

# Chemoselective reactions of dimethyl carbonate catalysed by alkali metal exchanged faujasites: the case of indolyl carboxylic acids and indolyl-substituted alkyl carboxylic acids

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At 160–180 °C, in the presence of alkali metal exchanged faujasites (MX or MY; M = Li, Na, K), the reaction of dimethyl carbonate with indolyl-3-acetic, -3-propionic, and -3-butyric acids proceeds towards the formation of the corresponding methyl esters or carbamate esters which can be isolated in 93–99% yields. The methylation of the indolyl-NH group is never observed. This high chemoselectivity is driven by the nature of the catalyst and the reaction temperature. In particular, among the six different zeolites used, the more basic MX faujasites show better performances in terms of both activity and selectivity than MY solids. A similar trend also holds for the reaction of dimethyl carbonate with indolyl-carboxylic acids, where MX compounds are still efficient catalysts for the formation of methyl esters. In this case, however, the overall reactivity/selectivity also reflects the relative positions of the NH and CO<sub>2</sub>H groups which may account for significant decarboxylation reactions observed for indolyl acids substituted at positions 2 and 3. This process is totally absent for indolyl-6-carboxylic acid.

## Introduction

In the past two decades, the non-toxic dimethyl carbonate (MeOCO<sub>2</sub>Me, DMC) has emerged as a green candidate for the replacement of highly noxious compounds such as phosgene and methyl halides/sulfate, in both methylation and methoxycarbonylation reactions.<sup>1</sup> A number of homogeneous and heterogeneous catalysts have been reported for DMC-mediated processes:<sup>1,2</sup> among them, we recently observed that alkali metal exchanged faujasites offered unique possibilities to catalyze methylation and esterification reactions. Most relevant examples were in the class of ambident nucleophiles. In the presence of NaY faujasite, the reaction of dimethyl carbonate with amino-phenols, -benzyl alcohols, -benzoic acids, and -benzamides not only showed a very high mono-*N*-methyl selectivity (up to 99%), but it proceeded with complete chemoselectivity towards the amino group [Scheme 1, path (a)].<sup>3</sup> The other nucleophilic functionalities (OH, CO<sub>2</sub>H, CH<sub>2</sub>OH, CONH<sub>2</sub>) were fully preserved from alkylation and/or transesterification reactions.

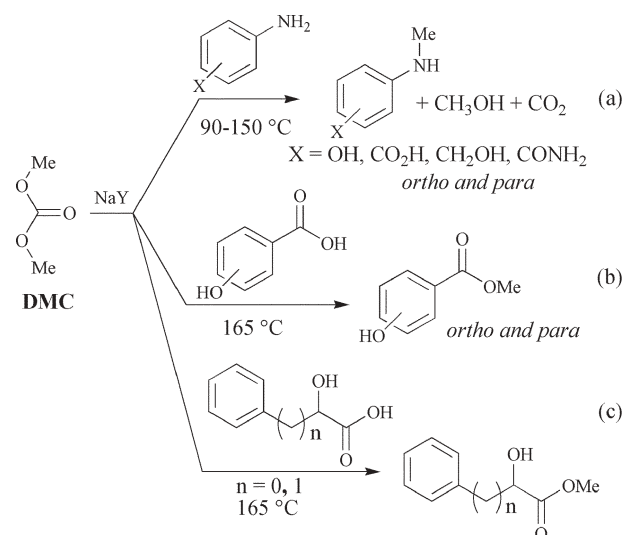
Likewise, at a higher temperature of 165 °C, the DMC/NaY system allowed the exclusive esterification of hydroxy-benzoic acids (*ortho*- and *para*-isomers), mandelic acid, and phenyllactic acid, without affecting aromatic and aliphatic OH-substituents [Scheme 1, paths (b) and (c)].<sup>4</sup>

All these processes were genuine green examples: they were truly catalytic, they did not require additional solvents (DMC served simultaneously as a reagent and solvent), and they released only MeOH and CO<sub>2</sub> as co-products. Moreover,

typical selectivities of reactions of Scheme 1 were in the range of 90–100%: in a single step, with no derivatization (protection/de-protection) sequences, the desired methylamines or methyl esters were isolated in 80–99% yields.

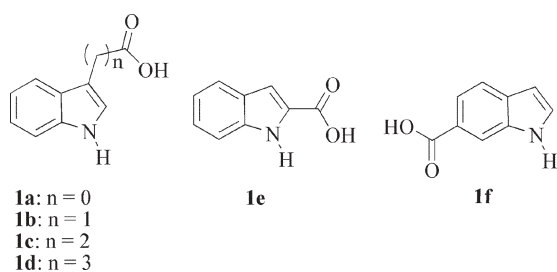
On the contrary, in the presence of basic catalysts (*i.e.* K<sub>2</sub>CO<sub>3</sub>), competitive reactions of *O*- and bis *N,N*-methylation, *N*- and *O*-methoxycarbonylation took place simultaneously.

These findings prompted us to face the problem of indolyl-substituted alkyl carboxylic acids and of indolyl carboxylic acids, which were both good models of ambident nucleophiles and examples of structural components of auxins and many pharmaceutical agents.<sup>5</sup> In particular, we focused our

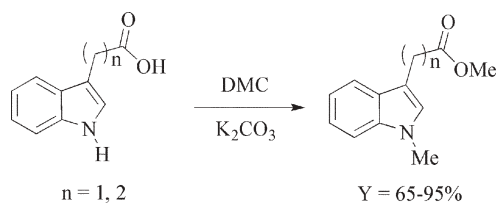


**Scheme 1** Chemoselective reactions of DMC in the presence of NaY catalyst.

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**Scheme 2**



**Scheme 3**

attention on indolyl-3-carboxylic, -acetic, -propionic, and -butyric acids (compounds **1a–d**), and on indolyl-2-carboxylic, and -6-carboxylic acids (compounds **1e** and **1f**) (Scheme 2).

At 130 °C, Jiang *et al.* already reported that reactions of DMC with acids **1a–d** were efficiently catalyzed by  $K_2CO_3$ ,<sup>6</sup> however, chemoselectivity was elusive because competitive processes of esterification and *N*-methylation occurred to comparable extents (Scheme 3).

In the case of **1a**, it was observed that a decarboxylation process also took place to give *N*-methylindole in 45% yield.

We wish to report herein that at 150–180 °C, the same reactions of acids **1b–d** and **1f**, became highly selective when carried out over alkali metal exchanged faujasites, particularly of the X type: only methyl esters were obtained in substantially quantitative yields, without affecting the NH group. For longer reaction times, carbamate esters coming from simultaneous esterification and *N*-methoxycarbonylation of indolyl substrates were isolated in up to 99% yield. Under these conditions, acids **1a** and **1e** underwent both decarboxylation and esterification reactions, but the methylation of the indolyl-NH group was not appreciable. The outcome was primarily driven by the acido-basic properties of the zeolite catalysts.

## Results

Six different faujasites, namely MY and MX (M = Li, Na, K) were used as catalysts: four of them (M = Li and K), were prepared through conventional ionic exchange reactions, starting from two commercially available samples of zeolites (NaY and NaX, respectively) and LiCl or KCl as precursors.<sup>7</sup> The main features of these catalysts are summarized in Table 1.

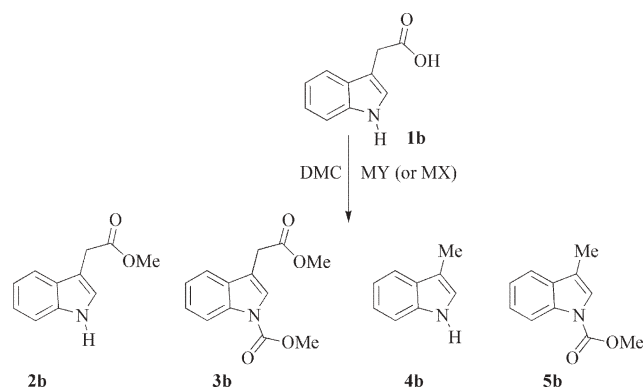
The reaction of DMC with indolyl-3-acetic acid **1b** was initially investigated. In the presence of MX or MY catalysts, a solution of **1b** in DMC ( $4.5 \times 10^{-2}$  M, 30 mL) was set to react at 160 and 180 °C, in a stainless-steel autoclave (90 mL). Weight ratios (*Q*) MX : **1b** or MY : **1b** ranged from 1 to 0.05, and different reaction times of 4–15 h were considered.

**Table 1** Faujasite catalysts used in the reaction of DMC with acids **1a–c**

Starting zeolite (Na, %) <sup>a</sup>	Product	Ionic exchange (%) <sup>b</sup>
NaX (7.5)	LiX	71
NaX (7.5)	KX	92
NaY (8)	LiY	67
NaY (8)	KY	86

<sup>a</sup> The Na content was evaluated through atomic absorption (AA).

<sup>b</sup> Percentage of ionic exchange (from NaX and NaY, respectively) was evaluated by AA (K) and emission (Li).



**Scheme 4**

After purification of reaction mixtures [flash-column chromatography (FCC): petroleum ether–diethyl ether, 2 : 3 v/v], four products were isolated and identified by GC/MS and by NMR (Scheme 4). The results are reported in Table 2.

In the absence of catalysts, the acid **2b** was recovered unreacted after 3 h at 180 °C (Table 2, entry 1). At the same temperature (180 °C, 4 h, *Q* = 1), reactions carried out over MY zeolites showed good conversions (68–75%) but modest selectivities (entries 2–4): the methyl ester **2b** was formed along with 3-methylindole (**4b**, 19–43%). The latter plausibly originated from the decarboxylation of indolyl-3-acetic acid.<sup>8</sup>

**Table 2** The reaction of DMC with **1b** in the presence of different zeolites

Entry	Cat.	Cat. : substr. ( <i>Q</i> ) <sup>a</sup>	<i>t</i> /h	<i>T</i> /°C	Conv. (%) <sup>b</sup>	Isolated product yield (%) <sup>c</sup>			
						<b>2b</b>	<b>3b</b>	<b>4b</b>	<b>5b</b>
1	None		3	180	<1				
2	LiY	1	4	180	68	25		43	
3	NaY	1	4	180	75	52		21	
4	KY	1	4	180	72	50		19	
5	NaY	0.1	15	180	75	56		16	
6	NaY	0.5	9	180	80	55		25	
7	NaY	0.5	15	180	100		61		35
8	LiX	1	4	180	95	87	10		
9	NaX	1	4	180	>99		97		
10	KX	1	4	180	>99		98		
11	NaX	1	3	160	>99	95			
12	NaX	0.1	9	160	>99	93			
13	NaX	0.05	9	160	46	44			
14	KX	0.1	8	160	>99	96			

<sup>a</sup> Weight ratio zeolite : **1b**. <sup>b</sup> Based on the recovered starting reagent **1b**. <sup>c</sup> Yields of **2b–5b** were evaluated after purification by flash-column chromatography on silica gel (eluant: petroleum ether–diethyl ether, 2 : 3 v/v).

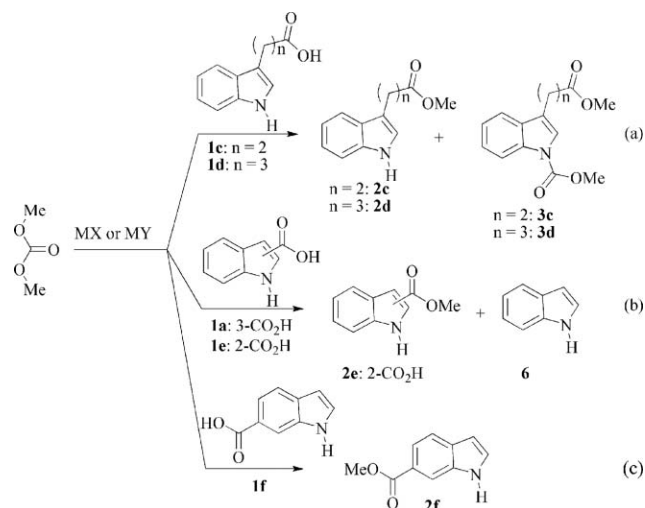
In the presence of NaY, a similar selectivity could be accomplished even by using lower  $Q$  ratios (NaY : **1b** = 0.1 and 0.5; **4b**: 16–25%, entries 5 and 6). If the reaction was continued for a longer time (15 h,  $Q = 0.5$ ), a quantitative conversion was reached, and products **2b** and **4b** were transformed into the corresponding *N*-methoxycarbonyl derivatives, **3b** (61%) and **5b** (35%), respectively (entry 7).

MX faujasites were superior catalysts in terms of both efficiency and selectivity. At 180 °C ( $Q = 1$ , 4 h), the methyl ester **2b** was isolated in a 87% yield over LiX (entry 8), while compound **3b** [methyl(*N*-methoxycarbonyl)-3-indolyl acetate] was obtained in 97 and 98% yields, in reactions catalyzed by NaX and KX, respectively (entries 9 and 10). At a lower temperature (160 °C), the esterification of **1b** was the exclusive process observed with NaX and KX, even at  $Q$  ratios of 0.05–0.1. Isolated yields of **2b** were of 93–96% (entries 11, 12 and 14) and of 44% (entry 13). In all cases, side-products **4b** and **5b** were never detected.

Reactions of DMC with indolyl-3-propionic, -3-butyric acids, -3-carboxylic, -2-carboxylic, and -6-carboxylic acids (**1c**, **1d**, **1a**, **1e**, and **1f**, respectively) were investigated under the same conditions used for **1b**. Solutions of compounds **1** in DMC ( $4.5 \times 10^{-2}$  M, 30 mL) were set to react at 160 and 180 °C, in the presence of NaY and MX (M = Na, Li) catalysts [weight ratios ( $Q$ ) of catalyst : substrate were of 0.1 and 1]. In the case of substrates **1c,d**, products coming from the esterification of the acid function (compounds **2c,d**), and from the *N*-methoxycarbonylation of the indolyl NH group (compounds **3c,d**) were observed [Scheme 5, path (a)]. The reactions of DMC with acids **1a**, and **1e** and **1f** yielded methyl esters (**2e,f**) along with indole (**6**) originated by the decarboxylation of reagents [Scheme 5, paths (b) and (c)]. Products were isolated and identified by GC/MS and NMR. The results are reported in Table 3.

### Acids **1c,d**

As in the case of indolyl-3-acetic acid (**1b**), MX faujasites were more active than NaY. At 180 °C ( $Q = 1$ ), reactions of acids



Scheme 5

**Table 3** The reaction of DMC with indolyl-3-propionic and indolyl-3-butyric acids (**1c** and **1d**) in the presence of different zeolites

Entry	Substrate	Cat.	Cat. : substr. ( $Q$ ) <sup>a</sup>	t/h	T/°C	Conv. (%) <sup>b</sup>	Isolated product yield (%) <sup>c</sup>
1	<b>1c</b>	NaY	0.1	20	180	21	<b>2c</b> : 19
2	<b>1c</b>	NaY	1	6	180	100	<b>2c</b> : 99
3	<b>1c</b>	NaX	1	3	160	100	<b>3c</b> : 98
4	<b>1c</b>	LiX	1	2	180	100	<b>3c</b> : 96
5	<b>1d</b>	NaY	0.1	12	180	30	<b>2d</b> : 28
6	<b>1d</b>	NaY	1	3	180	100	<b>2d</b> : 99
7	<b>1d</b>	NaX	1	3	160	100	<b>3d</b> : 99
8	<b>1a</b>	None		3	160	7	<b>6</b> : 5
9	<b>1a</b>	NaX	0.5	3	120	45	<b>6</b> : 43
10	<b>1a</b>	NaX	1	3	160	100	<b>6</b> : 99
11	<b>1a</b>	NaY	1	3	140	100	<b>6</b> : 99
12	<b>1e</b>	NaX	1	3	160	100 <sup>d</sup>	<b>2e</b> : 55
13	<b>1e</b>	NaY	1	3	160	100	<b>6</b> : 32
14	<b>1f</b>	NaX	0.1	5	160	22	<b>2f</b> : 19
15	<b>1f</b>	NaX	1	7	160	100	<b>2f</b> : 93
16	<b>1f</b>	NaY	1	3	180	40	<b>2f</b> : 36

**1c,d** catalyzed by NaY gave methyl esters **2c** and **2d** in substantially quantitative yields, after 6 and 3 h, respectively (Table 3, entries 2 and 6). Both processes were also possible with a lower  $Q$  ratio of 0.1 (entries 1 and 5).

Instead, in the presence of MX zeolites, simultaneous esterification and *N*-methoxycarbonylation reactions took place to yield compounds **3c** and **3d** as sole products (96–99%, entries 3, 4, and 7). These processes occurred at 160 and 180 °C, over NaX and LiX, respectively.

Crude esters **2c,d** and carbamate esters **3c,d** could be recovered in a very high purity (97–98%), by simple filtration of the zeolite and removal of DMC under vacuum.

It should be noted that, particularly for compounds **3**, very few synthetic methods are available in the literature, and they are always based on multistep sequences.<sup>9</sup>

### Acids **1a**, **1e**, and **1f**

Indolyl-carboxylic acids (**1a**, **1e**, and **1f**) showed quite a different behaviour with respect to **1b–d**. Regardless of the reaction conditions (catalyst, temperature, and time), acid **1a**, substituted at position 3, gave only the decarboxylation reaction to produce indole **6** in a substantially quantitative yield (Table 3, entries 9–11). In this case, a sluggish formation of indole (5%, 3 h, 160 °C) was observed also without any catalyst (entry 8). In the presence of NaX, acid **1e**, substituted at position 2, yielded a mixture of the methyl ester **2e** (55%) and indole **6** (32%) (entry 12), whereas the decarboxylation of **1e** was the sole reaction observed over the NaY catalyst (entry 13). Only indolyl-6-carboxylic acid **1f** underwent a highly chemoselective esterification process: the reaction was catalyzed by both NaX and NaY, at 160 and 180 °C, respectively (entries 14–16). The methyl ester **2f** was isolated in up to 93% yield (entry 15).

In all cases, faujasite catalysts were easily recyclable: after reactions of acids **1a–f**, they could be separated by filtration and re-activated by a mild thermal treatment (90 °C/0.1 mm, overnight). Both catalytic activity and selectivity were fully restored. For instance, when a re-activated NaX was used under the conditions of entry 11 of Table 2, the reaction of indolyl-3-acetic acid (**1b**) with DMC yielded the corresponding methyl ester (**2b**) in 92% isolated yield.

## Discussion

### Acids **1b–d**

Acid–base properties of MY and MX faujasites affect the results of Tables 2 and 3. In particular, according to the scale proposed by Barthomeuf (Scheme 6),<sup>10</sup> the more basic MX show better performances than MY. The latter, especially LiY, operates only at 180 °C: they promote either the competitive reactions of esterification and decarboxylation of **1b**, or the esterification of acids **1c,d**.<sup>11</sup>

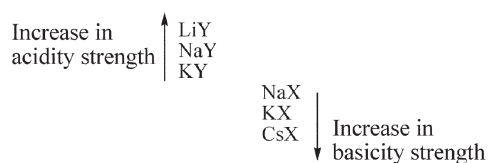
At 160 °C instead, NaX and KX faujasites selectively catalyze the formation of esters **2b** and carbamate esters **3c,d**. The same reactions require a higher temperature of 180 °C, with respect to the less basic LiX.

In the case of indolyl-3-acetic acid (**1b**), MX zeolites are further activated by the temperature: at 180 °C, NaX and KX allow a rapid and quantitative conversion of ester **2b** into **3b**. While, under the same conditions, a sluggish and not selective reaction is observed when NaY is the catalyst (Table 2, entry 6). Shieh *et al.* reported that the *N*-methoxycarbonylation of 5-bromoindole with DMC also takes place only in the presence of moderate-to-strong organic bases (DMAP and DBU).<sup>12</sup>

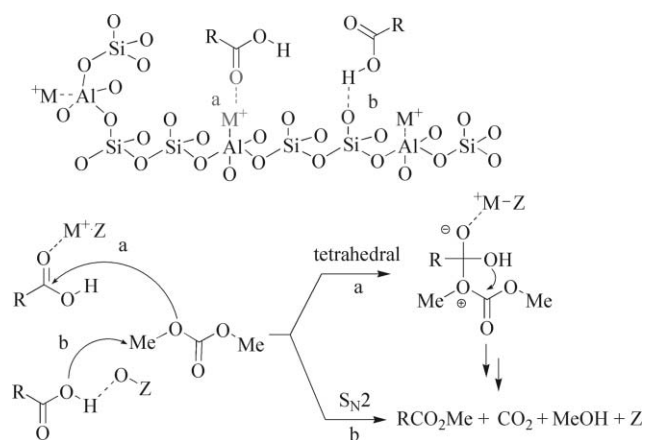
### Acids **1a, 1e,f**

For indolyl-carboxylic acids, the effect of the catalyst is evident for **1e** and, particularly, for **1f**: faster esterification reactions and better yields of products **2e** and **2f** are achieved over NaX faujasite with respect to NaY (entries 11–15, Table 3). However, the reactivity of compounds **1a**, and **1e** and **1f** also reflects the relative positions of the NH and CO<sub>2</sub>H groups. The high electron density of positions 2 and, especially, 3 of the pyrrole ring of the indoles<sup>13</sup> may account for the important, if not exclusive, decarboxylation reaction observed for reagents **1a** and **1e**. By contrast, this process is totally absent for indolyl-6-carboxylic acid. The lower reactivity of indolyl-3-acetic acid **1b** compared to its homologues **1c** and **1d** (Tables 2 and 3) can be explained accordingly.

Overall, the surface interactions between reagents and catalysts can be affected by the different acid–base features



Scheme 6



Scheme 7

of MY/MX solids. Scheme 7 describes two plausible modes of adsorption of carboxylic acids over alkali metal exchanged faujasites.<sup>14</sup>

The formation of methyl esters **2b,c** (Schemes 4 and 5) may proceed according to tetrahedral or S<sub>N</sub>2-type or both mechanisms, which are possibly favored over more basic X zeolites.

Indole-NH groups of acids **1** are also expected to bind to the polar surface of MY/MX faujasites.<sup>15</sup> Nevertheless, the reactivity of CO<sub>2</sub>H and NH functionalities is highly discriminated. Not to mention that compounds **1** never undergo *N*-methylation reactions which are always observed over conventional basic catalysts (Scheme 3).<sup>16,17</sup> This fine tuning of the selectivity suggests that the activation of acids **1** is a complex phenomenon where both the geometry of adsorption of reagents and the steric requisites of faujasites, can be involved.<sup>18</sup>

## Conclusions

The combination of dimethyl carbonate and Y or X faujasites allows a straightforward and high-yield synthesis of methyl esters **2** or methyl carbamate esters **3** derived from indolyl acids **1**. In particular, alkali metal exchanged X zeolites are superior catalysts in terms of both efficiency and selectivity. Typical chemoselectivity is up to 99% at quantitative conversions, a result hitherto not possible with standard basic catalysts (*i.e.* K<sub>2</sub>CO<sub>3</sub>), where only products of simultaneous esterification and *N*-methylation of acids **1** are obtained. Under the explored conditions, the reaction outcome is affected by the acid–base nature of MX/MY zeolites which likely alters the surface interactions between reagents and catalysts.

Although the procedure is rather energy-intensive, multiple *green* features can be recognized: (i) the non-toxic DMC is used as a reagent/solvent which can be recycled;<sup>19</sup> (ii) eco-safe solids (faujasites) are catalysts which can be easily separated and recycled; (iii) except for MeOH and CO<sub>2</sub>, no organic/inorganic by-products are observed; and (iv) thanks to the high chemoselectivity, not only derivatization sequences can be avoided, but also purification steps are much simplified.

## Experimental

Compounds **1** and DMC were ACS grade and were employed without further purification. Zeolites NaY and NaX were from Aldrich. Other MY and MX catalysts (M = Li, Na, K) were prepared according to a procedure previously reported by us.<sup>2h</sup> Before each reaction, all the faujasites were dehydrated by being heated at 65 °C under vacuum (10 mm Hg) overnight.

MS (EI, 70 eV) analyses were run using HP5/MS capillary columns (30 m). <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a 300 MHz spectrometer, using CDCl<sub>3</sub> as solvent.

### Reactions carried out in autoclave. General procedure

A stainless-steel autoclave (90 mL of internal volume) was charged with a solution (4.5 × 10<sup>-2</sup> M; 30 mL) of the chosen acid (**1**, 1.35 mmol), dimethyl carbonate (0.36 mol) and MY or NaX faujasites (catalyst : substrate in a 0.1–1 weight ratio, see Tables 2 and 3). At room temperature and before the reaction, air was removed by a purging valve with a N<sub>2</sub> stream. The autoclave was then heated by an oil-circulating jacket, while the mixture was kept under magnetic stirring throughout the reaction. A thermocouple fixed onto the autoclave head monitored the temperature (160–180 °C). After different time intervals (3–20 h), the autoclave was cooled to rt, purged from CO<sub>2</sub> and, finally, opened. The reaction mixture was analysed by GC/MS.

Crude esters **2b** and **2f**, and carbamate esters **3b–d** were isolated in 93–98% GC-purity by simple filtration of the NaX catalyst and removal of DMC under vacuum (35 °C/250 mm). Likewise, products **2c** and **2d** (98% GC) were obtained from reactions catalyzed by MY zeolites. Products **4b** and **5b** were obtained from the reaction of **1b** with DMC over MY faujasites (Table 2). Reaction mixtures were further purified by FCC on silica gel F60 (eluant: petroleum ether–diethyl ether in 2 : 3 v/v).

All compounds were characterized by GC/MS and <sup>1</sup>H NMR. Spectroscopic data of **2b–d**, **2f**, **3b**, **4b**, **5b**, and **6** were already reported in the literature.<sup>9,20–24</sup> The structures of new compounds **3c** and **3d** were confirmed also by <sup>13</sup>C NMR.

<sup>1</sup>H NMR spectra were recorded at 300 MHz, <sup>13</sup>C NMR at 75 MHz. Chemical shifts were reported in δ values downfield from TMS. CDCl<sub>3</sub> was used as the solvent.

The structures of esters **2b–d** and **2f**, and of indole **6** were confirmed also by comparison to authentic samples. Compound **2e** was not isolated: its structure was assigned by GC/MS.

### Methyl indolyl-3-acetate **2b**

Mp 42–44 °C (pale yellow solid) [lit.<sup>20a</sup> mp 47–48 °C]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 3.74 (s, 3H), 3.82 (s, 2H), 7.12–7.29 (m, 3H), 7.34–7.39 (m, 1H), 7.62–7.68 (m, 1H), 8.18 (brs, 1H). MS (EI), *m/z* (relative int.): 189 (M<sup>+</sup>, 32%), 131 (11), 130 (M<sup>+</sup> – CO<sub>2</sub>Me, 100), 103 (7), 77 (8).

### Methyl indolyl-3-propionate **2c**<sup>21</sup>

Mp 75–76 °C (white solid) [lit.<sup>20b</sup> mp 79–80 °C]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.75 (t, 2H, *J* = 8.1 Hz), 3.14 (t, 2H, *J* = 7.9 Hz), 3.7 (s, 3H), 7.03 (m, 1H), 7.10–7.26 (m, 2 H),

7.35–7.41 (m, 1H), 7.62–7.66 (m, 1H), 8.02 (brs, 1H). MS (EI), *m/z* (relative int.): 203 (M<sup>+</sup>, 18%), 131 (11), 130 (M<sup>+</sup> – CH<sub>2</sub>CO<sub>2</sub>Me, 100), 103 (4), 77 (6).

### Methyl indolyl-3-butyrate **2d**<sup>22</sup>

Mp 70–71 °C (colorless solid) [lit.<sup>20c</sup> mp 70–72 °C]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.06 (qui, 2H, *J* = 7.35 Hz), 2.41 (t, 2H, *J* = 7.54 Hz), 2.82 (t, 2H, *J* = 7.54 Hz), 3.67 (s, 3H), 7.00 (m, 1H), 7.08–7.24 (m, 2 H), 7.33–7.39 (m, 1H), 7.57–7.65 (m, 1H), 7.98 (brs, 1H). MS (EI), *m/z* (relative int.): 217 (M<sup>+</sup>, 28%), 186 (M<sup>+</sup> – OMe, 9), 143 (M<sup>+</sup> – CH<sub>2</sub>CO<sub>2</sub>Me – H, 21), 130 (M<sup>+</sup> – CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 77 (7).

### Methyl indolyl-2-carboxylate, **2e**<sup>23</sup>

MS (EI), *m/z* (relative int.): 175 (M<sup>+</sup>, 65%), 144 (M<sup>+</sup> – OMe, 21), 143 (100), 116 (M<sup>+</sup> – CO<sub>2</sub>Me, 12), 115 (53), 89 (28).

### Methyl indolyl-6-carboxylate **2f**

Mp 74–76 °C (pale yellow solid) [lit.<sup>24</sup> mp 71–72 °C]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 3.93 (s, 3H), 6.61 (m, 1H), 7.38 (m, 1H), 7.66 (d, 1H, *J* = 8.3 Hz), 7.82 (dd, 1H, *J*<sub>1</sub> = 8.5 Hz, *J*<sub>2</sub> = 1.5 Hz), 8.17 (m, 1H), 8.45 (brs, 1H). MS (EI), *m/z* (relative int.): 175 (M<sup>+</sup>, 73%), 145 (11), 144 (M<sup>+</sup> – OMe, 100), 116 (M<sup>+</sup> – CO<sub>2</sub>Me, 50), 89 (18).

### Methyl (*N*-methoxycarbonyl)indolyl-3 acetate **3b**

Mp 30–32 °C (white solid) [lit.<sup>9</sup> mp 34–35 °C]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 3.72 (s, 5H), 4.03 (s, 3H), 7.24–7.40 (m, 2H), 7.51–7.56 (m, 1H), 7.60 (s, 1H), 8.17 (d, 1H, *J* = 8.1 Hz). MS (EI), *m/z* (relative int.): 247 (M<sup>+</sup>, 56%), 189 (13), 188 (M<sup>+</sup> – CO<sub>2</sub>Me, 100), 143 (M<sup>+</sup> – CH<sub>2</sub>CO<sub>2</sub>Me, 40), 129 [M<sup>+</sup> – (CO<sub>2</sub>Me)<sub>2</sub>, 19], 128 (13), 102 (20), 76 (10).

### 3-Methylindole **4b**

Mp 96–98 °C (white solid) [lit.<sup>25</sup> mp 98–98.5 °C]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.35 (d, 3H, *J* = 1.1 Hz), 6.97 (m, 1H), 7.09–7.24 (m, 2H), 7.32–7.38 (m, 1H), 7.57–7.63 (m, 1H), 7.87 (brs, 1H). MS (EI), *m/z* (relative int.): 131 (M<sup>+</sup>, 58%), 130 (M<sup>+</sup> – H, 100), 102 (6), 77 (12).

### (*N*-Methoxycarbonyl)-3-methylindole **5b**

Viscous oil [lit.<sup>26</sup> bp 101–102 °C/0.5 torr]. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.19 (d, 3H, *J* = 1.1 Hz), 3.93 (s, 3H), 7.15–7.32 (m, 3H), 7.40–7.45 (m, 1H), 8.00 (m, 1H). MS (EI), *m/z* (relative int.): 190 (12), 189 (M<sup>+</sup>, 100%), 144 (82), 130 (M<sup>+</sup> – CO<sub>2</sub>Me, 48), 103 (16), 77 (24).

### Methyl (*N*-methoxycarbonyl)-3-indolyl propionate **3c**

Mp 40–43 °C (white solid); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.72 (t, 2H, *J* = 7.9 Hz), 3.01 (t, 2H, *J* = 8.0 Hz), 3.69 (s, 3H), 4.02 (s, 3H), 7.23–7.38 (m, 2H), 7.40 (s, 1H), 7.51–7.56 (m, 1H), 8.16 (d, 1H, *J* = 8.3 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 20.18, 33.46, 51.62, 53.58, 115.12, 118.75, 120.18, 122.03, 122.70, 124.62, 130.12, 135.46, 151.30, 173.19. MS (EI), *m/z* (relative int.): 261 (M<sup>+</sup>, 44%), 201 (M<sup>+</sup> – CO<sub>2</sub>Me – H, 11), 188

(M<sup>+</sup> – CH<sub>2</sub>CO<sub>2</sub>Me, 100), 144 (36), 143 [M<sup>+</sup> – (CO<sub>2</sub>Me)<sub>2</sub>, 20], 129 (13), 115 (22), 59 (14).

### Methyl (*N*-methoxycarbonyl)-3-indolyl butyrate 3d

Mp 63–65 °C (white solid); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 2.04 (qui, 2H, *J* = 7.4 Hz), 2.40 (t, 2H, *J* = 7.3 Hz), 2.73 (td, 2H, *J*<sub>1</sub> = 7.5 Hz, *J*<sub>2</sub> = 1.1 Hz), 3.67 (s, 3H), 4.02 (s, 3H), 7.22–7.37 (m, 2H), 7.39 (m, 1H), 7.51–7.56 (m, 1H), 8.16 (d, 1H, *J* = 7.9 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 24.17, 24.21, 33.45, 51.49, 53.59, 115.11, 118.98, 120.92, 122.11, 122.67, 124.55, 130.42, 135.59, 151.39, 173.78. MS (EI), *m/z* (relative int.): 276 (14), 275 (M<sup>+</sup>, 81%), 244 (M<sup>+</sup> – OMe, 16), 202 (17), 201 (M<sup>+</sup> – CO<sub>2</sub>Me – Me, 78), 188 (100), 156 (15), 144 (43), 143 (18), 129 (20), 115 (15).

### Indole 6

Mp 47–49 °C (yellow solid) [lit.<sup>27</sup> mp 52 °C].

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