

A Versatile, Practical, and Inexpensive Reagent, Pyridine-3-carboxylic Anhydride (3-PCA), for Condensation Reactions

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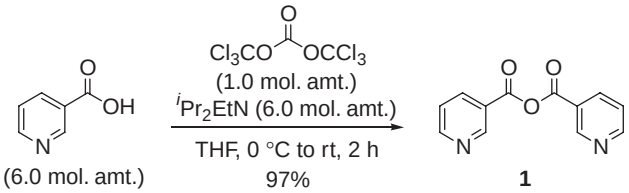
A highly useful method for the preparation of carboxylic esters and carboxamides from various carboxylic acids was established by using a novel condensing reagent, pyridine-3-carboxylic anhydride (3-PCA), in the presence of 4-(dimethylamino)pyridine as an activator. The reactions of various carboxylic acids with nucleophiles, such as alcohols or amines, afforded the corresponding carboxylic acids or carboxamides in good to high yields under mild conditions by using simple experimental procedure. In addition, it was confirmed that this protocol was applicable to a gram-scale synthesis and the by-products, including pyridine-3-carboxylic acid and pyridine-3-carboxylate (or pyridine-3-carboxamide) produced in situ, were easily removed by using a simple aqueous workup.

Since the synthesis of carboxylic esters and carboxamides from carboxylic acid and nucleophile, such as alcohol or amine, is considered to be one of the most important reactions in the field of synthetic organic chemistry, medicinal chemistry, and so forth, various condensation methods have been reported and are widely employed in the syntheses of natural and unnatural molecules that have carboxylic ester or carboxamide moieties.[1–12]

Benzoic acid derivatives, such as 2,4,6-trichlorobenzoyl chloride reported by Yamaguchi et al.[3] and 2-methyl-6-nitrobenzoic anhydride reported by Shiina et al.,[7] are used as effective condensing reagents in order to synthesize carboxylic esters under mild conditions, whereas an excess amount of bases, such as DMAP or triethylamine, is generally required to enhance the electrophilicity of the carboxylic acids in these reactions. In addition, these methods require purification by using silica-gel column chromatography to remove by-products, namely, the corresponding benzoic acid and benzoate produced from dehydrating agent and alcohol. Thus, it is still desired to develop more efficient reagent from the viewpoints of reactivity and purification. Then, pyridine carboxylic anhydride was chosen with the expectation that it would be reactive, because of the electron-withdrawing nature of pyridine ring.[13] In addition, the condensation reaction was expected to proceed without using any bases since the basicity was already inherent in the condensing reagent. Further, the hydrophilic pyridine carboxylic acid formed via this reaction would be readily removed by using a simple aqueous workup. We would like to report herein a convenient condensation reaction using pyridine-3-carboxylic anhydride (3-PCA, **1**), which is easily prepared from inexpensive pyridine-3-carboxylic acid (nicotinic acid) (Scheme 1).[14,15]



Scheme 1. Synthesis of pyridine-3-carboxylic anhydride (3-PCA).

Results and Discussion

Condensation Reaction between Carboxylic Acids and Alcohols with 3-PCA. First, we tried the synthesized various condensing agents, including pyridine carboxylic anhydride derivartives, such as pyridine-2-carboxylic anhydride (**2**) (quant.) and pyridine-4-carboxylic anhydride (**3**) (55%), furan carboxylic anhydride derivatives, such as furan-2-carboxylic anhydride (**4**) (98%) and furan-3-carboxylic anhydride (**5**) (98%), and thiophene carboxylic anhydride derivatives, such as thiophene-2-carboxylic anhydride (**6**) (99%) and thiophene-3-carboxylic anhydride (**7**) (99%), in good to excellent yields, as in the case of 3-PCA. Next, to evaluate the potential ability of hetero aryl carboxylic anhydrides as condensation reagent, the condensation reaction of 3-phenylpropionic acid (**8**) with 3-phenylpropan-1-ol (**9**) was initially examined in the presence of triethylamine, DMAP, and various dehydrating agents similar to the method using benzoic anhydride derivatives[3,7] (Table 1). When nicotinic anhydride (**1**) (pyridine-3-carboxylic anhydride, 3-PCA) was used, the reaction proceeded smoothly within 1 h, and the desired ester **10**, 3-phenylpropyl 3-phenylpropanoate, was afforded in 97% yield (Entry 1). However, the yield of **10** was smaller (72% or 87%) in the presence of a 3-PCA derivative, such as **2** or **3** (Entry 2 or 3). On the other hand, it was observed that the desired product was obtained in high yield when other carboxylic anhydrides, such as furoic anhydrides **4** and **5** or thenoic anhydrides **6** and **7**, were used (Entries 4–7). In regards to the reactivity and the ease of crystallization, 3-PCA (**1**) was chosen as a promising agent.

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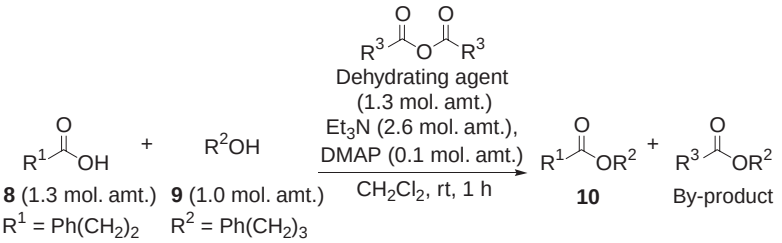
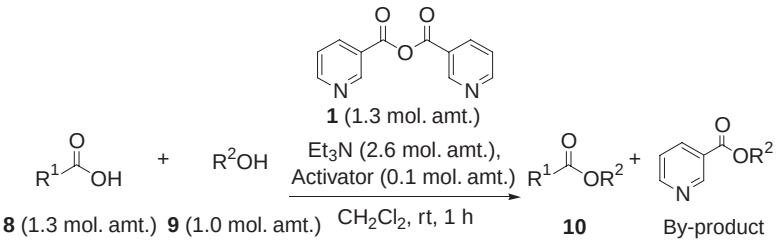
Table 1. Screening of Dehydrating Agents



Entry	R^3	Anhydride	Yield[a)]/%	
			10	By-product
1		**1**	97	3
2		**2**	72	28
3		**3**	87	5
4		**4**	98	1
5		**5**	quant.	trace
6		**6**	93	trace
7		**7**	quant.	trace

a) Isolated yield.

Table 2. Effect of Activators



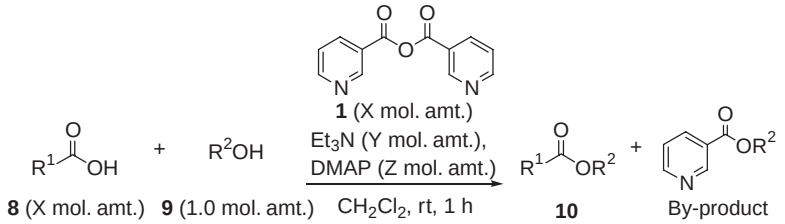
Entry	Activator	Yield[a)]/%	
		10	By-product
1	DMAP	97	3
2	PPY[b)]	95	4
3	HOBt[b)]	80	2
4	*N*-Methylimidazole	93	5
5	*N*-Butylimidazole	94	6

a) Isolated yield. b) PPY = 4-(1-pyrrolidinyl)pyridine, HOBt = 1-hydroxybenzotriazole.

Next, the effect of activators was examined (Table 2). When 4-(1-pyrrolidinyl)pyridine (PPY) was used, the desired ester **10** was obtained in high yield, just as in the case of DMAP (Entry 2). In the case of benzotriazole derivatives, such as 1-hydroxybenzotriazole (HOBt), the coupling reaction proceeded smoothly to afford **10** in good yield (Entry 3). Imidazole derivatives, such as *N*-methylimidazole or *N*-butylimidazole, which are known to be good nucleophilic bases,[16] also worked as activators for this coupling reaction (Entries 4 and 5).

Then, the reaction was further examined in order to reduce the amounts of the reagents, namely, carboxylic acid, triethylamine, DMAP, and 3-PCA (Table 3). It was observed that the corresponding ester formed in high yield even when the amounts of carboxylic acid, dehydrating reagent and triethylamine were all reduced to 1.1 molar amount (Entries 1–4). It is noteworthy that the desired carboxylic ester was obtained in high yield in the absence of triethylamine (Entry 5). This clearly indicates that the pyridine moiety of 3-PCA works as the base to capture pyridine-3-carboxylic acid formed in situ. In addition, it was found that the reaction proceeded smoothly

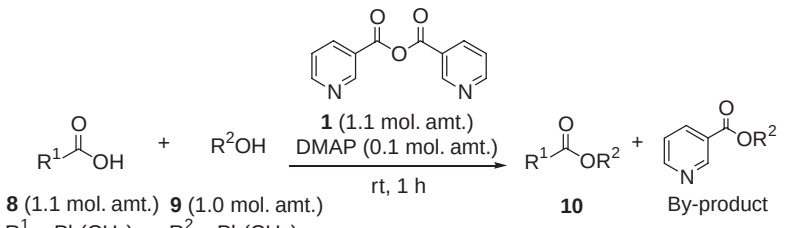
Table 3. Synthesis of Carboxylic Esters Using 3-PCA



Entry	X	Y	Z	Yield[a]/%	
				10	By-product
1	1.3	2.6	0.1	97	3
2	1.2	2.4	0.1	96	4
3	1.1	2.2	0.1	96	3
4	1.1	1.1	0.1	96	3
5	1.1	0	0.1	97	3
6	1.1	0	0.05	96	3
7	1.1	0	0.02	96	3
8[b]	1.1	0	0	49 (47)[c]	3

a) Isolated yield. b) The reaction mixture was stirred for 24 h. c) The unreacted starting material was recovered.

Table 4. Effect of Solvents



Entry	Solvent	Yield[a]/%	
		10	By-product
1	CH_2Cl_2	97	3
2[b]	CH_2Cl_2	97	3
3[c]	CH_2Cl_2	82	2
4	THF	94	3
5	Et_2O	93	4
6	DMF	95	4
7	DMSO	76	4
8	Toluene	91	4
9	MeCN	96	4

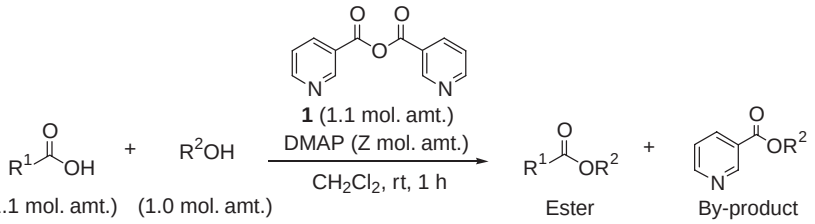
a) Isolated yield. b) The reaction was carried out at 0 °C. c) The reaction was carried out at −78 °C.

even when 0.02 molar amount of DMAP was used (Entry 7). Interestingly, the desired ester was obtained in 49% yield in the absence of DMAP (Entry 8).

Effect of solvents was examined (Table 4). It was shown that the reaction proceeded not only in a non-polar solvent, such as CH_2Cl_2 or toluene (Entries 1 and 8), but also in a polar solvent, such as THF, Et_2O, DMF, DMSO, or MeCN, and afforded ester **10** in good to excellent yields (Entries 1 and 4–9). In addition, it should be noted that the reaction well proceeded even at −78 °C (Entry 3).

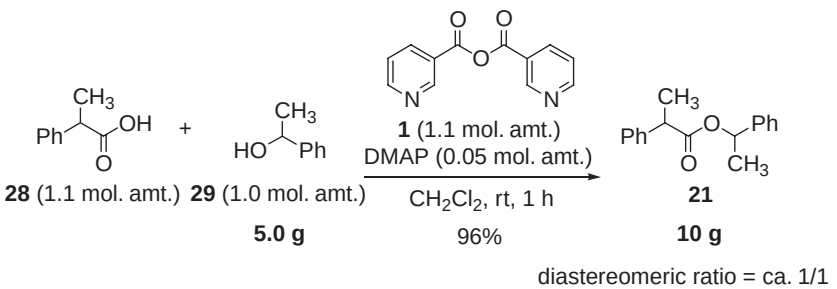
Results of the condensation reactions between various carboxylic acids and alcohols are shown in Table 5. Reactions of the primary and secondary aliphatic alcohols gave the desired carboxylic esters in high yields (Entries 1–6). On the other hand, in the case of tertiary alcohols, such as *t*-butyl alcohol, the corresponding ester was not detected (Entry 9). This reaction was applicable also to aromatic alcohols, which afforded ester **16** in high yield (Entry 7), and was effective even when a substrate possessing an acid-sensitive moiety in the same molecule (Entry 8). The corresponding products were likewise obtained rapidly in good to high yields when hindered α,α-disubstituted carboxylic acids or α,β-unsaturated carboxylic acids were used (Entries 10–17). In addition, it was observed that the yields of carboxylic esters increased

Table 5. Synthesis of Various Carboxylic Esters with 3-PCA



Entry	Carboxylic acid	Alcohol	Ester	Z	Yield[a]/%	
					Ester	By-product
1	$Ph(CH_2)_2CO_2H$	$Ph(CH_2)_3OH$	**10**	0.02	97	3
2	$Ph(CH_2)_2CO_2H$	$PhCH_2OH$	**11**	0.02	96	4
3	$Ph(CH_2)_2CO_2H$	$CH_2=CHCH_2OH$	**12**	0.02	93	3
4	$Ph(CH_2)_2CO_2H$	$PhCH(CH_3)OH$	**13**	0.02	95	3
5	$Ph(CH_2)_2CO_2H$	$Ph(CH_2)_2CH(CH_3)OH$	**14**	0.05	94	5
6	$Ph(CH_2)_2CO_2H$	*c*-$C_6H_{11}OH$	**15**	0.10	89	5
7	$Ph(CH_2)_2CO_2H$	PhOH	**16**	0.02	91	8
8	$Ph(CH_2)_2CO_2H$	$THPO(CH_2)_5OH$	**17**	0.02	95	5
9	$Ph(CH_2)_2CO_2H$	*t*-BuOH	—	0.10	ND[b]	ND[b]
10	*c*-$C_6H_{11}CO_2H$	$Ph(CH_2)_3OH$	**18**	0.05	90	10
11	*c*-$C_6H_{11}CO_2H$	$PhCH(CH_3)OH$	**19**	0.05	85	8
12	$PhCH(CH_3)CO_2H$	$Ph(CH_2)_3OH$	**20**	0.05	97	3
13	$PhCH(CH_3)CO_2H$	$PhCH(CH_3)OH$	**21**	0.05	95	3
14	Ph_2CHCO_2H	$Ph(CH_2)_3OH$	**22**	0.05	97	3
15	Ph_2CHCO_2H	$PhCH(CH_3)OH$	**23**	0.05	93	6
16	(*E*)-$PhCH=CHCO_2H$	$Ph(CH_2)_3OH$	**24**	0.05	70 (76)[c]	28 (23)[c]
17	(*E*)-$PhCH=CHCO_2H$	$PhCH(CH_3)OH$	**25**	0.05	60 (80)[c]	35 (14)[c]
18	$PhCO_2H$	$Ph(CH_2)_3OH$	**26**	0.10	26 (33)[c]	72 (62)[c]
19	*t*-$BuCO_2H$	$Ph(CH_2)_3OH$	**27**	0.10	10 (11)[c]	67 (57)[c]

a) Isolated yield. b) Not detected. c) The reaction was carried out at 0 °C.



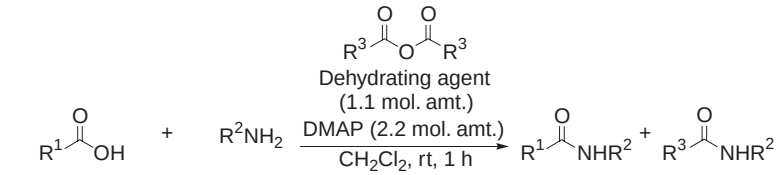
Scheme 2. Large-scale synthesis of 1-phenylethyl 2-phenylpropanecarboxylate with 3-PCA.

when the reactions were carried out at 0 °C (Entries 16 and 17). On the other hand, the reaction of benzoic acid with 3-phenylpropan-1-ol (**9**) gave the corresponding ester **26** (26%) along with a large amount of pyridine-3-carboxylate as a by-product (72%) (Entry 18). The reason of low yield may be due to the steric factor of the substrate, that is, there is not such a steric bulk difference between a phenyl ring and a pyridine ring in the mixed anhydride formed from 3-PCA and benzoic acid in situ. Further, when highly sterically hindered pivalic acid was used, corresponding ester **27** was afforded in low yield along with the undesirable by-product (67%) (Entry 19).

This method was also applicable to a gram-scale synthesis, from which ester **21** was obtained in 96% yield by using 3-PCA and a catalytic amount of DMAP (Scheme 2).[17] Importantly, the by-products, such as pyridine-3-carboxylic acid and 1-phenylethyl pyridine-3-carboxylate which were produced from 3-PCA and **29**, were easily removed by using an aqueous workup.[18]

Synthesis of Carboxamides from Nearly Molar Amounts of Carboxylic Acids and Amines Using 3-PCA. A condensation reaction for the synthesis of carboxamides from 3-phenylpropionic acid (**8**) and 3-phenylpropylamine (**30**) using various dehydrating agents in the presence of 2.2 molar amounts of DMAP at room temperature was tried to evaluate the potential ability of hetero aryl carboxylic anhydrides (Table 6). The reaction using 3-PCA proceeded smoothly within 1 h to provide the desired carboxamide **31**, 3-phenyl-*N*-(3-phenylpropyl)propanamide, in 91% yield along with 9% of *N*-(3-phenylpropyl)pyridine-3-carboxamide (Entry 1). In the case of using pyridine-4-carboxylic anhydride (**3**) the

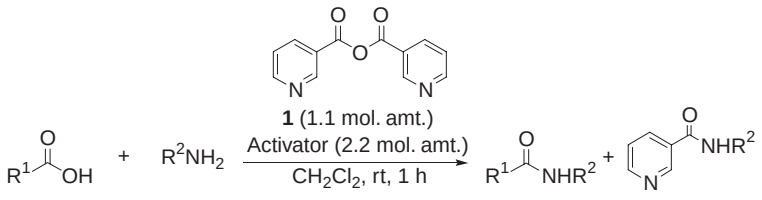
Table 6. Screening of Dehydrating Agents



Entry	R^3	Anhydride	Yield[a]/%	
			31	By-product
1		**1**	91	8
2		**2**	90	4
3		**3**	69	20
4		**4**	91	9
5		**5**	88	11
6		**6**	92	7
7		**7**	89	10

a) Isolated yield.

Table 7. Effect of Activators



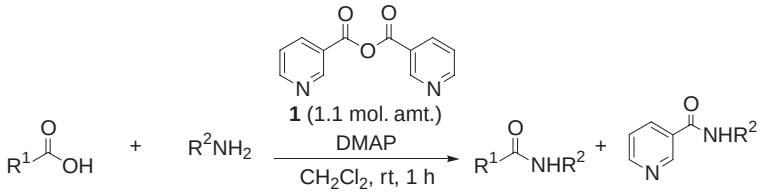
Entry	Activator	Yield[a]/%	
		31	By-product
1	DMAP	91	8
2	PPY[d]	78	3
3[b]	HOBt[d]	81	19
4	*N*-Methylimidazole	79	20
5	*N*-Butylimidazole	80	ND[c]
6	*N*-Methylmorpholine	67	32
7	none	9	91

a) Isolated yield. b) The reaction was carried out in the presence of *N*-methylmorpholine (2.2 equiv). c) Not detected. d) PPY = 4-(1-pyrrolidinyl)pyridine, HOBt = 1-hydroxybenzotriazole.

yield of **32** decreased to 69%, and the corresponding by-product was obtained in 20% yield (Entry 3). Pyridine-2-carboxylic anhydride (**2**) gave the desired product in 90% yield, but this reagent was liable to decomposition (Entry 2). Further, it was observed that other carboxylic anhydrides, such as furoic anhydrides **4** and **5** or thenoic anhydrides **6** and **7**, also provided the desired carboxamide in high yield (Entries 4–7). In regards to the reactivity and the ease of crystallization, 3-PCA (**1**) was chosen, as described in the section on esterification.

Next, the effect of the activators was further examined (Table 7). In the case of using 4-(1-pyrrolidinyl)pyridine (PPY) or 1-hydroxybenzotriazole (HOBt), these activators worked effectively to afford the desired carboxamides **31** in good yields (Entries 2 and 3). Imidazole derivatives, such as *N*-methylimidazole and *N*-butylimidazole, also gave good results (Entries 4 and 5), whereas the yield decreased to 67%

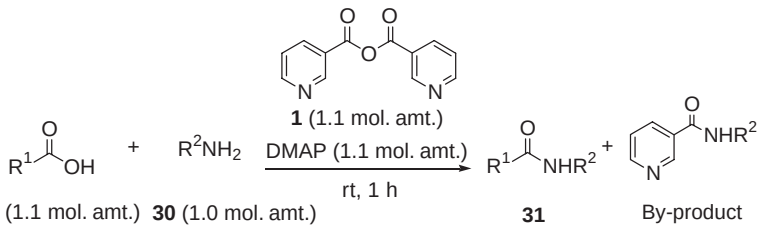
Table 8. Synthesis of Carboxamide Using DMAP as an Activator



Entry	DMAP/mol amt.	Yield[a]/%	
		31	By-product
1	3.3	75	8
2	2.2	91	8
3	1.1	92	8
4	0.55	84	15
5	0.05	79	20

a) Isolated yield.

Table 9. Effect of Solvents



Entry	Solvent	Yield[a]/%	
		31	By-product
1	CH_2Cl_2	92	8
2[b]	CH_2Cl_2	95	5
3[c]	CH_2Cl_2	97	3
4	THF	75	13
5	Et_2O	85	15
6	DMF	86	7
7	DMSO	88	10
8	Toluene	90	9
9	MeCN	92	8

a) Isolated yield. b) The reaction was carried out at 0 °C. c) The reaction was carried out at −78 °C.

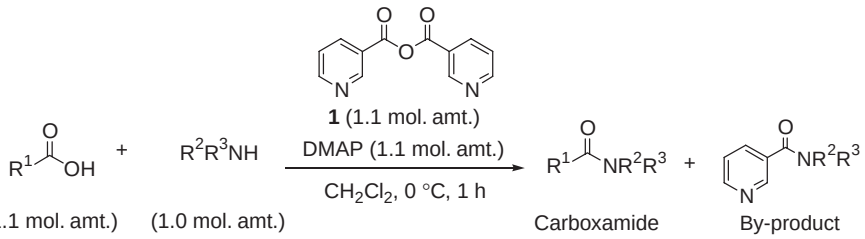
when *N*-methylmorpholine was used (Entry 6). In addition, the carboxamide was obtained in only 9%, and the remaining 91% was a by-product, *N*-(3-phenylpropyl)pyridine-3-carboxamide, in the absence of an activator (Entry 7). These results indicate the necessity of an effective activator in this reaction.

Next, the effect of DMAP was examined (Table 8). 3.3 molar amount of DMAP gave the desired product **31** in 75% yield and *N*-(3-phenylpropyl)pyridine-3-carboxamide 8% yield accompanied by a mixute of unknown compounds (Entry 1). In addition, the yield of carboxamide decreased to 79% when a catalytic amount of DMAP was used (Entry 5). On the other hand, it was observed that the desired product was obtained in high yield even when the amount of DMAP was reduced to 1.1 molar amount (Entries 1–3).

Finally, the effect of the solvents was examined (Table 9). Not only in a non-polar solvent, such as CH_2Cl_2 or toluene but also in a polar solvent such as THF, Et_2O, DMF, DMSO, or MeCN, the reaction was successfully carried out as similar to the section on esterification (Entries 1 and 4–9), and CH_2Cl_2 was found to be the best solvent, as shown in Entry 1. It is noteworthy that the reaction rapidly proceeded even at −78 °C, and the yield of desired carboxamide increased at lower temperatures (Entries 2 and 3).

The results obtained by using various carboxylic acids and amines under optimized conditions are summarized in Table 10. Even when nearly molar amounts of primary or secondary aliphatic amines were used, reactions of 3-phenylpropionic acid **8** with the respective amines proceeded smoothly to afford the corresponding carboxamides **31**–**36** in good to high yields (Entries 1–6). In the case of a tertiary amine, such

Table 10. Synthesis of Various Carboxamides with 3-PCA



Entry	Carboxylic acid	Amine	Carboxamide	Yield[a]/%	
				Carboxamide	By-product
1	$Ph(CH_2)_2CO_2H$	$Ph(CH_2)_3NH_2$	**31**	95	5
2	$Ph(CH_2)_2CO_2H$	$PhCH_2NHCH_3$	**32**	92	8
3	$Ph(CH_2)_2CO_2H$	$PhCH(NH_2)CH_3$	**33**	98	2
4	$Ph(CH_2)_2CO_2H$	$PhCH_2NH_2$	**34**	94	6
5	$Ph(CH_2)_2CO_2H$	Ph_2CHNH_2	**35**	97	2
6	$Ph(CH_2)_2CO_2H$	Piperidine	**36**	88	11
7	$Ph(CH_2)_2CO_2H$	*t*-$BuNH_2$	**37**	67	2
8	$Ph(CH_2)_2CO_2H$	$PhNH_2$	**38**	98	2
9[b]	$Ph(CH_2)_2CO_2H$	*o*-Cl-$C_6H_4NH_2$	**39**	85	2
10[c]	$Ph(CH_2)_2CO_2H$	$PhNH_2 \cdot HCl$	**38**	97	2
11[d]	$Ph(CH_2)_2CO_2H$	$EtNH_2 \cdot HCl$	**40**	95	3
12[e]	$Ph(CH_2)_2CO_2H$	$CH_3ONHCH_3 \cdot HCl$	**41**	98	2
13	*c*-$C_6H_{11}CO_2H$	$Ph(CH_2)_3NH_2$	**42**	90	10
14	*c*-$C_6H_{11}CO_2H$	$PhCH(NH_2)CH_3$	**43**	90	10
15	$PhCH(CH_3)CO_2H$	$Ph(CH_2)_3NH_2$	**44**	92	8
16	$PhCH(CH_3)CO_2H$	$PhCH(NH_2)CH_3$	**45**	98	2
17	Ph_2CHCO_2H	$Ph(CH_2)_3NH_2$	**46**	94	5
18	Ph_2CHCO_2H	$PhCH(NH_2)CH_3$	**47**	98	2
19	(*E*)-PhCH=$CHCO_2H$	$Ph(CH_2)_3NH_2$	**48**	85 (93)[f]	15 (6)[f]
20	(*E*)-PhCH=$CHCO_2H$	$PhCH(NH_2)CH_3$	**49**	80 (91)[f]	16 (8)[f]
21	$PhCO_2H$	$Ph(CH_2)_3NH_2$	**50**	43 (55)[f]	57 (44)[f]
22	$PhCO_2H$	$PhNH_2$	**51**	35 (50)[f]	56 (35)[f]
23	*t*-$BuCO_2H$	$Ph(CH_2)_3NH_2$	—	trace (trace)[f]	ND[g] (ND)[f,g]

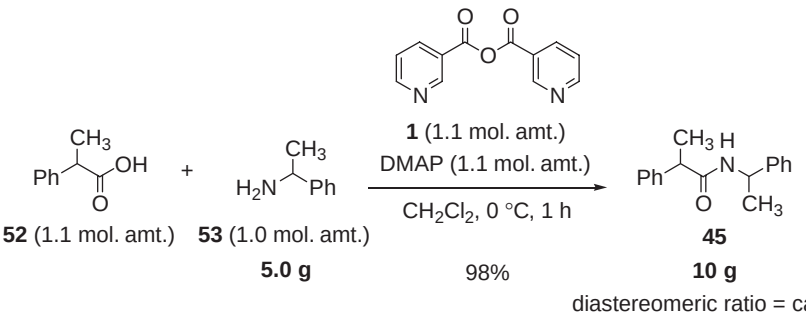
a) Isolated yield. b) The reaction was carried out for 24 h. c) The reaction was carried out for 12 h. d) The reaction was carried out for 6 h. e) The reaction was carried out for 3 h. f) The reaction was carried out at −78 °C. g) Not detected.

as *t*-butyl amine, the corresponding carboxamide was obtained in moderate yield (Entry 7). Aromatic amines including sterically hindered *o*-chloroaniline were successfully employed, and the corresponding carboxamides **38** and **39** were obtained in good to excellent yields (Entries 8 and 9). Importantly, this method was applicable to the reaction with amine hydrochloride, from which the desired carboxamides **38** and **40** were obtained in high yields (Entries 10 and 11). Further, *N*,*O*-dimethylhydroxylamine hydrochloride was also effectively converted to carboxamide **41**, as shown in Entry 12. This result indicates that the present procedure is a convenient method for the direct synthesis of *N*-methoxy-*N*-methylamides (Weinreb amides[19]) from free carboxylic acid under mild conditions. It was then confirmed that carboxamides **42–49** were also obtained in good yields in the cases of using hindered α,α-disubstituted and α,β-unsaturated carboxylic acids (Entries 13–20). In addition, the yields of carboxamides **48** and **49** increased when the reactions were carried out at −78 °C (Entries 19 and 20). On the other hand, the reaction with benzoic acid resulted in a low yield similar to that of the esterification reaction, and the reactions with pivalic acid also gave poor results (Entries 21–23).

The present protocol with 3-PCA was successfully employed for a gram-scale synthesis, and **45** was obtained in 98% yield (Scheme 3).[17] It is noteworthy that DMAP and by-products, such as pyridine-3-carboxylic acid and *N*-(1-phenylethyl)pyridine-3-carboxamide produced from 3-PCA and **53**, were easily removed by using an aqueous workup.[18]

Conclusion

A convenient and effective method for the synthesis of various carboxylic esters or carboxamides was successfully established. The reaction of various carboxylic acids and nucleophiles, such as alcohols or amines, with 3-PCA (**1**) and DMAP gave the corresponding products in good to high yields by using the simple experimental procedure. In addition, it is noted that the by-products produced in situ were easily removed by using an aqueous workup. Thus, pyridine-3-carboxylic anhydride is one of the most efficient and convenient reagents for the condensation reaction. Further study on the application and improvement of the present dehydrating reagent is now in progress.



Scheme 3. Large-scale synthesis of 2-phenyl-*N*-(1-phenylethyl)propanamide with 3-PCA.

Experimental

General. All melting points were determined on a Yanagimoto micro melting apparatus (Yanaco MP-S3) and are uncorrected. Infrared (IR) spectra were recorded by using an attenuated total reflection (ATR) method on a SensIR Technologies Travel *IR*™ spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM EX270L (270 MHz) or a Varian Mercury Plus 400 (400 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; brs, broad singlet. ^{13}C NMR spectra were recorded on a JEOL EX270L (68 MHz) or a Varian Mercury Plus 400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane, with the solvent resonance as the internal standard ($CDCl_3$; δ 77.0, acetone-d_6; δ 30.3). High-resolution mass spectra (HRMS) were recorded on a JMS-700V (JEOL) or Q-Tof-2-(micromass) mass spectrometer. Elemental analyses were conducted using a Yanaco MT-5 CHN corder. Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF254, 0.25 mm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Dry solvents were purchased from Kanto Chemical. All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Kokusan Chemical, or Aldrich Chemical. Carboxylic acids were used without further purification. Alcohols and amines were used after purification by distillation.

Experimental Procedure for the Preparation of 3-PCA (1). A solution of pyridine-3-carboxylic acid (1.00 g, 8.12 mmol) and diisopropylethylamine (1.41 mL, 8.12 mol) in THF (18 mL) was stirred for 10 min at 0 °C. To the reaction mixture, a solution of triphosgene (402 mg, 1.35 mmol) in THF (2 mL) was added at 0 °C, then stirred for 1 h. After addition of the solution, the reaction mixture was additionally stirred for 1 h at room temperature. After filtration of the reaction mixture to remove diisopropylethylammonium chloride formed, the filtrate was concentrated under reduced pressure. After EtOAc was added to the residue, the mixture was washed with water. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate. The solvent was evaporated to afford pyridine-3-carboxylic anhydride (898 mg, 97%).

Pyridine-3-carboxylic Anhydride (3-PCA, 1): White solid; mp 121–123 °C; IR (ATR) 1797, 1723 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 9.34 (dd, J = 0.8, 1.8 Hz, 2H), 8.92 (dd, J = 1.8, 4.8 Hz, 2H), 8.55 (ddd, J = 1.8, 1.8, 8.0 Hz, 2H), 7.66 (ddd, J = 0.8, 4.8, 8.0 Hz, 2H). ^{13}C NMR (100 MHz, acetone-d_6) δ 161.2, 155.3, 151.6, 138.1, 125.0, 124.2. Anal. Calcd for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28%. Found: C, 62.94; H, 3.49; N, 12.21%.

Pyridine-2-carboxylic Anhydride (2): Brown oil; IR (ATR) 1782, 1736 cm^{-1}; ^{1}H NMR (270 MHz, acetone-d_6) δ 8.80–8.50 (m, 2H), 8.40–8.20 (m, 2H), 8.20–7.90 (m, 2H), 7.75–7.50 (m, 2H). ^{13}C NMR (68 MHz, acetone-d_6) δ 206.0, 163.0, 150.2, 146.7, 138.3, 128.7, 126.7. HRMS (EI positive) Calcd for $C_{12}H_8N_2O_3$ M^+: 228.0535. Found: m/z 228.0530.

Pyridine-4-carboxylic Anhydride (3): White solid; mp 102–104 °C; IR (ATR) 1799, 1735 cm^{-1}; ^{1}H NMR (270 MHz, acetone-d_6) δ 8.93 (dd, J = 1.6, 4.6 Hz, 4H), 8.09 (dd, J = 1.6, 4.6 Hz, 4H). ^{13}C NMR (68 MHz, acetone-d_6) δ 205.8, 161.2, 151.8, 136.2, 123.8. Anal. Calcd for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28%. Found: C, 63.00; H, 3.64; N, 12.09%.

Furan-2-carboxylic Anhydride (4): White solid; mp 62–64 °C; IR (ATR) 1780, 1733 cm^{-1}; ^{1}H NMR (270 MHz, acetone-d_6) δ 8.03 (dd, J = 0.8, 1.6 Hz, 2H), 7.63 (dd, J = 0.8, 3.8 Hz, 2H), 6.79 (dd, J = 1.6, 3.8 Hz, 2H). ^{13}C NMR (68 MHz, acetone-d_6) δ 206.2, 153.4, 150.2, 143.4, 122.7, 113.5. Anal. Calcd for $C_{10}H_6O_5$: C, 58.26; H, 2.93%. Found: C, 58.12; H, 2.98%.

Furan-3-carboxylic Anhydride (5): White solid; mp 56–58 °C; IR (ATR) 1771, 1719 cm^{-1}; ^{1}H NMR (270 MHz, acetone-d_6) δ 8.65–8.45 (m, 2H), 7.77 (t, J = 1.6 Hz, 2H), 6.92 (dd, J = 0.5, 1.6 Hz, 2H). ^{13}C NMR (68 MHz, acetone-d_6) δ 206.3, 158.2, 151.1, 145.9, 119.0, 110.2. Anal. Calcd for $C_{10}H_6O_5$: C, 58.26; H, 2.93%. Found: C, 58.05; H, 3.02%.

Thiophene-2-carboxylic Anhydride (6): Brown solid; mp 57–59 °C; IR (ATR) 1757, 1700 cm^{-1}; ^{1}H NMR (270 MHz, acetone-d_6) δ 8.15–7.95 (m, 4H), 7.31 (dd, J = 3.8, 4.9 Hz, 2H). ^{13}C NMR (68 MHz, acetone-d_6) δ 205.9, 157.2, 136.9, 136.8, 132.2, 129.4. Anal. Calcd for $C_{10}H_6O_3S_2$: C, 50.41; H, 2.54%. Found: C, 50.51; H, 2.49%.

Thiophene-3-carboxylic Anhydride (7): Brown solid; mp 50–52 °C; IR (ATR) 1765, 1707 cm^{-1}; ^{1}H NMR (270 MHz, acetone-d_6) δ 8.57 (m, 2H), 7.70–7.55 (m, 4H). ^{13}C NMR (68 MHz, acetone-d_6) δ 206.1, 158.0, 136.9, 132.5, 128.4, 128.4. Anal. Calcd for $C_{10}H_6O_3S_2$: C, 50.41; H, 2.54%. Found: C, 50.51; H, 2.55%.

Preparation of Carboxylic Esters. To a stirred solution of 3-phenylpropionic acid (49.6 mg, 0.33 mmol) in CH_2Cl_2 (1.5 mL) were successively added pyridine-3-carboxylic anhydride (75.4 mg, 0.30 mmol) and DMAP (0.7 mg, 0.006 mmol) at room temperature. After stirring for 10 min, a solution of 3-phenylpropan-1-ol (40.9 mg, 0.30 mmol) in dichloromethane (1.5 mL) was added. After the reaction mixture was stirred for 1 h, it was quenched with saturated aqueous sodium hydrogen carbonate. The mixture was extracted with *tert*-butyl methyl ether. The organic layer was washed with 1 mol dm^{-3} hydrochloric acid (3 times), brine and dried over anhydrous Na_2SO_4, and the solvent was evaporated. The crude product was purified by preparative TLC (hexane/EtOAc = 9/1) to afford 3-phenylpropyl 3-phenylpropanoate (77.3 mg, 96%) as a colorless oil.

3-Phenylpropyl 3-Phenylpropanoate (10):[7c] Colorless oil; IR (ATR) 1731 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.36–7.15 (m, 10H), 4.12 (t, $J = 6.5$ Hz, 2H), 2.99 (t, $J = 7.9$ Hz, 2H), 2.67 (t, $J = 7.9$ Hz, 4H), 1.96 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.7, 141.0, 140.3, 128.4, 128.3, 128.2, 128.1, 126.1, 125.8, 63.8, 35.9, 32.2, 31.0, 30.2.

Benzyl 3-Phenylpropanoate (11):[7c] Colorless oil; IR (ATR) 1732 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.31–7.11 (m, 10H), 5.08 (s, 2H), 2.94 (t, $J = 7.7$ Hz, 2H), 2.65 (t, $J = 7.7$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.4, 140.2, 135.7, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 126.1, 66.1, 35.8, 30.9.

Allyl 3-Phenylpropanoate (12):[7c] Colorless oil; IR (ATR) 1734 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.05 (m, 5H), 5.87 (m, 1H), 5.45–5.10 (m, 2H), 4.56 (d, $J = 5.6$ Hz, 2H), 2.95 (t, $J = 7.8$ Hz, 2H), 2.65 (t, $J = 7.8$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.2, 140.2, 132.0, 128.3, 128.1, 126.1, 118.0, 65.0, 35.8, 30.9.

1-Phenylethyl 3-Phenylpropanoate (13): Colorless oil; IR (ATR) 1730 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.34–7.10 (m, 10H), 5.92–5.82 (m, 1H), 2.92 (t, $J = 7.7$ Hz, 2H), 2.62 (t, $J = 7.7$ Hz, 2H), 1.47 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 141.4, 140.2, 128.3, 128.2, 128.1, 127.6, 126.0, 125.8, 72.2, 36.1, 30.9, 22.1. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13%. Found: C, 80.27; H, 7.09%.

1-Methyl-3-phenylpropyl 3-Phenylpropanoate (14):[7c] Colorless oil; IR (ATR) 1727 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.35–7.00 (m, 10H), 4.93 (m, 1H), 2.93 (t, $J = 7.6$ Hz, 2H), 2.58 (t, $J = 7.6$ Hz, 2H), 2.70–2.40 (m, 2H), 2.00–1.60 (m, 2H), 1.19 (d, $J = 6.3$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.2, 141.3, 140.3, 128.3, 128.2, 128.1, 126.0, 125.7, 70.4, 37.5, 36.1, 31.7, 31.0, 20.0.

Cyclohexyl 3-Phenylpropanoate (15):[7c] Colorless oil; IR (ATR) 1727 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.35–7.05 (m, 5H), 4.74 (m, 1H), 2.92 (t, $J = 7.8$ Hz, 2H), 2.58 (t, $J = 7.8$ Hz, 2H), 1.85–1.05 (m, 10H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.9, 140.3, 128.1, 128.0, 128.0, 125.9, 72.4, 36.1, 31.5, 31.0, 25.3, 23.6.

Phenyl 3-Phenylpropanoate (16):[10b] Colorless oil; IR (ATR) 1755 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–6.94 (m, 10H), 3.03 (t, $J = 7.4$ Hz, 2H), 2.84 (t, $J = 7.4$ Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.0, 150.4, 139.9, 129.2, 128.4, 128.2, 126.2, 125.6, 121.3, 35.9, 30.9.

5-(Tetrahydropyranyloxy)pentyl 3-Phenylpropanoate (17):[7c] Colorless oil; IR (ATR) 1732 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.40–7.10 (m, 5H), 4.65–4.50 (m, 1H), 4.07 (t, $J = 6.5$ Hz, 2H), 3.95–3.80 (m, 1H), 3.80–3.65 (m, 1H), 3.60–3.45 (m, 1H), 3.45–3.30 (m, 1H), 2.94 (t, $J = 7.6$ Hz, 2H), 2.62 (t, $J = 7.6$ Hz, 2H), 2.00–1.25 (m, 12H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.7, 140.3, 128.2, 128.0, 126.0, 98.7, 67.2, 64.3, 62.2, 35.8, 30.9, 30.7, 29.3, 28.4, 25.4, 22.7, 19.6.

3-Phenylpropyl Cyclohexanecarboxylate (18):[7c] Colorless oil; IR (ATR) 1728 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.40–7.10 (m, 5H), 4.07 (t, $J = 6.4$ Hz, 2H), 2.68 (t, $J = 7.3$ Hz, 2H), 1.94 (m, 1H), 2.10–1.80 (m, 4H), 1.80–1.40 (m, 2H), 1.55–1.10 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 175.9, 141.1, 128.2, 125.8, 63.3, 43.2, 32.2, 30.3, 29.1, 25.8, 25.5.

1-Phenylethyl Cyclohexanecarboxylate (19): Colorless oil; IR (ATR) 1729 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.35–7.15 (m, 5H), 5.87 (q, $J = 6.6$ Hz, 1H), 2.31 (m, 1H), 1.90 (m, 2H), 1.72 (m, 2H), 1.51 (d, $J = 6.6$ Hz, 3H), 1.60–1.10 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 175.0, 141.9, 128.3, 127.5, 125.8, 71.7, 43.3, 29.0, 29.0, 25.8, 25.5, 25.5, 22.4. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%. Found: C, 77.23; H, 8.28%.

3-Phenylpropyl 2-Phenylpropanoate (20):[10b] Colorless oil; IR (ATR) 1730 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.12 (m, 8H), 7.04 (m, 2H), 4.05 (t, $J = 6.4$ Hz, 2H), 3.72 (q, $J = 6.9$ Hz, 1H), 2.54 (t, $J = 7.2$ Hz, 2H), 1.87 (t, $J = 7.2$ Hz, 2H), 1.50 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 174.3, 140.9, 140.5, 128.5, 128.2, 128.2, 127.4, 127.0, 125.8, 63.8, 45.6, 32.0, 30.2, 18.4.

1-(*RS*)-Phenylethyl 2-(*RS*)-Phenylpropanoate (21):[17] Colorless oil; IR (ATR) 1730 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.35–7.00 (m, 10H), 5.84 (q, $J = 6.6$ Hz, 1H), 3.74 (q, $J = 7.2$ Hz, 1H), 1.49 (d, $J = 7.2$ Hz, 3H), 1.48 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 173.3, 141.5, 141.4, 140.2, 128.3, 128.1, 127.4, 126.9, 125.5, 72.4, 45.7, 22.4, 18.4. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13%. Found: C, 80.35; H, 7.11%.

1-(*RS*)-Phenylethyl 2-(*SR*)-Phenylpropanoate (21):[17] White solid; mp 88–91 °C; IR (ATR) 1723 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.35–7.05 (m, 10H), 5.85 (q, $J = 6.6$ Hz, 1H), 3.73 (q, $J = 7.2$ Hz, 1H), 1.47 (d, $J = 7.2$ Hz, 3H), 1.40 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 173.4, 141.4, 141.4, 140.3, 128.4, 128.3, 127.6, 127.3, 125.8, 72.5, 45.6, 22.0, 18.4. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13%. Found: C, 80.21; H, 6.76%.

3-Phenylpropyl Diphenylacetate (22): Colorless oil; IR (ATR) 1731 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.00 (m, 15H), 5.03 (s, 1H), 4.14 (t, $J = 6.5$ Hz, 2H), 2.56 (t, $J = 7.3$ Hz, 2H), 1.92 (dt, $J = 6.5$, 7.3 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.2, 140.8, 138.5, 128.5, 128.4, 128.2, 127.1, 125.8, 64.3, 57.2, 32.0, 30.2. Anal. Calcd for $C_{23}H_{22}O_2$: C, 83.60; H, 6.71%. Found: C, 83.47; H, 6.64%.

1-Phenyethyl Diphenylacetate (23): Colorless oil; IR (ATR) 1731 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.35–7.10 (m, 15H), 5.94 (q, $J = 6.5$ Hz, 1H), 5.05 (s, 1H), 1.50 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.4, 141.1, 138.6, 138.4, 128.5, 128.4, 128.3, 128.2, 127.7, 127.1, 127.0, 125.9, 73.1, 57.2, 22.1. Anal. Calcd for $C_{22}H_{20}O_2$: C, 83.51; H, 6.37%. Found: C, 83.40; H, 6.49%.

3-Phenylpropyl (*E*)-3-Phenyl-2-propenoate (24):[7c] Colorless oil; IR (ATR) 1708 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.67 (d, $J = 16.0$ Hz, 1H), 7.60–7.45 (m, 2H), 7.45–7.10 (m, 8H), 6.44 (d, $J = 16.0$ Hz, 1H), 4.21 (t, $J = 6.6$ Hz, 2H), 2.73 (t, $J = 7.6$ Hz, 2H), 2.02 (tt, $J = 6.6$, 7.6 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 166.7, 144.5, 141.0, 134.2, 130.1, 128.7, 128.2, 128.2, 127.9, 125.8, 117.9, 63.8, 32.2, 30.3.

1-Phenylethyl (*E*)-3-Phenyl-2-propenoate (25): Colorless oil; IR (ATR) 1706 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.70 (d, $J = 16.0$ Hz, 1H), 7.60–7.45 (m, 2H), 7.45–7.20 (m, 8H), 6.47 (d, $J = 16.0$ Hz, 1H), 6.02 (q, $J = 6.6$ Hz, 1H), 1.61 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 166.0, 144.7, 141.6, 134.2, 130.1, 128.7, 128.4, 127.9, 127.7, 126.0, 118.2, 72.4, 22.3. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39%. Found: C, 80.54, H, 6.32%.

3-Phenylpropyl Benzoate (26):[7c] Colorless oil; IR (ATR) 1715 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.25–7.90 (m, 2H), 7.80–7.12 (m, 8H), 4.32 (t, $J = 6.5$ Hz, 2H), 2.77 (t, $J = 8.1$ Hz, 2H), 2.08 (tt, $J = 6.5$, 8.1 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 166.3, 141.0, 132.7, 130.2, 129.4, 128.4, 128.3, 128.2, 128.1, 125.8, 64.2, 32.3, 30.3.

3-Phenylpropyl 2,2-Dimethylpropanoate (27):[7c] Colorless oil; IR (ATR) 1727 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.14 (m, 5H), 4.07 (t, $J = 6.5$ Hz, 2H), 2.69 (t, $J = 8.1$ Hz, 2H), 1.95 (tt, $J = 6.5$, 8.1 Hz, 2H), 1.21 (s, 9H); ^{13}C NMR (68 MHz,

$CDCl_3$) δ 178.3, 141.1, 128.3, 128.3, 125.9, 63.5, 38.8, 32.2, 30.4, 27.3.

Typical Experimental Procedure for the Preparation of Carboxamides. To a stirred solution of 3-phenylpropionic acid (49.6 mg, 0.33 mmol) in CH_2Cl_2 (1.5 mL) were successively added pyridine-3-carboxylic anhydride (75.4 mg) and DMAP (40.4 mg) at 0 °C. After stirring for 10 min, a solution of 3-phenylpropylamine (40.6 mg, 0.30 mmol) in dichloromethane (1.5 mL) was added. After the reaction mixture was stirred for 1 h, it was quenched with saturated aqueous sodium hydrogencarbonate. The mixture was extracted with EtOAc. The organic layer was washed with 1 mol dm^{-3} hydrochloric acid (3 times), brine and dried over anhydrous Na_2SO_4, and the solvent was evaporated. The crude product was purified by preparative TLC (hexane/EtOAc = 1/9) to afford 3-phenyl-*N*-(3-phenylpropyl)propanamide (75.9 mg, 95%) as a white solid.

3-Phenyl-*N*-(3-phenylpropyl)propanamide (31):[7d] White solid; mp 54–56 °C; IR (ATR) 3305, 1627, 1538 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.35–6.85 (m, 10H), 6.57 (dr, 1H), 3.17 (dt, J = 6.4, 7.1 Hz, 2H), 2.88 (t, J = 7.6 Hz, 2H), 2.49 (t, J = 7.6 Hz, 2H), 2.41 (t, J = 7.6 Hz, 2H), 1.70 (tt, J = 7.1, 7.6 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.9, 141.0, 140.3, 128.3, 128.0, 127.9, 127.9, 127.8, 125.8, 125.7, 125.5, 38.8, 37.9, 32.9, 31.5, 30.8.

***N*-Benzyl-*N*-methyl-3-phenylpropanamide (32):**[7d] Mixture of two conformational isomers A and B. Colorless oil; IR (ATR) 1641 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.50–7.01 (m, 10H, A + B), 4.57 (s, 2aH, A), 4.40 (s, 2bH, B), 3.30–2.94 (m, 2H, A + B), 2.92 (s, 3bH, B), 2.78 (s, 3aH, A), 2.70–2.59 (m, 2H, A + B); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.0 (B), 171.7 (A), 140.9, 140.9, 136.9, 136.1, 128.5, 128.1, 128.1, 128.0, 127.6, 127.1, 126.9, 125.8, 125.7, 125.7, 52.9 (B), 50.5 (A), 35.1 (A), 34.7 (B), 34.5 (A), 33.7 (B), 31.3 (B), 31.1 (A).

3-Phenyl-*N*-(1-phenylethyl)propanamide (33):[7d] White solid; mp 52–54 °C; IR (ATR) 3307, 1636, 1534 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.70–7.35 (m, 10H), 6.51 (m, 1H), 5.03 (q, J = 7.2 Hz, 1H), 2.87 (t, J = 7.6 Hz, 2H), 2.40 (t, J = 7.6 Hz, 2H), 1.29 (d, J = 7.2 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.0, 143.0, 140.5, 128.2, 128.1, 128.0, 126.7, 125.8, 125.8, 48.3, 38.0, 31.6, 21.6.

***N*-Benzyl-3-phenylpropanamide (34):**[7d] White solid; mp 81–83 °C; IR (ATR) 3290, 1638, 1542 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.35–6.95 (m, 10H), 6.52 (brs, 1H), 4.25 (d, J = 5.8 Hz, 2H), 2.88 (t, J = 7.7 Hz, 2H), 2.42 (t, J = 7.7 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.9, 140.5, 138.0, 128.2, 128.2, 128.1, 127.2, 126.9, 125.9, 43.2, 38.0, 31.6.

***N*-(Diphenylmethyl)-3-phenylpropanamide (35):**[7d] White solid; mp 147–149 °C; IR (ATR) 3307, 1644, 1534 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.50–7.20 (m, 9H), 7.25–7.00 (m, 6H), 6.94 (d, J = 8.1 Hz, 1H), 6.21 (d, J = 8.1 Hz, 1H), 2.90 (t, J = 7.4 Hz, 2H), 2.47 (t, J = 7.4 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.0, 141.2, 140.4, 128.2, 128.1, 127.2, 126.9, 125.9, 56.5, 37.9, 31.5.

1-(3-Phenylpropanoyl)piperidine (36):[7d] Colorless oil; IR (ATR) 1635 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.55–7.10 (m, 5H), 3.54 (t, J = 5.4 Hz, 2H), 3.31 (t, J = 5.4 Hz, 2H), 2.96 (t, J = 7.6 Hz, 2H), 2.60 (t, J = 7.6 Hz, 2H), 1.90–1.35 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 169.9, 141.1, 128.1, 128.1, 125.7, 46.4, 42.5, 35.0, 31.4, 26.2, 25.4, 24.3.

***N*-(1,1-Dimethylethyl)-3-phenylpropanamide (37):**[20] White solid; mp 81–83 °C; IR (ATR) 3283, 1640, 1552 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.38–7.14 (m, 5H), 5.20 (brs, 1H), 2.93 (t, J = 7.3 Hz, 2H), 2.37 (t, J = 7.3 Hz, 2H), 1.28 (s, 9H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.1, 140.8, 128.2, 125.9, 50.9, 39.3, 31.8, 28.7.

***N*-Phenyl-3-phenylpropanamide (38):**[7d] White solid; mp 96–98 °C; IR (ATR) 3324, 1654, 1525 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.66 (brs, 1H), 7.54 (d, J = 7.6 Hz, 2H), 7.50–7.45 (m, 8H), 3.00 (t, J = 7.6 Hz, 2H), 2.65 (t, J = 7.6 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.1, 140.3, 137.7, 128.5, 128.2, 128.1, 128.0, 125.9, 124.0, 120.2, 38.7, 31.5.

***N*-(2-Chlorophenyl)-3-phenylpropanamide (39):**[21] White solid; mp 110–112 °C; IR (ATR) 3274, 1655, 1526 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.33 (d, J = 7.9 Hz, 1H), 7.57 (brs, 1H), 7.45–7.10 (m, 7H), 6.99 (t, J = 7.6 Hz, 1H), 3.05 (t, J = 7.6 Hz, 2H), 2.72 (t, J = 7.6 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.1, 140.1, 134.3, 128.8, 128.5, 128.2, 127.5, 126.2, 124.4, 122.5, 121.6, 39.4, 31.3.

***N*-Ethyl-3-phenylpropanamide (40):**[11] White solid; mp 52–54 °C; IR (ATR) 3292, 1629, 1549 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.50–7.00 (m, 5H), 6.19 (brs, 1H), 3.20 (t, J = 6.5 Hz, 2H), 2.93 (t, J = 7.6 Hz, 2H), 2.44 (t, J = 7.6 Hz, 2H), 1.05 (t, J = 6.5 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.8, 140.6, 128.1, 128.0, 125.8, 38.2, 34.2, 31.7, 14.6.

***N*-Methoxy-*N*-methyl-3-phenylpropanamide (41):** Colorless oil; IR (ATR) 2937, 1658 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.35–7.10 (m, 5H), 3.58 (s, 3H), 3.16 (s, 3H), 2.96 (t, J = 8.4 Hz, 2H), 2.73 (t, J = 8.4 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 141.0, 128.2, 128.2, 125.8, 61.0, 33.7, 30.6. Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25%. Found: C, 68.33; H, 7.49; N, 6.95%.

***N*-(3-Phenylpropyl)cyclohexanecarboxamide (42):**[11] White solid; mp 81–83 °C; IR (ATR) 3295, 1639, 1549 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.35–7.05 (m, 5H), 6.15 (brs, 1H), 3.24 (dt, J = 6.4, 6.6 Hz, 2H), 2.61 (t, J = 7.6 Hz, 2H), 2.05 (m, 1H), 1.95–1.55 (m, 6H), 1.50–1.05 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 175.9, 141.3, 128.1, 128.0, 125.6, 45.3, 38.8, 33.2, 31.2, 29.6, 25.6. Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71%. Found: C, 78.31; H, 9.38; N, 5.71%.

***N*-(1-Phenylethyl)cyclohexanecarboxamide (43):** White solid; mp 113–115 °C; IR (ATR) 3328, 1636, 1528 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40–7.15 (m, 5H), 6.05 (brs, 1H), 5.11 (q, J = 7.1 Hz, 1H), 2.08 (m, 1H), 1.90–1.55 (m, 4H), 1.45 (d, J = 7.1 Hz, 3H), 1.55–1.10 (m, 6H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 174.9, 143.3, 128.3, 126.9, 125.9, 48.1, 45.4, 29.6, 29.5, 25.7, 25.7, 21.8. Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.16; N, 6.05%. Found: C, 77.89; H, 9.22; N, 6.03%.

2-Phenyl-*N*-(3-phenylpropyl)propanamide (44):[7d] White solid; mp 91–93 °C; IR (ATR) 3240, 1640, 1560 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.40–7.10 (m, 8H), 7.10–6.95 (m, 2H), 5.84 (brs, 1H), 3.52 (q, J = 7.1 Hz, 1H), 3.17 (dt, J = 6.4, 6.6 Hz, 2H), 2.49 (t, J = 7.6 Hz, 2H), 1.70 (tt, J = 7.1, 7.6 Hz, 2H), 1.48 (d, J = 7.1 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 173.8, 141.3, 141.1, 128.5, 128.1, 128.0, 127.3, 126.9, 125.6, 46.8, 39.0, 33.0, 31.0, 18.4.

(2*RS*)-2-Phenyl-*N*-((1*RS*)-1-phenylethyl)propanamide (45):[7d] White solid; mp 116–118 °C; IR (ATR) 3244, 1639, 1543 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.45–7.00 (m, 10H), 5.76 (m, 1H), 5.08 (q, J = 6.9 Hz, 1H), 3.57 (q, J = 7.1 Hz, 1H), 1.49 (d, J = 7.1 Hz, 3H), 1.37 (d, J = 6.9 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 172.9, 143.1, 141.2, 128.7, 128.3, 127.4, 127.0, 126.9, 125.6, 48.6, 47.0, 21.9, 18.5. Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53%. Found: C, 80.51; H, 7.61; N, 5.43%.

(2*RS*)-2-Phenyl-*N*-((1*SR*)-1-phenylethyl)propanamide (45):[7d]

White solid; mp 116–118 °C; IR (ATR) 3244, 1639, 1543 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.10 (m, 10H), 5.82 (m, 1H), 5.07 (q, $J = 6.5$ Hz, 1H), 3.53 (q, $J = 7.0$ Hz, 1H), 1.49 (d, $J = 7.0$ Hz, 3H), 1.33 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 173.0, 143.0, 141.3, 128.7, 128.4, 127.4, 127.0, 127.0, 125.8, 48.6, 46.9, 21.6, 18.6. Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53%. Found: C, 80.27; H, 7.55; N, 5.42%.

***N*-(3-Phenylpropyl)diphenylacetamide (46):** White solid; IR (ATR) 3287, 1636, 1539 cm^{-1}; mp 139–141 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 7.45–7.00 (m, 15H), 5.72 (m, 1H), 4.89 (s, 1H), 3.27 (dt, $J = 6.2$, 7.0 Hz, 2H), 2.55 (t, $J = 7.3$ Hz, 2H), 1.78 (tt, $J = 7.0$, 7.3 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 171.6, 141.1, 139.3, 128.7, 128.6, 128.3, 128.2, 127.1, 125.8, 59.1, 39.4, 33.2, 31.1. Anal. Calcd for $C_{23}H_{23}NO$: C, 83.85; H, 7.04; N, 4.25%. Found: C, 83.43; H, 7.06; N, 4.15%.

***N*-(1-Phenylethyl)diphenylacetamide (47):** White solid; IR (ATR) 3270, 1637, 1545 cm^{-1}; mp 119–121 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 7.40–7.05 (m, 15H), 6.14 (m, 1H), 5.13 (q, $J = 7.0$ Hz, 1H), 4.89 (s, 1H), 1.37 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 170.7, 142.9, 139.3, 139.3, 128.7, 128.7, 128.5, 128.4, 127.0, 127.0, 127.0, 125.8, 58.8, 48.9, 21.8. HRMS (ESI positive) Calcd for $C_{22}H_{22}NO$ M^+: 316.1701. Found: m/z 316.1703.

(*E*)-3-Phenyl-*N*-(3-phenylpropyl)-2-propenamide (48): White solid; mp 115–118 °C; IR (ATR) 3244, 1639, 1543 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.62 (d, $J = 15.7$ Hz, 1H), 7.50–7.30 (m, 2H), 7.30–7.05 (m, 8H), 7.01 (m, 1H), 6.57 (d, $J = 15.7$ Hz, 1H), 3.39 (dt, $J = 6.4$, 6.6 Hz, 2H), 2.62 (t, $J = 7.6$ Hz, 2H), 1.87 (tt, $J = 7.2$, 7.6 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 166.0, 141.1, 140.2, 134.6, 129.2, 128.5, 128.1, 128.1, 127.4, 125.6, 121.0, 39.3, 33.2, 31.1. Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28%. Found: C, 81.53; H, 7.30; N, 5.25%.

(*E*)-3-Phenyl-*N*-(1-phenylethyl)-2-propenamide (49): White solid; mp 136–138 °C; IR (ATR) 3305, 1615, 1550 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.61 (d, $J = 15.7$ Hz, 1H), 7.50–7.05 (m, 11H), 6.59 (d, $J = 15.7$ Hz, 1H), 5.23 (q, $J = 6.9$ Hz, 1H), 1.48 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 165.1, 143.1, 140.6, 134.6, 129.2, 128.5, 128.3, 127.5, 126.9, 126.0, 120.9, 48.8, 21.8. Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57%. Found: C, 81.07; H, 7.06; N, 5.52%.

***N*-(3-Phenylpropyl)benzamide (50):**[11] White solid; mp 40–42 °C; IR (ATR) 3309, 1634, 1536 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.00–7.65 (m, 2H), 7.60–7.50 (m, 9H), 3.44 (dt, $J = 6.5$, 7.1 Hz, 2H), 2.66 (t, $J = 7.6$ Hz, 2H), 1.95 (tt, $J = 7.1$, 7.6 Hz, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 167.4, 141.2, 134.3, 130.9, 128.1, 128.1, 128.0, 126.7, 125.6, 39.7, 33.3, 30.9.

***N*-Phenylbenzamide (51):** White solid; mp 166–167 °C; IR (ATR) 3343, 1654, 1598 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 8.20–7.76 (m, 3H), 7.75–7.30 (m, 7H), 7.25–7.10 (m, 1H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 165.6, 137.8, 134.9, 131.7, 129.0, 128.7, 126.9, 124.5, 120.1. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10%. Found: C, 78.99; H, 5.62; N, 6.86%.

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