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## APPLICATION OF THE MILD-CONDITION PHTHALIMIDINE SYNTHESIS WITH USE OF 1,2,3-1*H*-BENZOTRIAZOLE AND 2-MERCAPTOETHANOL AS DUAL SYNTHETIC AUXILIARIES. EFFECTIVE SYNTHESIS OF PHTHALIMIDINES POSSESSING A VARIETY OF SUBSTITUENTS AT 2-POSITION<sup>†</sup>

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**Abstract** — The mild-condition phthalimidine synthesis based on Mannich type 1:1 condensation reaction between *o*-phthalaldehyde with a variety of primary amines in the presence of excess 2-mercaptoethanol and 1,2,3-1*H*-benzotriazole as “dual synthetic auxiliaries” in MeCN for 13 h at room temperature afford 2-substituted phthalimidines (2,3-dihydroisoindol-1-one) in fair to good isolated yields.

## INTRODUCTION

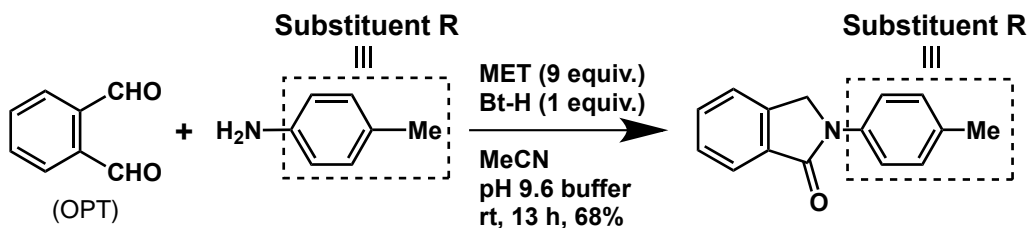
Heterocyclic compounds containing phthalimidine (2,3-dihydroisoindol-1-one) skeletons have attracted a considerable interest in recent years, because a number of fascinating natural/artificial bioactive compound have shown clinical utility.<sup>1</sup>

In the preceding paper,<sup>2</sup> we demonstrated the first possibility to “*regulate*” the double Mannich condensation-based mild condition phthalimidine synthesis between *o*-phthalaldehyde (OPT) and a primary amine (known as Thiele’s method<sup>3-5</sup>) in the presence of 1,2,3-1*H*-benzotriazole and 2-mercapto-

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<sup>†</sup> Dedicated to Professor Lutz F. Tietze on his 75th birthday

ethanol as dual synthetic auxiliaries. Roles of two auxiliaries interpreted in the present stage are as follows: *2H*-isoindole intermediate was first formed by assistance of excessive amount of MET, followed by the rearrangement of the intermediate *via* a tethered ion pair, which was assisted by stoichiometric amount of Bt-H. Optimized reaction condition utilizing *p*-toluidine as a primary amine is shown as Scheme 1.



Scheme 1

In this paper, we wish to describe the scope of this promising phthalimidine synthesis when a variety of primary amines are adopted.<sup>6</sup>

## RESULTS AND DISCUSSION

A number of commercially available primary amines were utilized to run the reaction exemplified as Scheme 1. Both aromatic and aliphatic primary amines were tested. The results are summarized as Table 1.

As we reported in the preceding papers,<sup>6</sup> in order at once to avoid the polymerization of intermediate *2H*-isoindoles and facilitate the isolation of phthalimidines, we carried out reaction work-ups based on filtrations whenever products were solids. Therefore, isolated yields do not necessarily reflect reaction conversions. However, the alternative work-up procedure, extractions, for compound **4** showed that the isolated yields may be improved from the results in Table 1, but in 10% or so (see EXPERIMENTAL). Therefore, we wish to evaluate the scope of our novel phthalimidine synthesis based on the isolated yields in Table 1.

When *p*-substituted anilines were used as primary amines, except for some compounds prepared in fair yields, the electronic effect of substituents (electron-donating or electron-withdrawal) did not greatly affect yields of products (compounds **1-11**). Further elongation of reaction time did not necessarily improve isolated yields because this factor would compete with polymerization of intermediate or product (compounds **8**, **11**, **18** and **19**). Similar tendencies were observed in cases of *m*-substituted anilines, where electronic effects were not likely to effect much on the nucleophilicity of amino groups (compounds **12-15**).

**Table 1.** Yields and Physical Properties of Phthalimidines

Compound	R-NH <sub>2</sub>	Yield (%)	mp (°C)/lit. mp (°C) <sup>g</sup>
1	<i>p</i> -NEt <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	72	149-152/180-182
2	<i>p</i> -NMe <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	73	191-191.5/-----
3	<i>p</i> -OMe-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	70	136-139/134
4	<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	68 <sup>e</sup>	140-141.5/139-140
5	C <sub>6</sub> H <sub>5</sub> -NH <sub>2</sub>	66	162-164.5/160
6	<i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	72	180-183/184-185
7	<i>p</i> -Br-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	62	181-182/183
8	<i>p</i> -I-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	34(44) <sup>f</sup>	196-198/200-201
9	<i>p</i> -COMe-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	84	237-239/243-244
10	<i>p</i> -CO <sub>2</sub> Me-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	80	214-217/-----
11	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	39(28) <sup>f</sup>	234-236/236
12	<i>m</i> -OMe-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	77	129-130/130-131
13	<i>m</i> -Me-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	60	148.5-149.5/145
14	<i>m</i> -Cl-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	44	186/185.5
15	<i>m</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	59	231-233/237-238
16	3-C <sub>5</sub> H <sub>4</sub> -NH <sub>2</sub> <sup>a</sup>	49	169-171/-----
17	<i>o</i> -Me-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	54	98-99/97.5-98
18	<i>o</i> -Cl-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	27(12) <sup>f</sup>	125/172-173
19	<i>o</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	18(33) <sup>f</sup>	161-162/164
20	2,6-Me <sub>2</sub> -C <sub>6</sub> H <sub>3</sub> -NH <sub>2</sub>	80	125-126.5/124-124.5
21	2,4,6-Me <sub>3</sub> -C <sub>6</sub> H <sub>2</sub> -NH <sub>2</sub>	49	104-106/-----
22	1-C <sub>10</sub> H <sub>7</sub> -NH <sub>2</sub> <sup>b</sup>	62	190-191/194-195
23	<i>p</i> -OMe-C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> -NH <sub>2</sub>	72	102-105/-----
24	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> -NH <sub>2</sub>	75	92-95/90-91
25	Me-NH <sub>2</sub>	47	112.5-114/116-117
26	MeCH <sub>2</sub> -NH <sub>2</sub>	67	oil/(bp <sub>2</sub> =120-121)
27	MeCH <sub>2</sub> CH <sub>2</sub> -NH <sub>2</sub>	76	oil/33.1-34.7
28	C <sub>18</sub> H <sub>36</sub> -NH <sub>2</sub> <sup>c</sup>	66	oil/(bp <sub>3</sub> =280-285)
29	<i>rac</i> -C <sub>6</sub> H <sub>5</sub> -CH(Me)-NH <sub>2</sub>	68	107-111/-----
30	<i>cyclo</i> -C <sub>6</sub> H <sub>11</sub> -NH <sub>2</sub> <sup>d</sup>	60	109-110.5/107-109
31	<i>t</i> -C <sub>4</sub> H <sub>9</sub> -NH <sub>2</sub>	53	60/53.5-54
32	NH <sub>3</sub>	70	142-148/150(dec)
33	C <sub>6</sub> H <sub>5</sub> -NHNH <sub>2</sub>	21	188-190/-----

(a) 3-aminopyridine. (b) 1-naphthylamine. (c) oleylamine.

(d) cyclohexylamine. (e) see preceding paper. (f) 49 h-mode reaction.

(g) see experimental section for references.

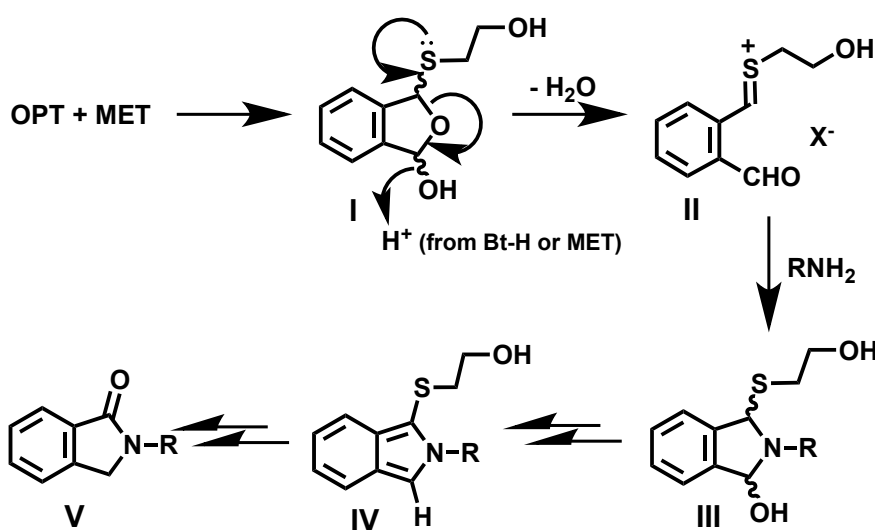
When *o*-substituted anilines were used, they were likely to retard the reaction process itself, which was not necessarily improved by elongated reaction periods (compounds **16-22**). In turn, use of 2,6-dimethylated anilines (compounds **20** and **21**) did not show as much yield decrements as those

observed in cases of *o*-chloro and *o*-nitroanilines (compounds **18** and **19**), suggesting that some specific conformational orientation reported in cases of 2-substituted phthalimidines may possibly become obstacles during phthalimidine-forming transition states, too.<sup>7,8</sup>

When aliphatic amines were used, isolated yields dropped more or less irrespective of alkyl groups, although *oily* phthalimidines required extractions and column chromatography during isolation (compounds **23-31**).

Interestingly, the use of ammonia as a source of “primary amine” gave 2-unsubstituted phthalimidine (**32**) in good isolated yields, although reaction media was alkaline.<sup>6</sup> Even with the use of phenylhydrazine, apparently competing hydrazone-forming reaction paths, gave desired phthalimidine (**33**) but in low yield.

<sup>1</sup>H and <sup>13</sup>C NMR spectra (see EXPERIMENTAL for those of new compounds) showed typical signal patterns of phthalimidine derivatives, of which diagnostic chemical shifts ( $\delta_{\text{ppm}}$ ) variations can be interpreted in terms of substituents' inductive effects (including spectra of known compounds, of course), as had been reported in our previous work concerning benzotriazole (Bt)-substituted isoindolines.<sup>9</sup> As for electron-donating abilities, alkylamines would be likely to react faster than arylamines, although in terms of isolated yields, significant differences were not observed. Considering that nucleophilicity do not effect on the reaction velocity, some reaction mechanism similar to S<sub>N</sub>1 format is to be assumed. Thus, when intermediate 2*H*-isoindole is formed, excessive amount of MET would work as a synthetic auxiliary to form an immonium cation (hard) *via* slow process, which is followed by the immediate attack of a nucleophile (Scheme 2).



Scheme 2. Supplementary Plausible Reaction Mechanism

The present results are compared with formerly reported ones (ascertained as Thiele's method) in Table 2.

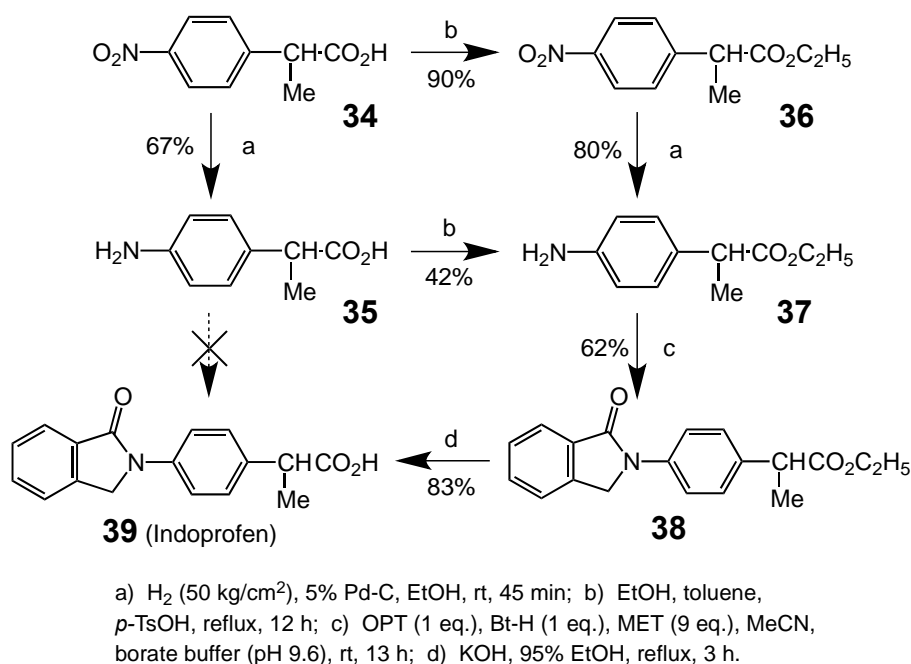
**Table 2.** Comparison of Isolated Yields

Compound	R-NH <sub>2</sub>	Yield (%)	
		This Work	Thiele's Method <sup>a</sup>
<b>3</b>	<i>p</i> -MeO-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	70	13
<b>4</b>	<i>p</i> -Me-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	68	16
<b>5</b>	C <sub>6</sub> H <sub>5</sub> -NH <sub>2</sub>	66	79
<b>6</b>	<i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	72	6
<b>7</b>	<i>p</i> -Br-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	62	57
<b>8</b>	<i>p</i> -I-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	44	37
<b>11</b>	<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	39	5
<b>12</b>	<i>m</i> -MeO-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	77	3
<b>13</b>	<i>m</i> -Me-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	60	9
<b>14</b>	<i>m</i> -Cl-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	44	27
<b>15</b>	<i>m</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	59	10
<b>18</b>	<i>o</i> -Cl-C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	27	10
<b>19</b>	<i>o</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>	33	12
<b>22</b>	1-C <sub>10</sub> H <sub>7</sub> -NH <sub>2</sub>	62	11
<b>29</b>	<i>rac</i> -C <sub>6</sub> H <sub>5</sub> -CH(Me)-NH <sub>2</sub>	68	21

(a) Based on ref. 4 except for **5** (ref. 3) and **29** (ref.5).

Our method as a whole provides phthalimidines in fair to good isolated yields based on facile and reliable procedures. In addition, our method is tolerant to the synthesis of 2-alkylphthalimidines, some of which have formerly been prepared but via methods other than Thiele's (see EXPERIMENTAL). These results proved that the Mannich-based synthetic method originated some 100 years ago was able to be regulated for the first time.

It had long been known that 2-phenylphthalimidine (**5**) was able to be prepared by Thiele's method in exceptionally high isolated yield. Therefore, phthalimidines possessing substituents on aromatic ring at 2-position had formerly been prepared from **5**, for which multistep procedure was indispensable. For example, industrial synthetic schemes of anti-inflammatory agent Indoprofen required more than 10 steps when started from **5** or 2-(4-acetylphenyl)phthalimidine (**9**).<sup>10,11</sup> Our method is tolerant to the structures of primary amines, and therefore, preparation of the amine sector in advance to phthalimidine-forming step would abate the number of reaction steps in the procedure. Based on this idea, we planned a short-step synthesis targeting indoprofen (Scheme 3).



**Scheme 3.** Short-Step Synthesis of *rac*-Indoprofen

First, aiming at shortest total synthesis (2 steps) from commercially available starting material, we reduced nitro group of **34** to give primary amine **35**. However, attempted phthalimidine synthesis using above obtained **35** to give indoprofen (**39**) was unsuccessful. Then **35** was converted into ester **37**, which was subjected to our phthalimidine synthesis to give indoprofen ethyl ester (**38**) of which isolated yield was consistent with the data shown in Table 1. Hydrolysis of **38** gave indoprofen (**39**). In addition, access to **38** was improved via ester (**36**) in view of chemical yield. These results proved that Indoprofen (**39**) can be prepared from commercially available **36** in as few as 4 steps (37% in total), exhibiting the utility of the “dual auxiliary assisted” Mannich condensation-based phthalimidine synthesis established by us.

## CONCLUSION

Utility of dual synthetic auxiliaries (Bt-H and MET) in Mannich type condensation reaction between OPT and primary amine exhibited that famous method originated by Thiele and co-workers became tacit and reliable phthalimidine-forming procedure for the first time. Further exploitation along this line is now underway in these laboratories.

## EXPERIMENTAL

**General Information.** All melting points are uncorrected. Infrared (ir) spectra were measured with a Shimadzu IR-430 grating infrared spectrophotometer and a JASCO FT/IR-8000 Fourier transform

infrared spectrometer.  $^1\text{H}$  (270 MHz) and  $^{13}\text{C}$  (67.5 MHz) nuclear magnetic resonance (nmr) spectral measurements were carried out with a JEOL JNM-GX200 Fourier transform NMR spectrometer. All signals are expressed as ppm downfield from tetramethylsilane (TMS) used as an internal reference ( $\delta$  value). The following abbreviations are used: singlet(s), doublet(d), triplet(t), quartet(q), multiplet(m), broad(b). Positional numbers are assembled as follows: no prime, isoindole ring; single prime, substituent at 2-position. Mass spectra (ms; EI and FAB modes) were taken with a JEOL JMS DX-303 mass spectrometer, where mass numbers of local maxima (relative intensities in parentheses) are recorded.

### Typical Experimental Procedure for the Preparation of Phthalimidine (2,3-Dihydroisoindol-1-one).

#### Method A. Preparation of 2-[*p*-(*N,N*-Diethylamino)phenyl]phthalimidine (**1**).

To a solution of *o*-phthaldehyde (OPT; 1.341 g, 10 mmol) in MeCN (30 mL) was added successively (i) a solution of 2-mercaptoethanol (MET; 6.0 mL, 86 mmol) in MeCN (10 mL) over 3 min, (ii) a solution of *N,N*-diethylphenylenediamine (1.720 g, 10 mmol) in MeCN (10 mL) over 2 min, (iii) 1,2,3-1*H*-benzotriazole (1.191 g, 10 mmol) portionwise over 2 min, and (iv) pH 9.6 buffer (0.05 *M*  $\text{H}_3\text{BO}_3\text{-KCl-NaOH}$ ; 5 mL) over 3 min with stirring at room temperature. After the additions were complete, the mixture was further stirred at room temperature for 13 h under  $\text{N}_2$ , and then evaporated. After storage in refrigerator for 3 h, the resulting solids were filtered, washed successively with ice-cold  $\text{Et}_2\text{O}$  and water, and then dried *in vacuo* to give crude phthalimidine (1.956 g, mp 145-206 °C). The filtrate was evaporated and diluted with water (100 mL). The further resulting solids were filtered, washed successively with ice-cold  $\text{Et}_2\text{O}$  and water, and then dried *in vacuo* to give another crop of crude product (0.376 g, mp 142-224 °C). Both of the crude samples were combined (2.432 g, 87%) and subjected to recrystallization from MeOH to give the analytically pure sample of 2-[4-(*N,N*-diethylamino)phenyl]phthalimidine (**1**; 2.094 g, 72%, mp 149-152 °C) as lemon-yellow needles.

Compounds **3-7**, **9-16**, **21**, **22**, **24**, and **30** were also prepared from the corresponding primary amines using the similar procedure to that described above. In cases of compounds **2** and **8**, precipitates appeared during 13 h reaction time, so the reaction mixture was first filtered to collect crude phthalimidine, followed by the work-up described above.

### Typical Experimental Procedure for the Preparation of Phthalimidine.

#### Method B. Preparation of 2-(*o*-chlorophenyl)phthalimidine (**18**).

To a solution of *o*-phthaldehyde (OPT; 1.341 g, 10 mmol) in MeCN (30 mL) was added successively (i) a solution of 2-mercaptoethanol (MET; 6.0 mL, 86 mmol) in MeCN (10 mL) over 5 min, (ii) a solution of

*o*-chloroaniline (1.276 g, 10 mmol) in MeCN (10 mL) over 5 min, (iii) 1,2,3-1*H*-benzotriazole (1.191 g, 10 mmol) portionwise over 4 min, and (iv) pH 9.6 buffer (0.05 *M* H<sub>3</sub>BO<sub>3</sub>-KCl-NaOH; 5 mL) over 1 min with stirring at room temperature. After the additions were complete, the mixture was further stirred at room temperature for 13 h under N<sub>2</sub>, and then evaporated. After storage in refrigerator for 1 h (no precipitates appeared), the residue was dissolved in CHCl<sub>3</sub>, washed successively with 2 *N* HCl, sat.aq. NaHCO<sub>3</sub>, and then dried over anhyd. Na<sub>2</sub>SO<sub>4</sub>. Filtration followed by evaporation *in vacuo* gave crude phthalimidine (1.72 g, 80%, mp 85-93 °C), which was recrystallized from Et<sub>2</sub>O to give the analytically pure sample of 2-(*o*-chlorophenyl)phthalimidine (**18**; 1.248 g, 60%, mp 109-110 °C) as colorless cubic prisms.

Compounds **8** (49 h-mode), **11** (49 h-mode), **17**, **18** (49 h-mode), **19** (both 13 h- & 49 h-modes), **20**, **23**, **29**, and **31-33** were also prepared from the corresponding primary amines using the similar procedure to that described above.

### Typical Experimental Procedure for the Preparation of Phthalimidine.

#### Method C. Preparation of 2-(1-propyl)phthalimidine (**27**).

To a solution of *o*-phthaldehyde (OPT; 1.341 g, 10 mmol) in MeCN (30 mL) was added successively (i) a solution of 2-mercaptoethanol (MET; 6.0 mL, 86 mmol) in MeCN (10 mL) over 2 min, (ii) a solution of *n*-propylamine (0.591 g, 10 mmol) in MeCN (10 mL) over 1 min, (iii) 1,2,3-1*H*-benzotriazole (1.191 g, 10 mmol) portionwise over 1 min, and (iv) pH 9.6 buffer (0.05 *M* H<sub>3</sub>BO<sub>3</sub>-KCl-NaOH; 5 mL) over 1 min with stirring at room temperature. After the additions were complete, the mixture was further stirred at room temperature for 13 h under N<sub>2</sub>, and then evaporated.

The crude material (3.60 g) was subjected to column chromatographic purifications (silica gel, C<sub>6</sub>H<sub>6</sub>-AcOEt = 4:1 in the first column; C<sub>6</sub>H<sub>6</sub>-AcOEt = 6:1 in the second column) to give the crude phthalimidine (0.687 g, lemon-yellow oil; pure from <sup>1</sup>H NMR spectra) and a mixture of phthalimidine and recovered Bt-H (2.183 g), the latter of which was washed with sat. a.q. NaHCO<sub>3</sub> to give another portion of phthalimidine (0.371 g, lemon-yellow oil; pure from <sup>1</sup>H NMR spectra). Total yield was 60%. Compounds **25**, **26**, and **28** were also prepared from the corresponding primary amines using the similar procedure to that described above.

<sup>1</sup>H NMR spectral and combustion analytical data were recorded for compounds **1** and **18** (known), because our melting points were apart from those previously reported. Physical data of phthalimidines (**1-33**) are as follows.

**2-[*p*-(*N,N*-Diethylamino)phenyl]phthalimidine (**1**).** Lemon-yellow needles from MeOH; mp 149-152



°C (lit.,<sup>12</sup> mp 180-182 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.90 (1H, dd, *J* = 7 Hz and 1 Hz, H-7), 7.60 (2H, d, *J* = 9 Hz, H-2' and 6'), 7.54 (1H, ddd, *J* = 7 Hz, 7 Hz, and 1 Hz, H-5), 7.52-7.40 (2H, m, H-4 and 6), 6.72 (2H, d, *J* = 9 Hz, H-3' and 5'), 4.76 (2H, s, H-3), 3.35 (4H, q, *J* = 7 Hz, NCH<sub>2</sub>), 1.16 (6H, t, *J* = 7 Hz, NCH<sub>3</sub>). *Anal.* Calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.06; H, 7.41; N, 10.02.

**2-[*p*-(*N,N*-Dimethylamino)phenyl]phthalimidine (2).** Lemon-yellow needles from MeOH; mp 191-191.5 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.90 (1H, dd, *J* = 8 Hz and 1 Hz, H-7), 7.65 (2H, d, *J* = 9 Hz, H-2' and 6'), 7.55 (1H, ddd, *J* = 7 Hz, 7 Hz, and 1 Hz, H-5), 7.51-7.43 (2H, m, H-4 and 6), 6.78 (2H, d, *J* = 9 Hz, H-3' and 5'), 4.76 (2H, s, H-3), 2.94 (6H, s, NCH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 166.8 (C=O), 147.7 (C-4'), 140.1 (C-3a), 133.3 (C-7a), 131.3 (C-5), 129.0 (C-1'), 127.9 (C-7), 123.5 (C-4), 122.3 (C-6), 121.1 (C-2' and 6'), 112.7 (C-3' and 5'), 50.9 (C-3), 40.5 (NCH<sub>3</sub>). IR (KBr): ν<sub>max</sub> (cm<sup>-1</sup>) 1676 (C=O), 1618, 816, 731. MS (EI): *m/z* (rel. intensities) 252 (*M*<sup>+</sup>, 29), 239 (100), 224 (69), 211 (6), 196 (14), 165 (32), 149 (13), 137 (9), 103 (12), 89 (16), 69 (33), 59 (52), 45 (31). *Anal.* Calcd for C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O: C, 76.16; H, 5.99 N, 11.10. Found: C, 76.32; H, 6.29; N, 11.15.

**2-(*p*-Methoxyphenyl)phthalimidine (3).** White leaflets from MeOH; mp 136-139 °C (lit.,<sup>13</sup> mp 134 °C).

**2-(*p*-Methylphenyl)phthalimidine (4).** White crystalline solids from MeOH; mp 140-141.5 °C.<sup>2</sup> Preparation using the procedure similar to that of method C raised the isolated yield of **4** upto 82%.

**2-Phenylphthalimidine (5).** White small leaflets from dioxane; mp 162-164.5 °C (lit.,<sup>13</sup> mp 160 °C).

**2-(*p*-Chlorophenyl)phthalimidine (6).** White small leaflets from dioxane; mp 180-183 °C (lit.,<sup>4</sup> mp 184-185 °C).

**2-(*p*-Bromophenyl)phthalimidine (7).** White small leaflets from dioxane; mp 181-182 °C (lit.,<sup>4</sup> mp 183 °C).

**2-(*p*-Iodophenyl)phthalimidine (8).** White small leaflets from dioxane; mp 196-198 °C (lit.,<sup>4</sup> mp 200-201 °C).

**2-(*p*-Acetylphenyl)phthalimidine (9).** Lemon-yellow leaflets from dioxane; mp 237-239 °C (lit.,<sup>10</sup> mp 243-244 °C).

**2-(*p*-Methoxycarbonylphenyl)phthalimidine (10).** Slightly lemon-yellow small leaflets from dioxane; mp 215-217 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.08 (2H, d, *J* = 9 Hz, H-3' and 5'), 7.98 (2H, d, *J* = 9 Hz, H-2' and 6'), 7.91 (1H, d, *J* = 7 Hz, H-7), 7.62 (1H, ddd, *J* = 7 Hz, 7 Hz, and 1 Hz, H-5), 7.52 (1H, d, *J* = 8 Hz, H-4), 7.51 (1H, dd, *J* = 8 Hz and 7 Hz, H-6), 4.87 (2H, s, H-3), 3.91 (3H, s, CO<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>) δ 166.7 (C=O of C-1), 165.6 (C=O of ester), 143.4 (C-1'), 140.7 (C-1'), 132.1 (C-5), 132.0 (C-7a), 129.8 (C-3' and 5'), 127.9 (C-7), 125.0 (C-4'), 123.1 (C-4), 122.9 (C-6), 118.3 (C-2' and 6'), 51.2 (CO<sub>2</sub>CH<sub>3</sub>), 50.2 (C-3). IR (KBr): ν<sub>max</sub> (cm<sup>-1</sup>) 1714 (C=O), 1603, 857, 772, 737. MS (EI): *m/z* (rel.

intensities) 267 ( $M^+$ , 100), 236 (77), 208 (16), 180 (4), 152 (4), 104 (8), 90 (11), 76 (9), 63 (4), 51 (3).

*Anal.* Calcd for  $C_{16}H_{13}NO_3$ : C, 71.90; H, 4.96; N, 5.24. Found: C, 71.76; H, 4.82; N, 5.04.

**2-(*p*-Nitrophenyl)phthalimidine (11).** Lemon-yellow small leaflets from dioxane; mp 234-236 °C (lit.,<sup>4</sup> mp 236 °C).

**2-(*m*-Methoxyphenyl)phthalimidine (12).** Beige crystalline solids from dioxane; mp 129-130 °C (lit.,<sup>4</sup> mp 130-131 °C).

**2-(*m*-Methylphenyl)phthalimidine (13).** White crystalline solids from dioxane; mp 148.5-149.5 °C (lit.,<sup>4</sup> mp 145 °C).

**2-(*m*-Chlorophenyl)phthalimidine (14).** White small needles from dioxane; mp 186 °C (lit.,<sup>4</sup> mp 185.5 °C).

**2-(*m*-Nitrophenyl)phthalimidine (15).** Lemon-yellow prisms from dioxane; mp 231-232 °C (lit.,<sup>4</sup> mp 237-238 °C).

**2-(3-Pyridyl)phthalimidine (16).** Beige powders from dioxane; mp 169-171 °C.  $^1H$  NMR ( $CDCl_3$ )  $\delta$  8.94 (1H, d,  $J = 3$  Hz, H-2'), 8.46 (1H, ddd,  $J = 7$  Hz, 3 Hz, and 2 Hz, H-4'), 8.40 (1H, dd,  $J = 5$  Hz and 1 Hz, H-6'), 7.88 (1H, d,  $J = 8$  Hz, H-7), 7.61 (1H, ddd,  $J = 8$  Hz, 8 Hz, and 6 Hz, H-5), 7.53 (1H, d,  $J = 7$  Hz, H-4), 7.49 (1H, dd,  $J = 7$  Hz and 7 Hz, H-6), 7.33 (1H, dd,  $J = 8$  Hz and 5 Hz, H-5'), 4.85 (2H, s, H-3).  $^{13}C$  NMR ( $CDCl_3$ )  $\delta$  167.8 (C=O), 145.3 (C-4'), 140.0 (C-3a), 139.9 (C-2'), 136.2 (C-1'), 132.5 (C-5), 132.3 (C-7a), 128.5 (C-7), 126.3 (C-6'), 124.1 (C-5'), 123.6 (C-4), 122.7 (C-6), 49.9 (C-3). IR (KBr):  $\nu_{max}$  ( $cm^{-1}$ ) 1701 (C=O), 1599, 804, 733, 702. MS (EI):  $m/z$  (rel. intensities) 211 [ $(M+1)^+$ , 100], 210 ( $M^+$ , 29), 183 (25), 168 (3), 155 (4), 133 (4), 119 (3), 105 (21), 89 (15), 78 (26), 63 (9), 51 (15). *Anal.* Calcd for  $C_{13}H_{10}N_2O$ : C, 74.27; H, 4.79; N, 13.32. Found: C, 74.07; H, 4.87; N, 13.42.

**2-(*o*-Methylphenyl)phthalimidine (17).** Slightly yellow prisms from  $Et_2O$ ; mp 98-99 °C (lit.,<sup>8</sup> mp 97.5-98 °C).

**2-(*o*-Chlorophenyl)phthalimidine (18).** White crystalline solids from dioxane; mp 125 °C (lit.,<sup>4</sup> mp 172-173 °C).  $^1H$  NMR (acetone- $d_6$ )  $\delta$  7.90 (1H, dd,  $J = 7$  Hz and 1 Hz, H-7), 7.63 (1H, ddd,  $J = 7$  Hz, 6 Hz, and 2 Hz, H-5), 7.53 (1H, ddd,  $J = 7$  Hz, 7 Hz, and 2 Hz, H-6), 7.52 (1H, d,  $J = 7$  Hz, H-4), 7.43 (1H, ddd,  $J = 7$  Hz, 7 Hz, and 2 Hz, H-5'), 7.40-7.30 (3H, m, H-3', 4' and 6'), 4.82 (2H, s, H-3). *Anal.* Calcd for  $C_{14}H_{10}ClNO$ : C, 69.00; H, 4.14; N, 5.75. Found: C, 69.15; H, 4.05; N, 5.55.

**2-(*o*-Nitrophenyl)phthalimidine (19).** Yellow powders from dioxane; mp 161-162 °C (lit.,<sup>4</sup> mp 164 °C).

**2-(2,6-Dimethylphenyl)phthalimidine (20).** White needles from hexane-AcOEt (2:1); mp 125-126.5 °C (lit.,<sup>8</sup> mp 124-124.5 °C).

**2-(2,4,6-Trimethylphenyl)phthalimidine (21).** Slightly yellow prisms from  $Et_2O$ ; mp 104-106 °C.

$^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.94 (1H, dd,  $J = 8$  Hz and 1 Hz, H-7), 7.58 (1H, ddd,  $J = 8$  Hz, 8 Hz, and 1 Hz, H-5), 7.50 (1H, d,  $J = 7$  Hz, H-4), 7.49 (1H, dd,  $J = 7$  Hz and 7 Hz, H-6), 6.96 (2H, s, H-3' and 5'), 4.56 (2H, s, H-3), 2.30 (3H, s,  $\text{CH}_3$ -4'), 2.13 (6H, s,  $\text{CH}_3$ -3' and 5').  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  167.8 (C=O), 141.6 (C-3a), 138.1 (C-4'), 136.3 (C-2' and 6'), 132.8 (C-4'), 132.3 (C-7a), 131.5 (C-5), 129.2 (C-3' and 5'), 128.0 (C-7), 124.1 (C-4), 122.8 (C-6), 51.2 (C-3), 20.9 ( $\text{ArCH}_3$ -4'), 17.8 ( $\text{ArCH}_3$ -2' and 6'). IR (KBr):  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 1694 (C=O), 1608, 852, 736. MS (EI):  $m/z$  (rel. intensities) 252 [ $(M+1)^+$ , 76], 251 ( $M^+$ , 5), 235 (5), 207 (5), 180 (2), 133 (37), 121 (99), 106 (19), 97 (4), 90 (13), 77 (10), 63 (5), 51 (4), 39 (6), [28 (100) =  $\text{N}_2$ ]. Anal. Calcd for  $\text{C}_{17}\text{H}_{17}\text{NO}$ : C, 81.24; H, 6.82; N, 5.57. Found: C, 81.24; H, 6.79; N, 5.29.

**2-(1-Naphthyl)phthalimidine (22).** Slightly beige prisms from dioxane; mp 190-191 °C (lit.,<sup>4</sup> mp 194-195 °C).

**2-[(*p*-Methoxyphenyl)methyl]phthalimidine (23).** Slightly gray small needles from AcOEt; mp 102-105 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.86 (1H, d,  $J = 7$  Hz, H-7), 7.48 (1H, ddd,  $J = 7$  Hz, 6 Hz and 1 Hz, H-5), 7.42 (1H, dd,  $J = 8$  Hz and 7 Hz, H-6), 7.35 (1H, d,  $J = 7$  Hz, H-4), 7.23 (2H, d,  $J = 8$  Hz, H-2' and 6'), 6.84 (2H, d,  $J = 8$  Hz, H-3' and 5'), 4.72 (2H, s, H-3), 4.21 (2H, s,  $\text{ArCH}_2$ ), 3.76 (3H, s,  $\text{OCH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  168.3 (C=O), 159.0 (C-4'), 141.1 (C-3a), 132.7 (C-7a), 131.2 (C-5), 129.4 (C-2' and 6'), 129.1 (C-1'), 127.9 (C-7), 123.7 (C-4), 122.6 (C-6), 114.0 (C-3' and 5'), 55.2 ( $\text{OCH}_3$ ), 49.2 (C-3), 45.7 (C- $\alpha$ ). IR (KBr):  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 1672 (C=O), 1585, 1242, 1028, 833, 814, 733. MS (EI):  $m/z$  (rel. intensities) 254 [ $(M+1)^+$ , 100], 253 ( $M^+$ , 47), 239 (6), 223 (7), 211 (2), 195 (2), 169 (2), 146 (12), 122 (67), 110 (9), 91 (31), 77 (19), 70 (4), 65 (9), 51 (9), 43 (48). Anal. Calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_2$ : C, 75.87; H, 5.97; N, 5.53. Found: C, 75.77; H, 5.94; N, 5.25.

**2-(Phenylmethyl)phthalimidine (24).** White crystalline solids from AcOEt; mp 92-95 °C (lit.,<sup>14</sup> mp 90-91 °C).

**2-Methylphthalimidine (25).** White crystalline solids from chromatographic purification; mp 112.5-114 °C (lit.,<sup>15</sup> mp 116-117 °C).

**2-Ethylphthalimidine (26).** Slightly yellow oil from chromatographic purification (lit.,<sup>15</sup> bp<sub>2</sub> 120-121 °C).

**2-Propylphthalimidine (27).** Lemon-yellow oil from chromatographic purification (lit.,<sup>16</sup> mp 33.1-34.7 °C).

**2-Oleylphthalimidine (28).** Lemon-yellow oil from chromatographic purification (lit.,<sup>17</sup> bp<sub>3</sub> 280-285 °C).

**2-(*rac*- $\alpha$ -Phenethyl)phthalimidine (29).** White small prisms from AcOEt-hexane (1:1); mp 107-111 °C (lit.,<sup>5,18</sup> no mp data indicated).

**2-Cyclohexylphthalimidine (30).** Colorless cubic prisms from  $\text{Et}_2\text{O}$ ; mp 109-110 °C (lit.,<sup>17</sup> mp 107-109 °C).

°C).

**2-(*tert*-Butyl)phthalimidine (31).** Colorless thin needles from dioxane; mp 60 °C (lit.,<sup>15</sup> mp 53.5-54 °C).

**Phthalimidine (32).** White crystalline solids from chromatographic purification; mp 142-148 °C (dec.) [lit.,<sup>19</sup> 150 °C (dec.)].

**2-(Phenylamino)phthalimidine (33).** Lemon-yellow powders from dioxane; mp 188-190 °C. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.85 (1H, d, *J* = 7 Hz, H-7), 7.70 (1H, s, NH), 7.63 (1H, dd, *J* = 8 Hz and 7 Hz, H-5), 7.58-7.48 (2H, m, H-4 and 6), 7.19 (2H, dd, *J* = 8 Hz and 7 Hz, H-3' and 5'), 6.82 (1H, t, *J* = 7 Hz, H-4'), 6.71 (2H, d, *J* = 7 Hz, H-2' and 6'), 4.63 (2H, s, H-3). <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 167.7 (C=O), 146.5 (C-1'), 139.8 (C-3a), 132.0 (C-5), 131.0 (C-7a), 129.2 (C-3' and 5'), 128.2 (C-7), 124.1 (C-4), 123.0 (C-6), 121.0 (C-4'), 113.3 (C-2' and 6'), 51.1 (C-3). IR (KBr): ν<sub>max</sub> (cm<sup>-1</sup>) 1691 (C=O), 1523, 1496, 1173, 736. MS (EI): *m/z* (rel. intensities) 224 (*M*<sup>+</sup>, 100), 132 (35), 104 (37), 90 (58), 77 (89), 65 (60), 51 (56), 39 (37). *Anal.* Calcd for C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O: C, 74.98; H, 5.39; N, 12.49. Found: C, 74.68; H, 5.37; N, 12.38.

#### Preparation of *rac*-2-(4-aminophenyl)propanoic acid (35) from 34.

A solution of 2-(4-nitrophenyl)propanoic acid (**34**; 5.00 g, 25 mmol) in EtOH (100 mL) was poured into an autoclave. After the suspension of 5% Pd-C (0.625 g), the apparatus was sealed and filled with H<sub>2</sub> (50 kg/cm<sup>2</sup>). The mixture was stirred at room temperature for 45 min. The reaction mixture was filtered and evaporated *in vacuo* to give the crude product (4.21 g, 100%, mp 131-132 °C; pure from <sup>1</sup>H NMR spectra). Recrystallization from dioxane gave the analytically pure sample of aminoacid (**35**; 3.96 g, 93%, mp 133-134 °C) (lit.,<sup>20</sup> no mp data indicated) as beige granules.

#### Preparation of ethyl *rac*-2-(4-nitrophenyl)propanoate (36) from 34.

Acid (**34**; 3.90 g, 20 mmol) and *p*-toluenesulfonic acid monohydrate (3.44 g, 20 mmol) were dissolved in anhyd. EtOH (80 mL) and the mixture was heated at reflux for 24 h with stirring, eliminating water by use of a Dean-Stark apparatus filled with molecular sieves (4A). After cooled to room temperature, the reaction mixture was evaporated *in vacuo*, and the residue was dissolved in AcOEt, washed successively with sat. aq. NaHCO<sub>3</sub> and sat. a.q. NaCl, and then dried over anhyd. MgSO<sub>4</sub>. Filtration followed by evaporation *in vacuo* gave the crude product as a yellow oil (5.30 g), which was further purified by column chromatography (silica gel, C<sub>6</sub>H<sub>6</sub>-AcOEt = 6:1) to give analytically pure sample of ethyl ester (**36**; 4.02 g, 90%) as a lemon-yellow oil.

Physical properties of compound **36** were as follows: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 8.19 (2H, d, *J* = 9 Hz, H-3 and 5), 7.49 (2H, d, *J* = 9 Hz, H-2 and 6), 4.15 (2H, AB-quartet type m, CH<sub>2</sub>CH<sub>3</sub>), 3.84 (1H, q, *J* = 7 Hz,

H-2'), 1.55 (3H, d,  $J = 7$  Hz, H-3'), 1.22 (3H, t,  $J = 7$  Hz, CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  173.0 (C=O), 147.8 (C-1), 146.8 (C-4), 128.4 (C-2), 123.6 (C-3), 61.0 (OCH<sub>2</sub>), 45.2 (C-2'), 18.2 (C-3'), 13.8 (CH<sub>2</sub>CH<sub>3</sub>). IR (neat):  $\nu_{\max}$  (cm<sup>-1</sup>) 2984, 1732, 1625, 1522, 1348, 1178, 1072, 1024, 858, 741, 698. MS (EI):  $m/z$  (rel. intensities) 223 ( $M^+$ , 15), 193 (4), 178 (6), 150 (41), 134 (12), 120 (15), 103 (60), 91 (100), 77 (33), 63 (7), 51 (9), 39 (10). Anal. Calcd for C<sub>11</sub>H<sub>13</sub>NO<sub>4</sub>: C, 59.19; H, 5.87; N, 6.27. Found: C, 58.96; H, 5.73; N, 5.99.

### Preparation of ethyl *rac*-2-(4-aminophenyl)propanoate (**37**) from **35**.

Aminoacid (**35**; 0.352 g, 2.09 mmol) and *p*-toluenesulfonic acid monohydrate (0.405 g, 2.13 mmol) were dissolved in anhyd. EtOH (30 mL) and the mixture was heated at reflux for 18 h with stirring, eliminating water by use of a Dean-Stark apparatus filled with molecular sieves (4A). After cooled to room temperature, the reaction mixture was evaporated *in vacuo*, and the residue was dissolved in AcOEt, washed successively with *conc.* NH<sub>4</sub>OH, sat. aq. NaHCO<sub>3</sub> and sat. a.q. NaCl, and then dried over anhyd. Na<sub>2</sub>SO<sub>4</sub>. Filtration followed by evaporation *in vacuo* gave the crude product (**37**; 0.386 g, 96%; pure from <sup>1</sup>H NMR spectra) as a red viscous oil (lit.,<sup>21</sup> bp<sub>0.8</sub> 120-122 °C). This sample was subjected to the reaction (preliminary) with OPT without further purification.

### Preparation of ester (**37**) from **36**.

A solution of ethyl 2-(4-nitrophenyl)propanoate (**36**; 3.35 g, 15 mmol) in EtOH (80 mL) was poured into an autoclave. After the suspension of 5% Pd-C (0.5 g), the apparatus was sealed and filled with H<sub>2</sub> (50 kg/cm<sup>2</sup>). The mixture was stirred at room temperature for 45 min. The reaction mixture was filtered and evaporated *in vacuo* to give the crude product (3.82 g), which was washed with AcOEt. After the removal of insoluble material (0.40 g, mp > 260 °C), purification by column chromatography (silica gel, C<sub>6</sub>H<sub>6</sub>-AcOEt = 4:1) gave the analytically pure sample of aminoester (**37**; 2.33 g, 80%) as a yellow oil. This sample was subjected to the reaction with OPT without further purification.

### Preparation of *rac*-Indoprofen ethyl ester (**38**) from **37**.

To a solution of *o*-phthalaldehyde (OPT; 1.340 g, 10 mmol) in MeCN (30 mL) was added successively (i) a solution of 2-mercaptoethanol (MET; 6.0 mL, 86 mmol) in MeCN (10 mL) over 2 min, (ii) a solution of ethyl ester (**37**; 1.930 g, 10 mmol) in MeCN (10 mL) over 2 min, (iii) 1,2,3-1*H*-benzotriazole (Bt-H; 1.191 g, 10 mmol) portionwise over 2 min, and (iv) pH 9.6 borate buffer (0.05 *M* H<sub>3</sub>BO<sub>3</sub>-KCl-NaOH; 5 mL) over 2 min with stirring at room temperature. After the additions were complete, the mixture was further stirred at room temperature for 13 h under N<sub>2</sub>, and then evaporated. The residue was dissolved in CHCl<sub>3</sub>, washed successively with sat. a.q. NaHCO<sub>3</sub>, 2*N* HCl, and sat. a.q. NaCl, and then dried over

anhyd. Na<sub>2</sub>SO<sub>4</sub>. Filtration followed by evaporation gave the crude material (3.40 g), which was purified by column chromatography (silica gel, C<sub>6</sub>H<sub>6</sub>-AcOEt = 5:1) to give the crude phthalimidine (**38**; 1.91 g, 62%, 105-107 °C; pure from <sup>1</sup>H NMR spectra) as beige crystalline solids. Chromatographically-purified sample was immediately subjected to combustion analyses.

Physical properties of compound **38** were as follows: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.92 (1H, dd, *J* = 7 Hz and 1 Hz, H-7), 7.82 (2H, d, *J* = 8 Hz, H-2'), 7.60 (1H, ddd, *J* = 7 Hz, 7 Hz, and 1 Hz, H-5), 7.52 (1H, d, *J* = 8 Hz, H-4'), 7.50 (1H, dd, *J* = 8 Hz and 8 Hz, H-6), 7.37 (2H, d, *J* = 8 Hz, H-3'), 4.85 (2H, s, H-3), 4.22-4.04 (2H, AB-quartet type m, CH<sub>2</sub>CH<sub>3</sub>), 3.72 (1H, q, *J* = 7 Hz, CHCH<sub>3</sub>), 1.51 (3H, d, *J* = 7 Hz, CHCH<sub>3</sub>), 1.22 (3H, t, *J* = 7 Hz, CH<sub>2</sub>CH<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 174.5 (C=O of ester), 167.5 (C=O of C-1), 140.1 (C-3a), 138.4 (C-4'), 136.8 (C-1'), 133.2 (C-7a), 132.1 (C-5), 128.4 (C-7), 128.2 (C-3' and 5'), 124.2 (C-4), 122.6 (C-6), 119.6 (C-2' and 6'), 60.8 (OCH<sub>2</sub>), 50.7 (C-3), 45.0 (CHCH<sub>3</sub>), 18.5 (CHCH<sub>3</sub>), 14.1 (CH<sub>2</sub>CH<sub>3</sub>). IR (KBr): ν<sub>max</sub> (cm<sup>-1</sup>) 3337, 2976, 2934, 1676 (C=O), 1516, 1385, 1205, 1172, 1055, 787, 747, 691. MS (EI): *m/z* (rel. intensities) 309 (*M*<sup>+</sup>, 36), 279 (18), 236 (100), 218 (25), 192 (15), 167 (38), 149 (54), 104 (50), 90 (39), 77 (44), 65 (34), 57 (52), 41 (71). Anal. Calcd for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub>: C, 73.77; H, 4.53; N, 6.19. Found: C, 73.47; H, 6.17; N, 4.39.

#### Preparation of *rac*-Indoprofen (**39**) from **38**.

To a solution of ester (**38**; 100 mg, 0.32 mmol) in EtOH (19 mL) was added 10% KOH (1 mL), and the mixture was heated at reflux for 3 h. After cooled to room temperature, the reaction mixture was evaporated *in vacuo*, and the residue was dissolved in cold water (10 mL). Acidification of aqueous solution gave precipitates, which were collected by filtration. Since the crude material was very hygroscopic, it was immediately recrystallized from EtOH to give the analytically pure sample of *rac*-indoprofen [**39**; 78 mg, 83%, mp 205-207 °C (lit.,<sup>10</sup> 213-214 °C); pure from <sup>1</sup>H NMR spectra] as slightly yellow crystalline solids.

The result of combustion analyses proved that our sample was hydrated: Anal. Calcd for C<sub>17</sub>H<sub>15</sub>NO<sub>3</sub>·1/3H<sub>2</sub>O: C, 71.07; H, 5.50; N, 4.87. Found: C, 71.01; H, 5.44; N, 4.63.

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