cm^{-1}: 3290 (NH), 1730, 1680, 1660 (CO). ^{1}H-NMR δ: 1.41 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.60 (3H, s, arom-$C\underline{H}_3$), 3.96 (3H, s, $OC\underline{H}_3$), 4.41 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.34 (1H, d, J=9 Hz, C_7-H), 7.96 (1H, dd, J=9, 2 Hz, C_6-H), 8.32 (1H, dif s, C_4-H), 9.20 (1H, br s, NH). MS m/z: 289 (M^+, 24% of BP), 230 (BP).

Ethyl 5-Methoxycarbonyl-3-methyl-1*H*-indole-2-carboxylate (**7**): Colorless needles from benzene–hexane, mp 157.5—160 °C. High-resolution MS: Calcd for $C_{14}H_{15}NO_4$: 261.1001. Found: 261.0964. IR ν_{max} cm^{-1}: 3300 (NH), 1710, 1675 (CO). ^{1}H-NMR δ: 1.42 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.61 (3H, s, arom-$C\underline{H}_3$), 3.90 (3H, s, $OC\underline{H}_3$), 4.40 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.30 (1H, d, J=9 Hz, C_7-H), 7.93 (1H, dd, J=9, 2 Hz, C_6-H), 8.41 (1H, dif s, C_4-H), 8.92 (1H, br s, NH). MS m/z: 261 (M^+, 69% of BP), 215 (BP).

Methyl 2-(2,2-Dimethoxymethyl-(2-ethoxycarbonyl-3-methyl-1*H*-indol-5-yl))acetate (**8**): Colorless needles from hexane–ethyl acetate, mp 139.5—142.5 °C. High-resolution MS: Calcd for $C_{18}H_{23}NO_6$: 349.1525. Found: 349.1512. IR ν_{max} cm^{-1}: 3310 (NH), 1730, 1675 (CO). ^{1}H-NMR (400 MHz) δ: 1.42 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.60 (3H, s, arom-$C\underline{H}_3$), 3.18, 3.48, and 3.69 (each 3H, s, $OC\underline{H}_3$), 3.99 and 5.04 [each 1H, d, J=9 Hz, arom-C$\underline{H}$($COOCH_3$)C$\underline{H}$(OCH_3)$_2$], 4.41 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.32 (1H, d, J=8 Hz, C_7-H), 7.37 (1H, dd, J=8, 2 Hz, C_6-H), 7.65 (1H, dif s, C_4-H), 8.64 (1H, br s, NH). MS m/z: 349 (M^+, 25% of BP), 47 (BP).

The Products from Ethyl 3-Methyl-5-propionyl-1*H*-indole-2-carboxylate (1f)[5] Methyl 2-(2-Ethoxycarbonyl-3-methyl-1*H*-indol-5-yl)-2-methylacetate (**2f**): Colorless needles from ethyl acetate, mp 112—113.5 °C. *Anal.* Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.30; H, 6.62; N, 5.00. IR ν_{max} cm^{-1}: 3300 (NH), 1735, 1673 (CO). ^{1}H-NMR δ: 1.38 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.53 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.55 (3H, s, arom-$C\underline{H}_3$), 3.60 (3H, s, $OC\underline{H}_3$), 3.78 (1H, q, J=7 Hz, arom-C$\underline{H}$$CH_3$), 4.36 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.20 (2H, s, C_6- and C_7-H), 7.47 (1H, s, C_4-H), 8.70 (1H, br s, NH). MS m/z: 289 (M^+, 70% of BP), 230 (BP).

Methyl 2-(2-Ethoxycarbonyl-3-methyl-1*H*-indol-5-yl)-2-methyl-2-methoxyacetate (**3f**): Colorless plates from ethyl acetate–hexane, mp 141—144 °C. *Anal.* Calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39. Found: C, 63.64; H, 6.60; N, 4.53. IR ν_{max} cm^{-1}: 3320 (NH), 1730, 1675 (CO). ^{1}H-NMR δ: 1.40 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.85 (3H, s, arom-C–$C\underline{H}_3$), 2.58 (3H, s, arom-$C\underline{H}_3$), 3.25 (3H, s, arom-C–$OC\underline{H}_3$), 3.68 (3H, s, arom-C–$COOC\underline{H}_3$), 4.37 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.28 (2H, s, C_6- and C_7-H), 7.70 (1H, dif s, C_4-H), 8.74 (1H, br s, NH). MS m/z: 319 (M^+, 9% of BP), 260 (BP).

Ethyl 5-(2-Methoxy)propionyl-3-methy-1*H*-indole-2-carboxylate (**9**): Colorless needles from ethyl acetate, mp 175—179 °C. High-resolution MS: Calcd for $C_{16}H_{19}NO_4$: 289.1314. Found: 289.1307. IR ν_{max} cm^{-1}: 3315 (NH), 1730, 1695, 1675 (CO). ^{1}H-NMR δ: 1.42 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.53 (3H, d, J=7 Hz, $COCHC\underline{H}_3$), 2.62 (3H, s, arom-$C\underline{H}_3$), 3.38 (3H, s, $CHOC\underline{H}_3$), 4.40 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.67 [1H, q, J=7 Hz, $COC\underline{H}$(OCH_3)CH_3], 7.31 (1H, d, J=8 Hz, C_7-H), 7.97 (1H, dd, J=8, 1.5 Hz, C_6-H), 8.42 (1H, dif s, C_4-H), 9.16 (1H, br s, NH). MS m/z: 289 (M^+, 13% of BP), 230 (BP).

General Procedure for the Reaction of Acylindoles (1) with TTN in Acetic Acid Acetic acid (1.8—2.0 ml) was added to a mixture of **1** (0.39 mmol) and TTN (0.39—0.47 mmol) under an argon atmosphere. The whole mixture was stirred until no further formation of the products was detected by TLC monitoring, and the reaction mixture was poured into ice-water, and worked up as described above to give the products (see Chart 2).

1*H*-3,4-Dihydropyrano[3,4-*b*]indole-1,4-dione (**11**): Pale yellow needles from ethyl acetate–hexane, mp 283—287 °C. *Anal.* Calcd for $C_{11}H_7NO_3$: C, 65.67; H, 3.51; N, 6.96. Found: C, 65.75; H, 3.51; N, 7.00. IR ν_{max} cm^{-1}: 3225 (NH), 1705, 1665 (CO). ^{1}H-NMR [$(CD_3)_2SO$] δ: 5.12 (2H, s, $COC\underline{H}_2O$), 7.10—7.78 (3H, m, arom-H), 8.00 (1H, m, arom-H), 13.20 (1H, br s, NH). MS m/z: 201 (M^+, 73% of BP), 143 (BP).

Ethyl 5-(Acetoxy)acetyl-1*H*-indole-2-carboxylate (**12**): Colorless prisms from ethyl acetate–hexane, mp 167—170.5 °C. High-resolution MS: Calcd for $C_{15}H_{15}NO_5$: 289.0950. Found: 289.0906. IR ν_{max} cm^{-1}: 3310 (NH), 1760, 1695, 1670 (CO). ^{1}H-NMR δ: 1.41 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.21 (3H, s, $OC\underline{H}_3$), 4.43 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 5.40 (2H, s, $COC\underline{H}_2O$), 7.21—8.37 (4H, m, arom-H), 9.30 (1H, br s, NH). MS m/z: 289 (M^+, 14% of BP), 216 (BP).

Ethyl 5-Acetyl-2,3-dihydro-3-methyl-2-oxo-1*H*-indole-3-carboxylate (**10e**): Colorless needles from ethyl actate, mp 170—172 °C. *Anal.* Calcd for $C_{14}H_{15}NO_4$: C, 64.35; H, 5.79; N, 5.36. Found: C, 64.51; H, 5.78; N, 5.28. IR ν_{max} cm^{-1}: 3289 (NH), 1725, 1675 (CO). ^{1}H-NMR δ: 1.16 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.71 (3H, s, C_3-$C\underline{H}_3$), 2.56 (3H, s, $COC\underline{H}_3$), 4.14 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.00 (1H, d, J=9 Hz, C_7-H), 7.81 (1H, s, C_4-H), 7.90 (1H, dd, J=9, 2 Hz, C_6-H), 9.59 (1H, br s, NH). ^{13}C-NMR δ: 13.92 ($OCH_2\underline{C}H_3$), 20.05 (C_3-$\underline{C}H_3$), 26.40 ($CO\underline{C}H_3$), 55.56 (C_3), 62.35 ($O\underline{C}H_2CH_3$), 110.00, 123.56, and 130.80 (C_4, C_6, and C_7), 131.20, 132.61, and 145.48 (C_{3a}, C_5, and C_{7a}), 168.96 and 177.95 (C_2 and C_3–$\underline{C}OO$), 196.64 (C_5-$\underline{C}OCH_3$). MS m/z: 261 (M^+, 43% of BP), 188 (BP).

Ethyl 2,3-Dihydro-3-methyl-2-oxo-1*H*-indole-3-carboxylate (**10g**): Pale yellow prisms from ethyl acetate–hexane, mp 78—85 °C. High-resolution MS: Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0882. IR ν_{max} cm^{-1}: 3150 (NH), 1735, 1715 (CO). ^{1}H-NMR δ: 1.15 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.68 (3H, s, C_3-$C\underline{H}_3$), 4.11 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 6.80—7.43 (4H, m, arom-H), 9.40 (1H, br s, NH). MS m/z: 219 (M^+, 36% of BP), 146 (BP).

2-(2-Ethoxycarbonyl-1*H*-indol-3-yl)-2-methylacetic Acid (13) A mixture of methyl 2-(2-ethoxycarbonyl-1*H*-indol-3-yl)-2-methylacetate (**2b**) (710 mg, 2.6 mmol), AcOH (13.1 ml), and 30% H_2SO_4 (5.6 ml) was stirred at 60 °C for 11.5 h, and then poured into ice-water. Filtration with suction gave crude **13** (598 mg, 89%). Recrystallization from ethyl acetate–hexane gave pure **13** as colorless needles (515 mg, 76%), mp 146—162 °C. High-resolution MS: Calcd for $C_{14}H_{15}NO_4$: 261.1001. Found: 261.0985. IR ν_{max} cm^{-1}: 3325 (NH), 1710, 1690, 1685 (CO). ^{1}H-NMR [$(CD_3)_2SO$] δ: 1.34 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.42 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 4.32 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 4.69 (1H, q, J=7 Hz, arom-C$\underline{H}$$CH_3$), 6.80—7.80 (4H, m, arom-H), 11.55 (1H, br s, NH). MS m/z: 261 (M^+, 37% of BP), 170 (BP).

2-(2-Ethoxycarbonyl-1*H*-indol-5-yl)-2-methylacetic Acid (14) A mixture of methyl 2-(2-ethoxycarbonyl-1*H*-indol-5-yl)-2-methylacetate (**2d**) (734 mg, 2.7 mmol), AcOH (13.5 ml), and 10% H_2SO_4 (6.0 ml) was stirred at 65 °C for 10.0 h, and then poured into ice-water. Filtration with suction gave crude **14** (666 mg, 96%). Recrystallization from ethyl acetate–hexane gave pure **14** as colorless needles (354 mg, 51%), mp 178—182 °C. High-resolution MS: Calcd for $C_{14}H_{15}NO_4$: 261.1001. Found: 261.0988. IR ν_{max} cm^{-1}: 3300 (NH), 1695 (CO). ^{1}H-NMR [$(CD_3)_2SO$]

δ: 1.35 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.41 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 3.70 (1H, q, J=7 Hz, arom-$C\underline{H}CH_3$), 4.32 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.00—7.60 (4H, m, arom-H), 11.75 (1H, br s, NH). MS m/z: 261 (M^+, 60% of BP), 216 (BP).

General Procedure for the Reaction of Acetylindoles (1c, 16) with TTN in Trifluoroacetic Acid Trifluoroacetic acid (2 ml) was added to a mixture of ethyl acetyl-1*H*-indole-2-carboxylate **1c**, **16** (0.43 mmol) and TTN (0.48 mmol), under an argon atmosphere. The whole mixture was stirred under the conditions given in Chart 4, poured into ice-water, and filtered on Celite. The residue was washed with ethyl acetate. The separated organic layer was washed with saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residue was subjected to column chromatography on silica gel using a gradient of benzene–ethyl acetate to give the C_3-nitrated compounds **15**, **17**.

Ethyl 5-Acetyl-3-nitro-1*H*-indole-2-carboxylate (**15**): Pale yellow prisms from ethyl acetate–hexane, mp 187—189 °C. *Anal.* Calcd for $C_{13}H_{12}N_2O_5$: C, 56.52; H, 4.38; N, 10.14. Found: C, 56.34; H, 4.27; N, 10.19. IR ν_{max} cm^{-1}: 3200 (NH), 1735, 1665 (CO). ^{1}H-NMR [$(CD_3)_2SO$] δ: 1.40 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.67 (3H, s, $COC\underline{H}_3$), 4.48 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.63 (1H, d, J=8 Hz, C_7-H), 7.97 (1H, dd, J=8, 2 Hz, C_6-H), 8.58 (1H, d, J=2 Hz, C_4-H), 13.45 (1H, br s, NH). MS m/z: 276 (M^+, 56% of BP), 261 (BP).

Ethyl 7-Acetyl-3-nitro-1*H*-indole-2-carboxylate (**17**): Pale yellow prisms from ethyl acetate–hexane, mp 118—121 °C. *Anal.* Calcd for $C_{13}H_{12}N_2O_5$: C, 56.52; H, 4.38; N, 10.14. Found: C, 56.66; H, 4.48; N, 10.18. IR ν_{max} cm^{-1}: 3250 (NH), 1740, 1660 (CO). ^{1}H-NMR δ: 1.46 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.70 (3H, s, $COC\underline{H}_3$), 4.50 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.38 (1H, t, J=8 Hz, C_5-H), 7.93 (1H, dd, J=8, 1 Hz, C_6-H), 8.28 (1H, d, J=8 Hz, C_4-H), 11.08 (1H, br s, NH). MS m/z: 276 (M^+, BP).

Reaction of Ethyl 3-Methyl-5-propionyl-1*H*-indole-2-carboxylate (1f) with $PhI(OAc)_2$. Methyl 2-(2-Ethoxycarbonyl-1*H*-indol-5-yl)-2-methylacetate (2f) A mixture of 97% H_2SO_4 (d=1.84, 80 mg, 0.79 mmol), $PhI(OAc)_2$ (149 mg, 0.46 mmol), **1f** (100 mg, 0.39 mmol), and methyl orthoformate (5 ml) was stirred at room temperature for 6 days under an argon atmosphere. Then 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*. The residue was subjected to column chromatography on silica gel using toluene–ethyl acetate gradient elution to give crude **2f** (8 mg, 8%), and **1f** (43 mg, 43% recovery). The compound **2f** obtained by this method was identical with **2f** obtained from the other reaction of **1f** with TTN, based on TLC and NMR comparisons.

Reaction of Ethyl 3-Acetyl-1*H*-indole-2-carboxylate (1a) with $Pb(OAc)_4$. Methyl 3-Acetyl-1*H*-indole-2-carboxylate (19) A solution of **1a** (111 mg, 0.48 mmol) and BF_3OEt_2 (0.5 ml, 4.1 mmol) in absolute methanol (4 ml) was added to a mixture of $Pb(OAc)_4$ (90%, 354 mg, 0.72 mmol) and benzene (2 ml) under an argon atmosphere. The whole mixture was stirred for 23 h at room temperature, 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 a residue (94 mg). The residue was then subjected to column chromatography using benzene–ethyl acetate (5 : 1) to give crude **19** (40 mg, 38%) as colorless crystals and **1a** (10 mg, 9% recovery). Recrystallization from ethyl acetate–hexane gave pure **19** as colorless plates, mp 159.5—161.5 °C. *Anal.* Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.30; H, 5.12; N, 6.46. IR ν_{max} cm^{-1}: 3250 (NH), 1720, 1645 (CO). ^{1}H-NMR δ: 2.73 (3H, s, $COC\underline{H}_3$), 3.95 (3H, s, $COOC\underline{H}_3$), 7.10—7.51 (3H, m, C_5-, C_6-, and C_7-H), 8.00 (1H, m, C_4-H), 9.41 (1H, br s, NH). MS m/z: 217 (M^+, 71% of BP), 170 (BP).

5-Acetyl-3-methyl-2,3-dihydro-1*H*-indol-2-one (20) A mixture of ethyl 5-acetyl-3-methyl-2,3-dihydro-2-oxo-1*H*-indole-3-carboxylate (**10e**) (80 mg, 0.31 mmol), AcOH (0.9 ml), and 97% H_2SO_4 (0.45 ml) was stirred at 70 °C for 6.5 h. After cooling, 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*. The residue (59 mg) was chromatographed on silica gel with benzene–ethyl acetate to give crude **20** (37 mg, 64%). Recrystallization from hexane–ethyl acetate gave pure **20** as colorless needles (30 mg, 52%), mp 158—161 °C. High-resolution MS: Calcd for $C_{11}H_{11}NO_2$: 189.0790. Found: 189.0794. IR ν_{max} cm^{-1}: 3150 (NH), 1705, 1675 (CO). ^{1}H-NMR δ: 1.53 (3H, d, J=8 Hz, $CHC\underline{H}_3$), 2.56 (3H, s, $COC\underline{H}_3$), 3.51 (1H, q, J=8 Hz, $COC\underline{H}CH_3$), 6.96 (1H, d, J=8 Hz, C_7-H), 7.70—8.00 (2H, m, C_4- and C_6-H), 9.71 (1H, br s, NH). MS m/z: 189 (M^+, 55% of BP), 174 (BP).

Methyl 4-(2-Ethoxycarbony-1*H*-indol-3-yl)butyrate (34) Triethylsilane (12 ml, 73.8 mmol) was added dropwise to a solution of ethyl 3-(3-methoxycarbonyl)propionyl-1*H*-indole-2-carboxylate (**33**)[5c] (6.00 g, 19.8 mmol) in trifluoroacetic acid (69.3 ml) and the mixture was stirred for 3 h at room temperature. Distillation of trifluoroacetic acid under reduced pressure gave an oily residue. The residue was dissolved in ethyl acetate and the organic layer was washed with saturated $NaHCO_3$ and saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give a colorless crystalline residue (6.66 g). The residue was chromatographed on silica gel with benzene to give **34** as colorless crystals (5.50 g, 96.1%). Recrystallization from methylene chloride–hexane gave pure **34** as colorless needles (4.97 g, 87%), mp 80—81 °C. *Anal.* Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.50; H, 6.69; N, 4.69. IR ν_{max} cm^{-1}: 3325 (NH), 1719, 1675 (CO). ^{1}H-NMR δ: 1.40 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 1.72—2.60 (4H, m, arom-$C\underline{H}_2C\underline{H}_2CH_2$), 3.16 (2H, t, J=7.5 Hz, $CH_2C\underline{H}_2COOCH_3$), 3.62 (3H, s, $OC\underline{H}_3$), 4.41 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 6.90—7.50 (3H, m, C_5-, C_6-, and C_7-H), 7.68 (1H, m, C_4-H), 8.98 (1H, br s, NH). MS m/z: 289 (M^+, 88% of BP), 156 (BP).

4-(2-Ethoxycarbonyl-1*H*-indol-3-yl)butyric Acid (24b)[11] A solution of methyl 4-(2-ethoxycarbonyl-1*H*-indol-3-yl)butyrate (**34**) (5.55 g, 19.2 mmol) in AcOH (14.4 ml) and 30% H_2SO_4 (7.2 ml) was stirred for 4.5 h at 70 °C. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The organic layer was extracted with saturated Na_2CO_3. The alkaline solution was acidified with 5% HCl and extracted with ethyl acetate. The organic layer was washed with saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give **24b** (4.53 g, 86%). Recrystallization from benzene–ethyl acetate gave pure **24b** as colorless needles (4.20 g, 79.5%), mp 132—134 °C [lit.[11] colorless prisms (from benzene), mp 135 °C]. *Anal.* Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.56; H, 6.16; N, 4.90. IR ν_{max} cm^{-1}: 3330 (NH), 1707 (CO). ^{1}H-NMR [$(CD_3)_2SO$] δ: 1.39 (3H, t, J=7.5 Hz, $CH_2C\underline{H}_3$), 1.68—2.70 (4H, m, arom-$C\underline{H}_2C\underline{H}_2CH_2$), 3.10 (2H, t, J=7 Hz, $CH_2C\underline{H}_2COOH$), 4.36 (2H, q, J=7.5 Hz, $OC\underline{H}_2CH_3$), 6.83—7.79 (4H, m, arom-H), 11.35 (1H, br s, NH or OH), 11.85 (1H, br s, OH or NH). MS m/z: 275 (M^+, 64% of BP), 156 (BP).

Ethyl 3,4,5,6-Tetrahydro-6-oxo-1*H*-cyclohept[*c*,*d*]indole-2-carboxylate (25b)[11] Oxalyl chloride (3.8 ml, 43.6 mmol) was added dropwise to a suspension of **24b** (4.00 g, 14.5 mmol) in chloroform (60 ml). The reaction mixture was stirred at room temperature for 0.5 h then at 40 °C for 15 min. It changed to a clear solution during the formation of the acid chloride and generated carbon monoxide. After the solvent was distilled off, 1,2-dichloroethane (300 ml) and $AlCl_3$ (7.86 g, 60.5 mmol) were added successively. The whole mixture was stirred for 2 h at room temperature, then at 60 °C for 0.5 h. The reaction mixture was poured into ice-water, and extracted with chloroform. The organic layer was washed with saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give a residue (3.55 g). The residue was subjected to column chromatography on silica gel with chloroform to give **25b** (2.92 g, 78%). Recrystallization from ethanol–hexane gave pure **25b** as colorless prisms (2.43 g, 65%), mp 155—158 °C [lit.[11] pale yellow prisms (from ethanol), mp 154—156 °C]. *Anal.* Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.77; H, 5.88; N, 5.42. IR ν_{max} cm^{-1}: 3330 (NH), 1690, 1655 (CO). ^{1}H-NMR δ: 1.43 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 2.18 (2H, m, $CH_2C\underline{H}_2CH_2$), 3.05 (2H, m, $CH_2C\underline{H}_2CO$ or arom-$C\underline{H}_2CH_2$), 3.40 (2H, m, arom-$C\underline{H}_2CH_2$ or $CH_2C\underline{H}_2CO$), 4.44 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.33 (1H, t, J=8 Hz, C_8-H), 7.60 (1H, dd, J=8, 2 Hz, C_9- or C_7-H), 7.93 (1H, dd, J=8, 2 Hz, C_7- or C_9-H), 9.30 (1H, br s, NH). MS m/z: 257 (M^+, 82% of BP), 228 (BP).

Methyl 2-Ethoxycarbonyl-1,3,4,5-tetrahydro-1*H*-benz[*c*,*d*]indole-5-carboxylate (35) 1) In Methyl Orthoformate with Sulfuric Acid: Successively, **25b** (0.40 mmol) and TTN (0.60 mmol) was added to a mixture of 97% H_2SO_4 (d=1.84, 0.95 mmol) and methyl orthoformate (3 ml) under an argon atmosphere. The whole mixture was stirred for 1 h at 0 °C, then poured into ice-water, and filtered on Celite. The residue was washed with ethyl acetate. Combined filtrates were 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 a residue (115 mg). The residue was subjected to column chromatography on silica gel with benzene–ethyl acetate to give a pro-

duct (**35**, 107 mg, 93%) and **25b** (4 mg, 4%). Recrystallization from benzene–hexane gave pure **35** as colorless prisms (86 mg, 75%).

2) In Methanol: Methanol (2 ml) was added to a mixture of **25b** (0.78 mmol) and TTN (0.78 mmol) under an argon atmosphere. The reaction mixture was stirred for 24 h at room temperature, 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 a residue (237 mg). The residue was subjected to column chromatography on silica gel with ethyl acetate–hexane gave a product (**35**, 102 mg, 46%) and **25b** (40 mg, 20%). Recrystallization from hexane–benzene gave pure **35** as colorless prisms (91 mg, 41%), mp 121—123 °C. *Anal.* Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.96; N, 4.88. Found: C, 66.96; H, 5.97; N, 4.83. IR ν_{max} cm^{-1}: 3300 (NH), 1708, 1675 (CO). ^{1}H-NMR δ: 1.42 (3H, t, J=7 Hz, CH_2CH_3), 2.00—2.73 (2H, m, arom-CH_2CH_2 or CH_2CH_2CH), 3.15—3.50 (2H, m, CH_2CH_2CH or arom-CH_2CH_2), 3.78 (3H, s, OCH_3), 4.10 [1H, t, J=6 Hz, arom-CH(COOCH$_3$)CH$_2$], 4.47 (2H, q, J=7 Hz, OCH_2CH_3), 6.90—7.45 (3H, m, arom-H), 8.86 (1H, br s, NH). ^{13}C-NMR δ: 14.50 (CH_2CH_3), 20.75 and 27.28 (arom-CH_2CH_2CH), 43.09 (arom-$CHCH_2$), 52.01 (OCH_3), 60.67 (OCH_2CH_3), 110.09, 117.28, and 126.38 (C_6, C_7, and C_8), 120.99, 121.47, 126.70, 130.22, and 134.61 (*tert*-carbon), 162.54 and 173.93 ($COOCH_3$ and $COOCH_2CH_3$). MS *m/z*: 287 (M^+, BP).

2a-Ethoxycarbonyl-2,2a,3,4,5,6-hexahydro-1*H*-cyclohept[*c,d*]indole-2,6-dione (36) AcOH (2 ml) was added to a mixture of **25b** (0.39 mmol) and TTN (0.39 mmol) under an argon atmosphere. The mixture was stirred overnight at room temperature, then poured into ice-water, and filtered on Celite. The residue was washed with hot ethyl acetate, and the combined filtrates were 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 a residue (96 mg). The residue was subjected to column chromatography on silica gel with ethyl acetate–hexane to give a product (**36**, 67 mg, 64%). Recrystallization from benzene–ethyl acetate gave **36** as pale yellow prisms, mp 137—143 °C. *Anal.* Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.68; H, 5.51; N, 5.10. IR ν_{max} cm^{-1}: 3140 (NH), 1730, 1720, 1680 (CO). ^{1}H-NMR (400 MHz) δ: 1.12 (3H, t, J=7 Hz, CH_2CH_3), 1.81 and 2.19 (each 1H, m, $CH_2CH_2CH_2$), 1.96 and 3.05 [each 1H, m, CH_2CH_2C(COOEt)] 2.77 (2H, dd, J=7, 5 Hz, CH_2CH_2CO), 7.13 (1H, d, J=8 Hz, C_7- or C_9-H), 7.40 (1H, t, J=8 Hz, C_8-H), 7.49 (1H, dd, J=8, 1 Hz, C_9- or C_7-H), 8.55 (1H, br s, NH). MS *m/z*: 273 (M^+, 68% of BP), 200 (BP).

β-Methyl *N*-Trifluoroacetyl-L-aspartate (37)[14] Trifluoroacetic anhydride (5 ml, 35.4 mmol) was added dropwise to a solution of β-methyl L-aspartate hydrochloride[12] (3.3 g, 18 mmol) in trifluoroacetic acid (16 ml) at 0 °C under an argon atmosphere. The mixture was allowed to warm to room temperature, and stirred for 6 h. Distillation of trifluoroacetic acid under reduced pressure gave **37** (4.1 g, 94%) as colorless oil. $[\alpha]_D^{22}$ −1.23° (c=0.062, AcOEt). *Anal.* Calcd for $C_7H_8F_3NO_5$: C, 34.58; H, 3.32; N, 5.76. Found: C, 34.14; H, 3.41; N, 5.76. IR ν_{max} cm^{-1}: 3395 (NH), 3600—2300 (OH), 1735, 1720 (CO). ^{1}H-NMR (400 MHz) δ: 2.96 (1H, dd, J=18, 4 Hz, one of $CHCH_2CO$). 3.15 (1H, dd, J=18, 4 Hz, one of $CHCH_2CO$), 3.74 (3H, s, OCH_3), 4.90 (1H, dt, J=8, 4 Hz, CH_2CHNH), 7.64 (1H, d, J=8 Hz, CHNHCO). MS *m/z*: 212 ($M^+ - OCH_3$, 5% of BP), 198 (BP).

Acylation of Ethyl 1*H*-Indole-2-carboxylate (26) with β-Methyl *N*-Trifluoroacetyl-L-aspartyl α-Chloride (27) Oxalyl chloride (4.3 ml, 49.3 mmol) was added to a solution of **37** (1.195 g, 4.92 mmol) in methylene chloride (5 ml) under an argon atmosphere and the mixture was stirred overnight at room temperature, then for 2 h at 30 °C, and evaporated to dryness *in vacuo* to give **27** as a yellow oil. A solution of **26** (300 mg, 1.6 mmol) in nitrobenzene (5 ml) was added to a mixture of **27**, $AlCl_3$ (635 mg, 4.8 mmol), and nitrobenzene (5 ml). The whole mixture was stirred for 1 h at 0 °C and for 5 h at room temperature, then 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 give a residue. The residue was subjected to column chromatography on silica gel; gradient elution with benzene–ethyl acetate gave a mixture of methyl (2*S*)-4-(2-ethoxycarbonyl-1*H*-indol-3-yl)-4-oxo-2-trifluoroacetoamidobutyrate (**39**) and methyl (2*S*)-4-(2-ethoxycarbonyl-1*H*-indol-5-yl)-4-oxo-2-trifluoroacetoamidobutyrate (**38**) (535 mg, 81%, **39** : **38** = 10.8 : 1). The ratio of the yields of **39** and **38** was measured on a Hitachi 635A liquid chromatograph (HPLC) [column, Waters Radial Pack Silica (5 μm) (8 × 100 mm); wavelength, 258 nm; solvent, methylene chloride : ethyl acetate = 10 : 1]. The mixture was then subjected to column chromatography on silica gel; gradient elution with methylene chloride–ethyl acetate to give **39** (489 mg, 74%) and **38** (45 mg, 7%) as yellow crystals, respectively. Recrystallizations of both crude **39** and **38** from ethyl acetate–hexane gave the pure C-3 acylated compound **39** and its C-5 isomer **38**, respectively.

38: Colorless prisms from ethyl acetate–hexane, mp 202—203 °C. *Anal.* Calcd for $C_{18}H_{17}F_3N_2O_6$: C, 52.18; H, 4.14; N, 6.76. Found: C, 52.51; H, 4.23; N, 6.56. IR ν_{max} cm^{-1}: 3290 (NH), 1758, 1710, 1680, 1670 (CO). ^{1}H-NMR [400 MHz, $(CD_3)_2SO$] δ: 1.36 (3H, t, J=7 Hz, CH_2CH_3), 3.62—3.78 (2H, m, $COCH_2CH$), 3.69 (3H, s, OCH_3), 4.37 (2H, q, J=7 Hz, OCH_2CH_3), 4.93 (1H, dt, J=7, 5 Hz, $CH_2CHNHCO$), 7.35 (1H, m, C_3-H), 7.54 (1H, d, J=9 Hz, C_7-H), 7.88 (1H, dd, J=9, 2 Hz, C_6-H), 8.46 (1H, dif s, C_4-H), 9.89 (1H, br d, J=7 Hz, CHNHCO), 12.32 (1H, br s, indolic-NH). MS *m/z*: 414 (M^+, 39% of BP), 216 (BP).

39: Colorless prisms from ethyl acetate–hexane, mp 123—124.5 °C. $[\alpha]_D^{22}$ +22.0° (c=0.5, EtOH). *Anal.* Calcd for $C_{18}H_{17}F_3N_2O_6$: C, 52.18; H, 4.14; N, 6.76. Found: C, 51.97; H, 4.17; N, 6.78. IR ν_{max} cm^{-1}: 3300 (NH), 1758, 1742, 1703, 1640 (CO). ^{1}H-NMR (400 MHz) δ: 1.45 (3H, t, J=7 Hz, CH_2CH_3), 3.72 (1H, dd, J=18, 4 Hz, one of $COCH_2CH$), 3.80 (3H, s, OCH_3), 4.05 (1H, dd, J=18, 5 Hz, one of $COCH_2CH$), 4.47 (2H, q, J=7 Hz, OCH_2CH_3), 5.00 (1H, m, $CH_2CHNHCO$), 7.29 (1H, dt, J=7, 1 Hz, C_5- or C_6-H), 7.39 (1H, dt, J=7, 1 Hz, C_6- or C_5-H), 7.43 (1H, dif d, J=7 Hz, C_7-H), 7.76 (1H, br d, J=8 Hz, CHNHCO), 8.10 (1H, d, J=8 Hz, C_4-H), 9.39 (1H, br s, indolic-NH). MS *m/z*: 414 (M^+, 25% of BP), 216 (BP).

Methyl (+)-(2*S*)-4-(2-Ethoxycarbonyl-1*H*-indol-3-yl)-2-trifluoroacetoamidobutyrate (40) Triethylsilane (2 ml, 12.5 mmol) was added to a solution of **39** (1.78 g, 4.3 mmol)in trifluoroacetic acid (14 ml), and the whole mixture was stirred for 2 h at room temperature. Then the reaction mixture was poured into ice-water, and extracted with ethyl acetate. The organic layer was washed with 5% NaOH and saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give a residue. The residue was then subjected to column chromatography on silica gel; gradient elution with benzene–ethyl acetate gave crude **40** (1.54 g, 95%). Recrystallization from ethyl acetate–hexane gave pure **40** as colorless prisms, mp 163—164.5 °C. $[\alpha]_D^{22}$ +11.4° (c=0.367, EtOH). *Anal.* Calcd for $C_{18}H_{19}F_3N_2O_5$: C, 54.00; H, 4.78; N, 7.00. Found: C, 54.05; H, 4.79; N, 7.10. IR ν_{max} cm^{-1}: 3340, 3310 (NH), 1750, 1705, 1685 (CO). ^{1}H-NMR (400 MHz) δ: 1.43 (3H, t, J=7 Hz, CH_2CH_3), 2.28—2.42 (2H, m, CH_2CH_2CH), 3.15 and 3.32 (each 1H, m, arom-CH_2CH_2), 4.44 (2H, m, OCH_2CH_3), 4.70 (1H, dt, J=7.5, 5 Hz, $CH_2CHNHCO$), 7.17 (1H, ddd, J=8, 6, 2 Hz, C_5- or C_6-H), 7.34 (1H, ddd, J=8, 7, 1 Hz, C_6- or C_5-H), 7.38 (1H, dif d, J=8 Hz, C_7-H), 7.64 (1H, dd, J=8, 1 Hz, C_4-H), 7.91 (1H, br d, J=7.5 Hz, CHNHCO), 8.73 (1H, br s, indolic-NH). MS *m/z*: 400 (M^+, 75% of BP), 156 (BP).

(+)-(2*S*)-4-(2-Ethoxycarbonyl-1*H*-indol-3-yl)-2-trifluoroacetoamidobutyric Acid (41) AcOH (4.5 ml) and 30% H_2SO_4 (2.25 ml) were successively added to **40** (266 mg, 0.66 mmol). The whole mixture was stirred for 5 h at 70°C, poured into ice-water, and extracted with ethyl acetate. The organic layer was washed with saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give a crude product (**41**; 211 mg, 82%). Recrystallization from ethyl acetate–hexane gave pure **41** as colorless prisms, mp 190—192 °C. $[\alpha]_D^{22}$ +23.7° (c=0.279, EtOH). *Anal.* Calcd for $C_{17}H_{17}F_3N_2O_5$: C, 52.85; H, 4.44; N, 7.25. Found: C, 52.79; H, 4.42; N, 7.35. IR ν_{max} cm^{-1}: 3310 (NH), 1737, 1700, 1670 (CO). ^{1}H-NMR [400 MHz, $(CD_3)_2SO$] δ: 1.35 (3H, t, J=7 Hz, CH_2CH_3), 2.10 and 2.21 (each 1H, m, $CH_2CH_2CHNHCO$), 3.08 and 3.21 (each 1H, m, arom-CH_2CH_2), 4.16 (1H, m, $CH_2CHNHCO$), 4.35 (2H, q, J=7 Hz, OCH_2CH_3), 7.06 (1H, ddd, J=8, 7, 1 Hz, C_5- or C_6-H), 7.26 (1H, ddd, J=8, 7, 1 Hz, C_6- or C_5-H), 7.43 (1H, d, J=8 Hz, C_7-H), 7.67 (1H, dif d, J=8 Hz, C_4-H), 9.84 (1H, br d, J=7.5 Hz, CHNHCO), 11.57 (1H, br s, indolic-NH). MS *m/z*: 386 (M^+, 83% of BP), 156 (BP).

(+)-(5*S*)-2-Ethoxycarbonyl-5-trifluoroacetoamido-6-oxo-3,4,5,6-tetrahydro-1*H*-cyclohept[*c,d*]indole (42) Oxalyl chloride (0.4 ml, 4.5 mmol) was added to a solution of **41** (100 mg, 0.26 mmol) in chloroform (1 ml) under an argon atmosphere and the reaction mixture was stirred for 2 h at 60 °C. Then the solvent was evaporated off *in vacuo* to give a residue. 1,2-Dichloroethane (10 ml) and $AlCl_3$ (207 mg, 1.56 mmol) were added to the above residue under an argon atmosphere and the reaction mixture was stirred for 1.3 h at room temperature. The 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*. The residue was subjected to column chromatography; gradient elution with benzene–ethyl acetate

gave crude **42** (55 mg, 58%). Recrystallization from ethyl acetate–hexane gave pure **42** (45 mg, 47%) as pale yellow needles, mp 224—226 °C. $[\alpha]_D^{22}$ +132.2° (c=0.45, EtOH). *Anal.* Calcd for $C_{17}H_{15}F_3N_2O_4$: C, 55.44; H, 4.11; N, 7.61. Found: C, 55.34; H, 4.09; N, 7.66. IR ν_{max} cm^{-1}: 3275 (NH), 1710, 1678, 1665 (CO). ^{1}H-NMR [40 MHz, $(CD_3)_2SO$] δ: 1.38 (3H, t, J=7 Hz, CH_2CH_3), 2.22 (1H, dif dddd, J=14, 13, 10, 4 Hz, one of $CH_2CH_2CHNHCO$), 2.32 (1H, dt, J=13, 4 Hz, one of $CH_2CH_2CHNHCO$), 3.22 (1H, ddd, J=18, 14, 4 Hz, one of arom-CH_2CH_2), 3.67 (1H, dt, J=18, 4 Hz, one of arom-CH_2CH_2), 4.39 (2H, q, J=7 Hz, OCH_2CH_3), 4.84 (1H, dd, J=10, 8 Hz, $CH_2CHNHCO$), 7.44 (1H, t, J=8 Hz, C_8-H), 7.80 (2H, d, J=8 Hz, C_7- and C_9-H), 9.87 (1H, br d, J=8 Hz, CHNHCO), 12.21 (1H, br s, indolic-NH). ^{13}C-NMR [$(CD_3)_2SO$] δ: 14.23 (CH_2CH_3), 25.97 and 28.04 (C_3 and C_4), 60.50 (OCH_2CH_3 and C_5), 115.98 (CF_3), 115.98 (CF_3), 118.57, 122.34, and 124.03 (C_7, C_8, and C_9), 121.05, 124.03, 124.52, 126.89, and 136.97 (*tert*-carbon), 155.94 ($NHCOCF_3$), 161.32 (arom-COO), 193.74 (arom-COCHNH). MS m/z: 368 (M^+, 39% of BP), 255 (BP).

(+)-(5*S*)-2-Ethoxycarbonyl-3-methoxy-5-trifluoroacetoamido-6-oxo-3,4,5,6-tetrahydro-1*H*-cyclohept[*c*,*d*]indole (43) A mixture of **42** (0.41 mmol) and TTN (1.63 mmol) in MeOH (10 ml) was stirred overnight at room temperature. The reaction mixture was then poured into ice-water and acidified by adding 10% HCl. The whole mixture was filtered on Celite, and the residue was washed with ethyl acetate. The combined filtrates were extracted with ethyl acetate. The organic layer was washed with saturated NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo* to give a residue. The residue was subjected to column chromatography on silica gel; gradient elution with ethyl acetate–benzene gave crude **43** (56 mg, 49%) and **42** (19 mg, 15%). Recrystallization from ethyl acetate–hexane gave pure **43** (36 mg, 32%) as pale yellow prisms, mp 188—193 °C. $[\alpha]_D^{22}$ +135.3° (c=0.36, EtOH). High-resolution MS: Calcd for $C_{18}H_{17}F_3N_2O_5$: 398.1091. Found: 398.1143. IR ν_{max} cm^{-1}: 3290 (NH), 1710, 1685 (CO). ^{1}H-NMR (400 MHz) δ: 1.49 (3H, t, J=7 Hz, CH_2CH_3), 2.19 [1H, ddd, J=15, 11, 2 Hz, one of $CH(OCH_3)CH_2CHNHCO$], 3.00 [1H, ddd, J=15, 5, 1 Hz, one of $CH(OCH_3)CH_2CHNHCO$], 3.77 (3H, s, OCH_3), 4.51 (2H, q, J=7 Hz, OCH_2CH_3), 5.34 [1H, dd, J=5, 2 Hz, arom-$CH(OCH_3)CH_2$], 5.50 (1H, dd, J=11, 5 Hz, CH_2CHCO), 7.46 (1H, t, J=8 Hz, C_8-H), 7.72 (1H, dd, J=8, 1 Hz, C_9-H), 8.09 (1H, dd, J=8, 1 Hz, C_7-H), 8.15 (1H, br d, J=5 Hz, $CHNHCOCF_3$), 9.51 (1H, br s, indolic-NH). ^{13}C-NMR δ: 14.52 (CH_2CH_3), 31.77 (C_4), 54.28 (C_5), 57.56 (OCH_3), 61.85 (OCH_2CH_3), 70.69 (C_3), 115.96 (CF_3), 118.48, 124.91, and 124.89 (C_7, C_8 and C_9), 121.29, 123.81, 126.68, 127.13, and 135.83 (*tert*-carbon), 156.38 ($NHCOCF_3$), 161.17 (arom-COO), 194.88 (arom-COCHNH). MS m/z: 398 (M^+, 48% of BP), 269 (BP).

Acknowledgements This work was supported in part by a Grant-in-Aid for Scientific Research (No. 03671017) from the Ministry of Education, Science and Culture of Japan and a grant from the Japan Research Foundation for Optically Active Compounds. We thank Dr. Hirashima, Daiichi Pharmaceutical Co., Ltd., for conducting biological tests.

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