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Effective esterification of carboxylic acids using (6-oxo-6*H*-pyridazin-1-yl)phosphoric acid diethyl ester as novel coupling agents

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Abstract—(6-Oxo-6*H*-pyridazin-1-yl)phosphoric acid diethyl esters (**3**) are efficient and selective coupling agents for equimolar esterification of carboxylic acids and alcohols. Esterification of aliphatic and aromatic carboxylic acids with aliphatic and aromatic alcohols using **3** afforded the corresponding esters chemoselectively in good to excellent yield.

1. Introduction

Effective esterification of carboxylic acids with alcohols is the most fundamental reaction in organic synthesis.[1] It has long been known that the process of esterification is enormously accelerated by the addition of strong acid such as sulfuric acid. There are also many methods of esterification that use specific dehydrating reagents.[2] However, the classical esterifications have some disadvantages of the corrosiveness of strong acid, with accompanying side reactions such as carbonization and oxidation. Although many reagents for esterification of carboxylic acid have been developed,[2–5] the research in this field is still very active even now.[6] For direct esterification of carboxylic acid in the absence of strong acid, carboxylic acid must be activated to more reactive species by using an activator.

In our previous paper,[3,5] we have reported on the synthesis of anhydrides and esters using 4,5-dichloro-2-[(4-nitrobenzensulfonyl)]pyridazin-3(2*H*)-one as an activator. Because this esterification proceeds via the corresponding anhydrides as the intermediate,[5] 2 equiv of carboxylic acids are required in this reaction. Therefore, we attempted to develop more effective coupling agents that contain pyridazinone derivatives for high-yielding esterifications with equimolar reactions of carboxylic acids and alcohols. Pyridazin-3(2*H*)-one is a stable and good leaving group, and shows an electron withdrawing ability.[3,5,7–9] Also various organophosphorus compounds have been developed as carboxylic acid activators.[10] Therefore, we designed and synthesized some (6-oxo-6*H*-pyridazin-1-yl)phosphoric acid diethyl esters as carboxylic acid activator. In this paper, we report on effective and convenient esterification of carboxylic acids with alcohols by using (6-oxo-6*H*-pyridazin-1-yl)phosphoric acid diethyl esters in one port.

2. Results and discussion

Some 4,5-disubstituted-pyridazin-3(2*H*)-ones were readily prepared by the reported methods.[11] From preliminary experiments (Table 1, entries 1–5),[12] we selected triethylamine and acetonitrile as a suitable base/solvent system for the synthesis of **3**.

The reaction of 4,5-disubstituted-pyridazin-3(2*H*)-ones (**1**) with diethyl chlorophosphate (**2**) in the presence of triethylamine in acetonitrile at room temperature afforded the corresponding **3a**–**3e** in excellent yields (Table 1, entries 1 and 6–9) (Scheme 1).

Initially, direct esterification of 4-nitrobenzoic acid (**4a**) with methanol (**5a**) using **3a** was studied in a variety of

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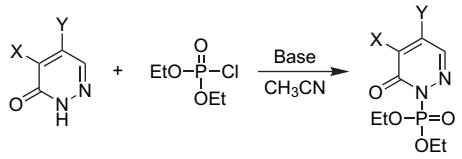
Table 1. Synthesis of diethyl 6-oxo-6*H*-pyridazin-1-ylphosphonate **3**[a]



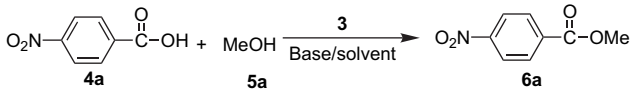
1 **2** **3**

Entry	1			Base	Time (h)	Yield[b] (%)
		X	Y			
1	**a**	Cl	Cl	Et_3N	1	**3a** (96)
2	**a**	Cl	Cl	DMAP[c]	28	**3a** (65)
3	**a**	Cl	Cl	NaH	26	**3a** (58)
4	**a**	Cl	Cl	K_2CO_3	10	**3a** (89)
5	**a**	Cl	Cl	Cs_2CO_3	18	**3a** (78)
6	**b**	Cl	OMe	Et_3N	6	**3b** (89)
7	**c**	Cl	N_3	Et_3N	4	**3c** (86)
8	**d**	Cl	OPh	Et_3N	8	**3d** (88)
9	**e**	Br	Br	Et_3N	19	**3e** (79)

[a] Reaction was carried out at room temperature.
[b] Isolated yield.
[c] DMAP=*N*,*N*-dimethylaminopyridine.

representative organic solvents and bases (Table 2, entries 1–10). Exclusive esterification in excellent yields was obtained in triethylamine/THF (or toluene, acetone, acetonitrile, diethyl ether, and ethyl acetate),[13] potassium carbonate/ethyl acetate (or THF), and *N*,*N*-dimethylaminopyridine/THF (or ethyl acetate). Among these systems, we selected the potassium carbonate/ethyl acetate system for direct esterification of carboxylic acid using **3a**. The efficacy of **3b**–**3e** for esterification was evaluated using the reaction of 4-nitrobenzoic acid (**4a**) with methanol (**5a**) in the presence of

Table 2. Esterification of compound **4a** with methanol (**5a**) using **3** at reflux temperature



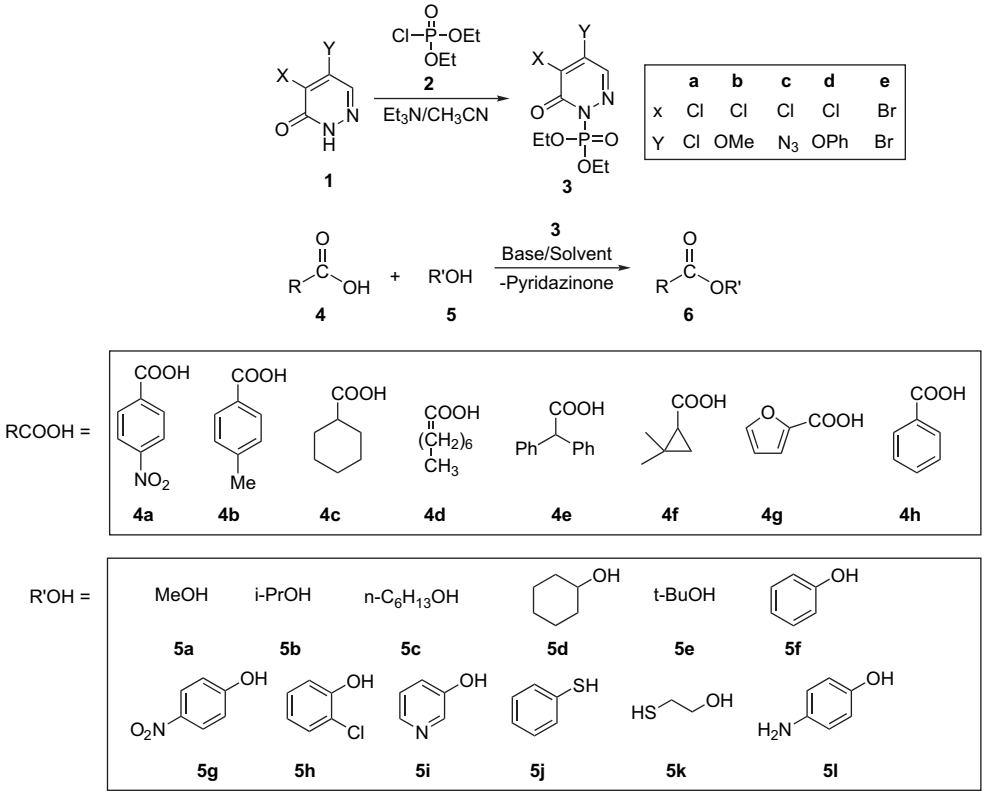
4a **5a** **6a**

Entry	3	Base	Solvent	Time (h)	**6a** Yield[a] (%)
1	**3a**	Et_3N	THF	0.5	95
2	**3a**	Et_3N	EtOAc	0.5	97
3	**3a**	Et_3N	H_2O	20	9[d]
4	**3a**	K_2CO_3	THF	0.3	98
5	**3a**	K_2CO_3	EtOAc	0.5	99
6	**3a**	K_2CO_3	H_2O	6	17[d]
7	**3a**	DMAP[b]	THF	2	98
8	**3a**	DMAP[b]	EtOAc	2	95
9	**3a**	DMAP[b]	H_2O	42	11[d]
10	**3a**	Resin[c]	THF	43	17
11	**3a**	Resin[c]	EtOAc	20	66
12	**3a**	Resin[c]	H_2O	50	11[d]
13	**3b**	K_2CO_3	EtOAc	1	97
14	**3c**	K_2CO_3	EtOAc	0.5	98
15	**3d**	K_2CO_3	EtOAc	0.8	96
16	**3e**	K_2CO_3	EtOAc	0.5	89

[a] Isolated yield. 4,5-Dichloropyridazin-3(2*H*)-one was isolated quantitatively.
[b] DMAP=*N*,*N*-dimethylaminopyridine.
[c] Resin is Amberite-IRA66.
[d] Compound **3** was decomposed.

potassium carbonate in ethyl acetate at reflux temperature (Table 2, entries 13–16).

Compounds **3a**–**3d** showed similar efficacy for esterification under this condition. Therefore, we selected compound **3a** as a novel coupling agent for the esterification of carboxylic acid because **1b**–**1d** were prepared by the conversion of



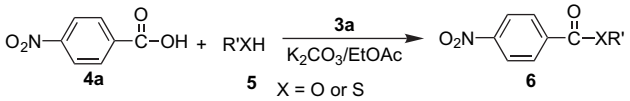
Scheme 1.

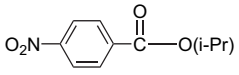
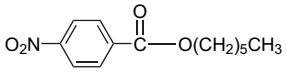
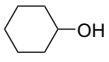
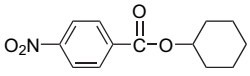
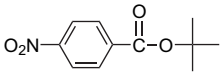
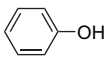
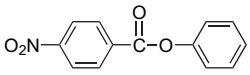
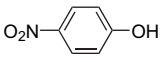
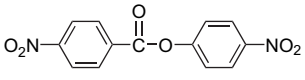
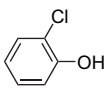
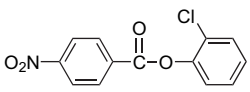
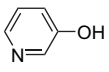
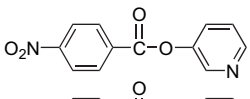
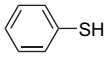
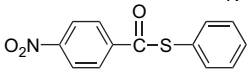
1a. Esterification of 4-nitrobenzoic acid (**4a**) with various aliphatic and aromatic alcohols **5b**–**5i** using **3a** in the presence of potassium carbonate in refluxing ethyl acetate afforded the corresponding esters **6b**–**6i** except for **6e** in good to excellent yields (Table 3, entries 1–8).

The reaction of 4-nitrobenzoic acid (**4a**) with benzenethiol (**5j**) under the same condition also afforded the corresponding thioester **6j** in excellent yields, whereas reaction of 4-nitrobenzoic acid (**4a**) with *tert*-butyl alcohol (**5e**) under the same condition obtained 4-nitrobenzoic anhydride instead of the corresponding ester **6e** in 21% yield (Table 3, entry 4). This result may be attributed to the steric hindrance of *tert*-butanol. Treatment of aliphatic or aromatic carboxylic acids **4b**–**4g** with various alcohols **5a**, **5c**, **5f**, and **5i** in the presence of potassium carbonate in refluxing ethyl acetate easily afforded the corresponding ester **6k**–**6ag** in good to excellent yields (Table 4).

Selective esterification of primary alcohol in mixed alcohol such as 1°/2° alcohol and 1°/3° alcohol is also often required. Therefore we examined the selective esterification of a mixture of two alcohols such as 1°/2° alcohols, 1°/3° alcohols, 2°/3° alcohols, aromatic/aliphatic alcohols, or bifunctional alcohols such as 2-mercaptoethanol (**5k**) and 4-aminophenol (**5l**). The esterification of octanoic acid (**4d**) with a mixture of 1°/2° alcohols or 1°/3° alcohols afforded primary alkyl ester **6t** selectively (Table 5, entries 1 and 3). But we found the corresponding anhydrides as the main products in the competition reaction of 2°/3° alcohols with octanoic acid (**4d**) and benzoic acid (**4h**) (Table 5, entries 5 and 6). This selectivity may be due to the steric hindrance of the carbonyl carbon of acyl phosphate and alcohols (2° or 3°). In the reaction of carboxylic acids with 2° or 3° alcohol under our reaction condition, the formation of anhydride may be more favorable than esterification. Esterification of octanoic acid (**4d**) with a mixture of cyclohexanol (**5d**)/phenol (**5f**) afforded phenyl ester **6u** selectively in good yield (Table 5, entry 7). We investigated the chemoselectivity in the esterification of a mixture of phenol (**5f**)/benzenethiol (**5j**) and bifunctional alcohols such as 2-mercaptoethanol (**5k**) and 4-aminophenol (**5l**). The esterification of a mixture of phenol (**5f**)/benzenethiol (**5j**) with octanoic acid (**4d**) afforded the corresponding ester **6u** chemoselectively as the main product instead of the thioester. Also diphenyldisulfide was obtained as the side product (Table 5, entry 11). The reaction of 2-mercaptoethanol (**5k**) with octanoic acid (**4d**) under the same condition also afforded the thioester **6ak** selectively in 86% yield (Table 5, entry 13). However, the reaction of 4-aminophenol (**5l**) with octanoic acid (**4d**) under the same condition yielded the corresponding amide **6am** chemoselectively in 99% yield (Table 5, entry 15).

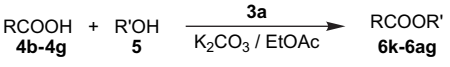
Table 3. Esterification of compound **4a** with alcohols **5** using **3a** at reflux temperature

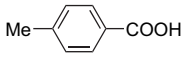
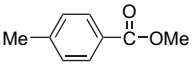
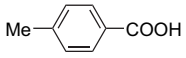
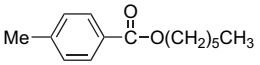
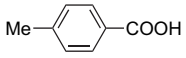
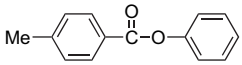
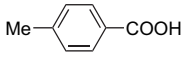
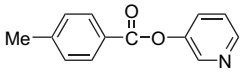
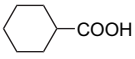
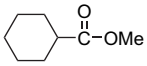
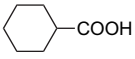
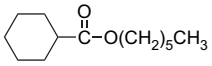
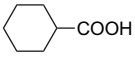
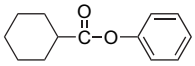
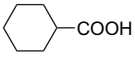
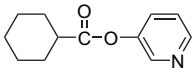
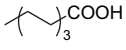
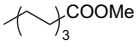
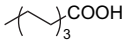
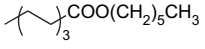
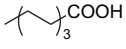
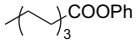
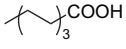
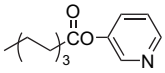
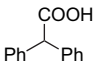
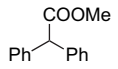
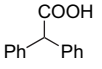
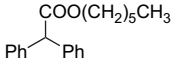
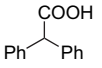
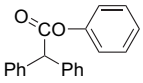
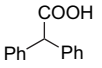


Entry		5	Time (h)	Product **6**	Yield[a] (%)
1	**5b**	*i*-PrOH	1.5		**6b** (86)
2	**5c**	$CH_3(CH_2)_5OH$	2		**6c** (80)
3	**5d**		5.5		**6d** (77)
4	**5e**		3		**6e** (—)[b]
5	**5f**		2		**6f** (98)
6	**5g**		0.5		**6g** (99)
7	**5h**		0.5		**6h** (99)
8	**5i**		0.5		**6i** (97)
9	**5j**		1		**6j** (98)

[a] Isolated yield. 4,5-Dichloropyridazin-3(2*H*)-one was isolated quantitatively.
[b] 4-Nitrobenzoic anhydride instead of **6e** was obtained in 21% yield.

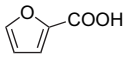
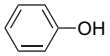
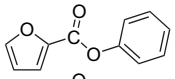
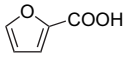
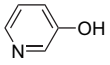
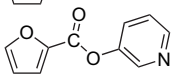
Table 4. Esterification of some carboxylic acids **4b**–**4g** with **5a**, **5c**, **5f**, and **5i** using **3a** in the presence of potassium carbonate in refluxing ethyl acetate



Entry	4		5		Time (h)	Product **6**	Yield[a] (%)
1	**4b**		**5a**	MeOH	2		**6k** (95)
2	**4b**		**5c**	$CH_3(CH_2)_5OH$	9		**6l** (71)
3	**4b**		**5f**		3.5		**6m** (86)
4	**4b**		**5i**		4		**6n** (89)
5	**4c**		**5a**	MeOH	1		**6o** (81)
6	**4c**		**5c**	$CH_3(CH_2)_5OH$	4		**6p** (83)
7	**4c**		**5f**		0.5		**6q** (80)
8	**4c**		**5i**		0.5		**6r** (96)
9	**4d**		**5a**	MeOH	1.3		**6s** (91)
10	**4d**		**5c**	$CH_3(CH_2)_5OH$	5		**6t** (76)
11	**4d**		**5f**		3		**6u** (95)
12	**4d**		**5i**		1.5		**6v** (94)
13	**4e**		**5a**	MeOH	0.5		**6w** (92)
14	**4e**		**5c**	$CH_3(CH_2)_5OH$	0.5		**6x** (93)
15	**4e**		**5f**		2		**6y** (87)
16	**4e**		**5i**		0.5		**6z** (95)
17	**4f**		**5c**	$CH_3(CH_2)_5OH$	9		**6aa** (70)
18	**4f**		**5f**		1		**6ab** (86)
19	**4f**		**5i**		0.5		**6ac** (97)
20	**4g**		**5a**	MeOH	1.5		**6ad** (92)
21	**4g**		**5c**	$CH_3(CH_2)_5OH$	1		**6ae** (77)

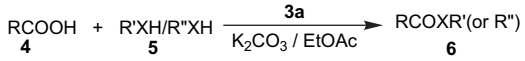
(*continued*)

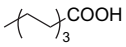
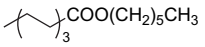
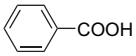
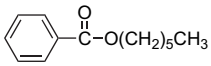
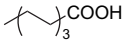
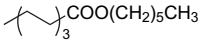
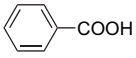
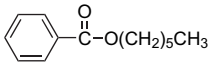
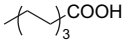
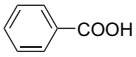
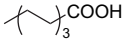
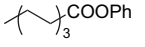
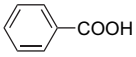
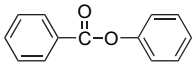
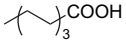
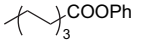
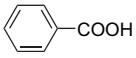
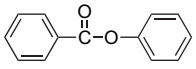
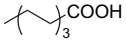
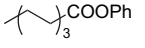
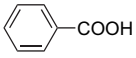
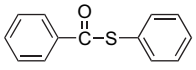
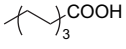
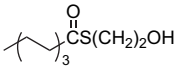
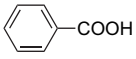
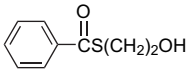
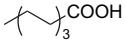
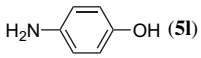
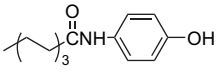
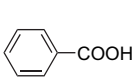
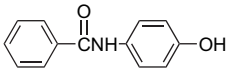
Table 4. (*continued*)

Entry		4		5	Time (h)	Product **6**	Yield[a] (%)
22	**4g**		**5f**		3		**6af** (95)
23	**4g**		**5i**		2.5		**6ag** (95)

[a] Isolated yield. 4,5-Dichloropyridazin-3(2*H*)-one was isolated quantitatively.

Table 5. Competition reaction of octanoic acid (**4d**) or benzoic acid (**4h**) with mixed alcohols at room temperature



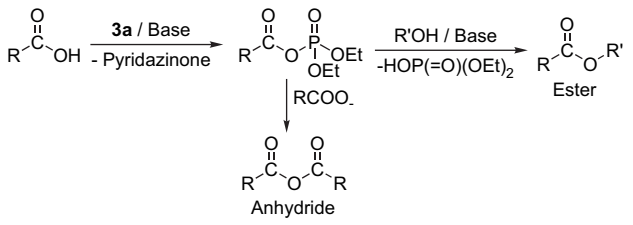
Entry		4	R′XH/R″XH (**5**)	Time (h)	Product **6**	Yield[a] (%)
1	**4d**		$CH_3(CH_2)_5OH$ (**5c**)/*i*-PrOH(**5b**)	1		**6t** (87)
2	**4h**			5[b]		**6ah** (90)
3	**4d**		$CH_3(CH_2)_5OH$ (**5c**)/*t*-BuOH(**5e**)	0.3		**6t** (82)
4	**4h**			11		**6ah** (22)[c]
5	**4d**		*i*-PrOH(**5b**)/*t*-BuOH(**5e**)	3.5	—	—[d]
6	**4h**			3.5	—	—[c]
7	**4d**		c-$C_6H_{11}OH$(**5d**)/C_6H_5OH(**5f**)	2		**6u** (80)
8	**4h**			2		**6ai** (86)
9	**4d**		$CH_3(CH_2)_5OH$(**5c**)/C_6H_5OH(**5f**)	0.5		**6u** (88)
10	**4h**			4		**6ai** (82)
11	**4d**		C_6H_5OH (**5f**)/C_6H_5SH (**5j**)	6		**6u** (71)[e]
12	**4h**			3.5		**6aj** (50)[e]
13	**4d**		$HSCH_2CH_2OH$ (**5k**)	1.5		**6ak** (86)
14	**4h**			4		**6al** (93)
15	**4d**		 (**5l**)	1.5		**6am** (99)
16	**4h**			2.5[f]		**6an** (92)

[a] Isolated yield. 4,5-Dichloropyridazin-3(2*H*)-one was isolated quantitatively.
[b] Reaction temperature=at reflux temperature.
[c] Benzoic anhydride was obtained in 54% yield.
[d] Octanoic anhydride was obtained in 75% yield.
[e] Diphenyldisulfide was also obtained.
[f] The solvent was THF.

The reaction of benzoic acid (**4h**) with a mixture of 1°/2° alcohols afforded primary alkyl ester **6ah** in excellent selectivity and in high yield (Table 5, entry 2). The esterification of benzoic acid (**4h**) with a mixture of 1°/3° alcohols afforded primary alkyl ester **6ah** (22%) and benzoic anhydride (54%) (Table 5, entry 4). The reaction of a mixture of 2°/3° alcohols with benzoic acid (**4h**) isolated only benzoic anhydride instead of the corresponding ester (Table 5, entry 6). Aromatic alcohols were selectively esterified with benzoic acid (**4h**) in the competition reaction of aliphatic/aromatic alcohol under our condition (Table 5, entries 8 and 10). The esterification of a mixture of phenol (**5f**)/benzenethiol (**5i**) with benzoic acid (**4h**) using **3a** afforded the corresponding thioester **6aj** (50%) chemoselectively and diphenyldisulfide (Table 5, entry 12). The reaction of 2-mercaptoethanol (**5k**) with benzoic acid (**4h**) using **3a** under same condition also afforded selectively thioester **6al** in 93% yield (Table 5, entry 14). The structure of **6al** was established by IR, NMR, and elemental analysis. However, the reaction of 4-aminophenol (**5l**) with benzoic acid (**4h**) using **3a** under the same condition yielded the corresponding amide **6an** chemoselectively in 92% yield (Table 5, entry 16).

In the esterification of octanoic acid (**4d**) or benzoic acid (**4h**), the different selectivity of cyclohexanol (**5d**) and phenol (**5f**) may be attributed to the steric hindrance and/or the difference of pK_a for two alcohols. Also, the different chemoselectivity for esterification of octanoic acid (**4d**) or benzoic acid (**4h**) with phenol (**5f**) or benzenethiol (**5j**) may be due to the different nucleophilicity of two nucleophiles (**5f** and **5j**) and/or the different electrophilicity of the carbonyl carbons for aliphatic and aromatic carboxylic acids.

In all the reactions described above, reusable 4,5-dichloropyridazin-3(2*H*)-one (**1a**) was also isolated quantitatively. On the other hand, acid anhydride was not detected during these reactions when monitored with TLC except for the use of 2° and 3° alcohols. Actually, only 1 equiv of carboxylic acid was required for the esterification under these reaction conditions. This esterification mechanism is different from that of the esterification of carboxylic acid with alcohol by using 4,5-dichloro-2-[(4-nitrobenzenesulfonyl)]pyridazin-3(2*H*)-one.[6] The esterification of carboxylic acid using compound **3** may be proceeded via two steps, the formation of acyl phosphate in the first step and then alcohol reacts with acyl phosphate to give the ester in the second step. Therefore, diethyl 6-oxo-6*H*-pyridazin-1-ylphosphonate is a more effective coupling agent than 4,5-dichloro-2-[(4-nitrobenzenesulfonyl)]pyridazin-3(2*H*)-one[6] for equimolar esterification of carboxylic acids and alcohols. The structures of all the products were established by IR, NMR, and elemental analyses (Scheme 2).



Scheme 2.

3. Conclusion

Compound **3a** is an efficient coupling agent for equimolar esterification of carboxylic acids with alcohols under the basic condition. It also has some advantages: (i) the reaction condition is basic, (ii) this method shows excellent selectivity for primary or secondary alcohols, (iii) the coupling agent is easily prepared from commercially available compound **1**, and (iv) compound **1** can be recovered quantitatively for reuse. We also believe that these coupling agents would be applicable particularly to solid-phase syntheses and amidation of carboxylic acid.

4. Experimental

4.1. General

Column chromatography was carried out on silica gel 60 (70–230 mesh). Melting points were determined with a Thomas–Hoover capillary apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz spectrophotometer with chemical shift values reported in δ units (part per million) relative to an internal standard (tetramethylsilane). IR spectra were obtained on a Hitachi 270-50 or Mattson Genesis Series FT-IR spectrophotometer. Elemental analyses were performed with CHNS-932 (Leco).

4.2. 4,5-Disubsituted-6-oxo-6*H*-pyridazin-1-ylphosphonates (3a–3e)

A solution of diethyl chlorophosphate (10.4 mmol) in solvent such as CH_2Cl_2, THF, CH_3CN, acetone, or toluene was added slowly to a solution of 4,5-disubsituted-pyridazin-3(2*H*)-ones[10] (9.4 mmol) in solvent such as CH_2Cl_2, THF, CH_3CN, acetone, or toluene in the presence of a base (10.4 mmol) at the appropriate temperature with stirring. The mixture was stirred at room temperature until compound **1** disappeared. After filtering the mixture, water (150 mL) was added to the filtrate. The product was extracted with methylene chloride (150 mL). The methylene chloride solution was dried over anhydrous magnesium sulfate. The resulting solution was evaporated under reduced pressure to give compound **3** as liquid.

4.2.1. Diethyl-4,5-dichloro-6-oxo-(6*H*)-pyridazin-1-ylphosphonate (3a). Liquid. R_f=0.33 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3020, 2970, 1700, 1610, 1560, 1460, 1430, 1400, 1380, 1310, 1180, 1150, 1120, 1050, 980, 940 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 9.04 (s, 1H), 4.52–4.42 (m, 4H), 1.48–1.43 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 157.6, 149.6, 138.3, 127.2, 65.9, 16.0. Elemental analysis calcd for $C_8H_{11}Cl_2N_2O_4P$: C, 31.92; H, 3.68; N, 9.30. Found: C, 31.93; H, 3.74; N, 9.33.

4.2.2. Diethyl-5-chloro-4-methoxy-6-oxo-(6*H*)-pyridazin-1-ylphosphonate (3b). Liquid. R_f=0.33 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3010, 2960, 2940, 1695, 1620, 1580, 1480, 1460, 1400, 1360, 1290, 1170, 1120, 1040, 980 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.91 (s, 1H), 4.50–4.40 (m, 4H), 4.15 (s, 3H), 1.44 (t, 6H, J=7.1 Hz). ^{13}C NMR ($CDCl_3$) δ: 157.8, 156.9, 137.3, 113.8, 65.5, 57.7,

16.0. Elemental analysis calcd for $C_9H_{14}ClN_2O_5P$: C, 36.44; H, 4.76; N, 9.44. Found: C, 36.46; H, 4.77; N, 9.52.

4.2.3. Diethyl-4-azido 5-chloro-6-oxo-(6*H*)-pyridazin-1-ylphosphonate (3c). Liquid. R_f=0.30 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3010, 2960, 2260, 1690, 1580, 1460, 1380, 1360, 1300, 1250, 1210, 1180, 1080, 1050, 1020, 860 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.90 (s, 1H), 4.96–4.40 (m, 4H), 1.46–1.41 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 157.7, 141.9, 141.1, 116.8, 65.8, 16.0. Elemental analysis calcd for $C_8H_{11}ClN_5O_4P$: C, 31.23; H, 3.60; N, 22.77. Found: C, 31.34; H, 3.69; N, 22.78.

4.2.4. Diethyl-5-chloro-4-phenoxy-6-oxo-(6*H*)-pyridazin-1-ylphosphonate (3d). Liquid. R_f=0.40 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3010, 1690, 1580, 1500, 1380, 1320, 1300, 1230, 1210, 1050, 980, 900, 820, 780 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.51 (s, 1H), 7.52–7.13 (m, 5H), 4.53–4.44 (m, 4H), 1.48–1.43 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 158.3, 155.3, 153.2, 140.3, 130.7, 126.6, 120.1, 115.5, 65.7, 16.1. Elemental analysis calcd for $C_{14}H_{16}ClN_2O_5P$: C, 46.88; H, 4.50; N, 7.81. Found: C, 46.91; H, 4.52; N, 7.84.

4.2.5. Diethyl-4,5-dibromo-6-oxo-(6*H*)-pyridazin-1-ylphosphonate (3e). Liquid. R_f=0.30 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3030, 2980, 2950, 1700, 1600, 1540, 1430, 1420, 1380, 1300, 1180, 1100, 1050, 970 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 9.04 (s, 1H), 4.52–4.42 (m, 4H), 1.47–1.42 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 158.5, 151.5, 132.4, 121.4, 65.9, 16.1. Elemental analysis calcd for $C_8H_{11}Br_2N_2O_4P$: C, 24.64; H, 2.84; N, 7.18. Found: C, 24.66; H, 2.95; N, 7.21.

4.3. Esterification of carboxylic acid derivatives with alcohol derivatives

A solution of carboxylic acid (4.1 mmol, 1 equiv), alcohol (4.5 mmol, 1.1 equiv), base (4.5 mmol, 1.1 equiv), coupling agent **3** (6.1 mmol, 1.5 equiv), and solvent (30 mL) was stirred at reflux temperature or at room temperature until carboxylic acid disappeared by TLC monitoring. After cooling to room temperature, the mixture was filtered. The solvent was evaporated under reduced pressure. The resulting residue was applied to the top of an open-bed silica gel column (2.5×10 cm). The column was eluted with methylene chloride. Fractions containing the ester were combined, and evaporated under reduced pressure to give the ester. And fractions containing pyridazinone derivative were combined, and evaporated under reduced pressure to give pyridazinone derivative.

4.3.1. Methyl 4-nitrobenzoate (6a). Mp 94–95 °C. R_f=0.58 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3120, 3080, 2950, 2850, 1720, 1610, 1530, 1440, 1350, 1310, 1280, 1100, 960, 880, 820, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.29 (d, 2H, *J*=9.0 Hz), 8.21 (d, 2H, *J*=9.0 Hz), 3.99 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 165.2, 150.6, 136.5, 130.7, 123.6, 52.9. Elemental analysis calcd for $C_8H_7NO_4$: C, 53.04; H, 3.89; N, 7.73. Found: C, 49.96; H, 3.97; N, 7.80.

4.3.2. Isopropyl 4-nitrobenzoate (6b). Mp 106–108 °C. R_f=0.67 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3110, 3070, 3050, 2990, 2940, 2870, 1710, 1610, 1520, 1460, 1340, 1290, 1090, 1000, 830, 710 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.28 (d, 2H, *J*=8.9 Hz), 8.20 (d, 2H, *J*=8.8 Hz), 5.29 (m, 1H), 1.41 (d, 6H, *J*=6.3 Hz). ^{13}C NMR ($CDCl_3$) δ: 164.2, 150.4, 136.3, 130.6, 123.4, 69.7, 21.9. Elemental analysis calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.49; H, 5.31; N, 6.72.

4.3.3. Hexyl 4-nitrobenzoate (6c). Liquid. R_f=0.71 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3140, 2950, 2890, 1730, 1610, 1540, 1470, 1360, 1320, 1280, 1110, 1020, 880, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.29 (d, 2H, *J*=9.0 Hz), 8.21 (d, 2H, *J*=9.0 Hz), 4.38 (t, 2H, *J*=6.7 Hz), 1.85–1.75 (m, 2H), 1.51–1.26 (m, 6H), 0.91 (t, 3H, *J*=7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 165.7, 151.4, 136.9, 131.6, 124.5, 67.1, 32.3, 29.5, 26.6, 23.5, 14.9. Elemental analysis calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.20; H, 6.89; N, 5.59.

4.3.4. Cyclohexyl 4-nitrobenzoate (6d). Liquid. R_f=0.73 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3150, 2970, 2900, 1730, 1610, 1530, 1460, 1410, 1360, 1340, 1290, 1180, 1110, 1020, 960, 890 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.28 (d, 2H, *J*=9.0 Hz), 8.21 (d, 2H, *J*=9.0 Hz), 5.11–5.03 (m, 1H), 2.00–1.95 (m, 2H), 1.83–1.75 (m, 2H), 1.68–1.57 (m, 3H), 1.53–1.33 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 164.0, 150.4, 136.4, 130.6, 123.4, 74.4, 31.5, 25.3, 23.6. Elemental analysis calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.67; H, 6.10; N, 5.67.

4.3.5. Phenyl 4-nitrobenzoate (6f). Mp 127–129 °C. R_f=0.75 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3130, 1750, 1610, 1530, 1490, 1360, 1320, 1280, 1190, 1080, 1020, 870, 850, 760, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.40–8.33 (m, 4H), 7.46 (t, 2H, *J*=8.1 Hz), 7.31 (t, 1H, *J*=7.4 Hz), 7.23 (d, 2H, *J*=7.5 Hz). ^{13}C NMR ($CDCl_3$) δ: 163.3, 150.9, 150.5, 135.0, 131.3, 129.7, 126.4, 123.7, 121.4. Elemental analysis calcd for $C_{13}H_9NO_4$: C, 64.20; H, 3.73; N, 5.76. Found: C, 64.23; H, 3.75; N, 5.78.

4.3.6. 4-Nitrophenyl 4-nitrobenzoate (6g). Mp 158–159 °C. R_f=0.77 (CH_2Cl_2). IR (KBr) 3150, 1760, 1600, 1560, 1540, 1500, 1360, 1340, 1270, 1220, 1080, 870, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.40 (s, 4H), 8.36 (d, 2H, *J*=9.1 Hz), 7.96 (d, 2H, *J*=9.1 Hz). ^{13}C NMR ($CDCl_3$) δ: 162.5, 155.1, 151.2, 145.8, 133.9, 131.5, 125.5, 123.9, 122.5. Elemental analysis calcd for $C_{13}H_8N_2O_6$: C, 54.18; H, 2.80; N, 9.72. Found: C, 54.22; H, 2.88; N, 9.81.

4.3.7. 2-Chlorophenyl 4-nitrobenzoate (6h). Mp 119–121 °C. R_f=0.77 (CH_2Cl_2). IR (KBr) 3130, 3100, 1760, 1620, 1540, 1490, 1370, 1290, 1270, 1220, 1090, 900, 860, 780, 730 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.45–8.37 (m, 4H), 7.53 (d, 1H, *J*=7.9 Hz), 7.39–7.28 (m, 4H). ^{13}C NMR ($CDCl_3$) δ: 162.5, 151.1, 146.8, 134.3, 131.5, 130.5, 128.0, 127.6, 126.8, 123.8, 123.6. Elemental analysis calcd for $C_{13}H_8ClNO_4$: C, 56.23; H, 2.90; N, 5.04. Found: C, 56.31; H, 2.97; N, 5.09.

4.3.8. Pyridin-3-yl 4-nitrobenzoate (6i). Mp 111–112 °C. R_f=0.24 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3120, 1740, 1620, 1600, 1560, 1520, 1480, 1420, 1340, 1320, 1260, 1200, 1060, 1000, 840, 700 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.61–8.58 (m, 2H), 8.39 (s, 4H), 7.66 (d, 1H, *J*=8.4 Hz), 7.46–7.41 (m, 1H). ^{13}C NMR ($CDCl_3$) δ:

162.9, 151.1, 147.5, 143.2, 137.2, 134.1, 131.4, 129.2, 124.1, 123.8. Elemental analysis calcd for $C_{12}H_8N_2O_4$: C, 59.02; H, 3.30; N, 11.47. Found: C, 59.05; H, 3.38; N, 11.49.

4.3.9. *S*-Phenyl 4-nitrobenzothioate (6j). Mp 155–157 °C. R_f=0.71 (CH_2Cl_2). IR (KBr) 3100, 3070, 1670, 1600, 1520, 1480, 1440, 1340, 1320, 1200, 1100, 920, 850, 750, 680 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.34 (d, 2H, J=8.8 Hz), 8.18 (d, 2H, J=8.8 Hz), 7.53–7.48 (m, 5H). ^{13}C NMR ($CDCl_3$) δ: 188.8, 150.7, 141.3, 134.9, 130.1, 129.5, 128.5, 125.2, 124.0. Elemental analysis calcd for $C_{13}H_9NO_3S$: C, 60.22; H, 3.50; N, 5.40. Found: C, 60.24; H, 3.53; N, 5.48.

4.3.10. 4-Nitrobenzoic anhydride. Mp 55–56 °C. R_f=0.84 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3150, 3000, 1730, 1620, 1540, 1360, 1280, 1110, 1030, 880, 810, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.12 (d, 2H, J=9.0 Hz), 8.12 (d, 2H, J=9.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 164.7, 150.5, 135.8, 130.6, 123.5. Elemental analysis calcd for $C_{15}H_{10}N_2O_6$: C, 57.33; H, 3.21; N, 8.91. Found: 57.37; H, 3.33; N, 8.96.

4.3.11. Methyl 4-methylbenzoate (6k). Liquid. R_f=0.77 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3030, 1740, 1620, 1450, 1290, 1190, 1120, 1030, 850, 760 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.91 (d, 2H, J=8.2 Hz), 7.20 (d, 2H, J=8.2 Hz), 3.87 (s, 3H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 167.1, 143.5, 129.6, 129.0, 127.4, 51.8, 21.5. Elemental analysis calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 72.03; H, 6.79.

4.3.12. Hexyl 4-methylbenzoate (6l). Liquid. R_f=0.81 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 2940, 2850, 1720, 1620, 1460, 1380, 1270, 1180, 1100, 1020, 760 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.93 (d, 2H, J=8.2 Hz), 7.21 (d, 2H, J=8.2 Hz), 4.29 (t, 2H, J=6.7 Hz), 2.39 (s, 3H), 1.79–1.70 (m, 2H), 1.36–1.30 (m, 6H), 0.92–0.87 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 166.7, 143.3, 129.5, 129.0, 127.8, 64.8, 31.5, 28.7, 25.7, 22.5, 21.6, 14.0. Elemental analysis calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.11; H, 8.36.

4.3.13. Phenyl 4-methylbenzoate (6m). Mp 75–76 °C. R_f=0.72 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3050, 2950, 1720, 1610, 1590, 1480, 1460, 1400, 1270, 1250, 1190, 1170, 1090, 1020, 840, 750 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.09 (d, 2H, J=8.2 Hz), 7.42 (t, 2H, J=8.1 Hz), 7.30 (d, 2H, J=8.3 Hz), 7.25–7.19 (m, 3H), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 165.3, 151.1, 144.1, 130.2, 129.5, 129.3, 126.9, 125.8, 121.8, 21.8. Elemental analysis calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.18; H, 5.82.

4.3.14. Pyridin-3-yl 4-methylbenzoate (6n). Mp 75–76 °C. R_f=0.45 (EtOAc/CH_2Cl_2=1:5, v/v). IR (KBr) 3120, 3050, 3000, 2930, 2850, 1740, 1650, 1610, 1580, 1470, 1430, 1280, 1210, 1180, 1140, 940 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.56 (d, 1H, J=2.1 Hz), 8.53 (d, 1H, J=4.2 Hz), 8.09 (d, 2H, J=8.2 Hz), 7.61 (d, 1H, J=8.3 Hz), 7.41–7.36 (m, 1H), 7.33 (d, 2H, J=8.0 Hz), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 164.8, 147.4, 146.9, 145.0, 143.6, 130.3, 129.4 (2), 126.0, 123.9, 21.8. Elemental analysis calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.25; H, 5.25; N, 6.64.

4.3.15. Methyl cyclohexanecarboxylate (6o). Liquid. R_f=0.73 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 2970, 2900, 1760, 1470, 1270, 1210, 1190, 1150, 1050 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.55 (s, 3H), 2.24–2.15 (m, 1H), 1.18–1.76 (m, 2H), 1.66–1.59 (m, 2H), 1.55–1.52 (m, 1H), 1.40–1.27 (m, 2H), 1.24–1.05 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 176.2, 51.2, 42.9, 28.9, 25.6, 25.3. Elemental analysis calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.59; H, 10.01.

4.3.16. Hexyl cyclohexanecarboxylate (6p). Liquid. R_f=0.85 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 2970, 2900, 1750, 1690, 1470, 1400, 1330, 1260, 1180, 1140, 1050 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 4.05 (t, 2H, J=6.7 Hz), 2.33–2.24 (m, 1H), 1.19–1.86 (m, 2H), 1.77–1.72 (m, 2H), 1.66–1.57 (m, 3H), 1.51–1.23 (m, 11H), 0.89 (t, 3H, J=6.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 166.7, 143.3, 129.5, 129.0, 127.8, 64.8, 31.5, 28.7, 25.7, 22.5, 21.6, 14.0. Elemental analysis calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.23; H, 10.60.

4.3.17. Phenyl cyclohexanecarboxylate (6q). Liquid. R_f=0.71 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3100, 2960, 2900, 1770, 1610, 1500, 1460, 1390, 1330, 1260, 1210, 1170, 1140, 1040, 950 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.30 (t, 2H, J=8.2 Hz), 7.14 (t, 1H, J=7.4 Hz), 7.03 (d, 2H, J=7.4 Hz), 2.56–2.46 (m, 1H), 2.05–2.00 (m, 2H), 1.80–1.75 (m, 2H), 1.66–1.50 (m, 3H), 1.38–1.21 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 176.1, 64.2, 43.2, 31.4, 29.0, 28.6, 25.7, 25.6, 25.4, 22.5, 13.4. Elemental analysis calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.50; H, 7.98.

4.3.18. Pyridin-3-yl cyclohexanecarboxylate (6r). Liquid. R_f=0.50 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3100, 2960, 2900, 1720, 1600, 1500, 1460, 1280, 1210, 1190, 1110, 1050, 810 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.43 (d, 1H, J=4.5 Hz), 8.40 (d, 1H, J=2.2 Hz), 7.44 (d, 1H, J=8.3 Hz), 7.30–7.26 (m, 1H), 2.62–2.52 (m, 1H), 2.07–2.02 (m, 2H), 1.83–1.78 (m, 2H), 1.69–1.51 (m, 3H), 1.42–1.23 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 173.7, 147.5, 146.5, 143.3, 129.1, 123.7, 42.9, 28.7, 25.6, 25.1. Elemental analysis calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.24; H, 7.41; N, 6.85.

4.3.19. Methyl octanoate (6s). Liquid. R_f=0.86 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 2960, 2890, 1760, 1470, 1450, 1380, 1210, 1180 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.66 (s, 3H), 2.31 (t, 2H, J=7.4 Hz), 1.62 (t, 2H, J=7.4 Hz), 1.33–1.29 (m, 8H), 0.88 (t, 3H, J=6.6 Hz). ^{13}C NMR ($CDCl_3$) δ: 174.1, 51.2, 34.0, 31.6, 29.0, 28.8, 24.9, 22.5, 13.9. Elemental analysis calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.33; H, 11.51.

4.3.20. Hexyl octanoate (6t). Liquid. R_f=0.82 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 2960, 2900, 1760, 1580, 1400, 1380, 1270, 1190, 1120 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 4.06 (t, 2H, J=6.7 Hz), 2.29 (t, 2H, J=7.6 Hz), 1.66–1.57 (m, 4H), 1.40–1.23 (m, 14H), 0.92–0.86 (m, 6H). ^{13}C NMR ($CDCl_3$) δ: 173.9, 64.3, 34.4, 31.6, 31.4, 29.1, 28.9, 28.6, 25.6, 25.0, 22.5, 22.4, 14.0, 13.0. Elemental analysis calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. Found: C, 74.33; H, 11.61.

4.3.21. Phenyl octanoate (6u). Liquid. R_f=0.66 (CH_2Cl_2). IR (KBr) 3090, 2950, 2880, 1770, 1600, 1500, 1470, 1380, 1300, 1200, 1140, 1100, 1030, 930 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.34 (t, 2H, J=7.4 Hz), 7.18 (t, 1H, J=7.4 Hz),

7.08–7.03 (m, 2H), 2.52 (t, 2H, J=7.4 Hz), 1.78–1.69 (m, 2H), 1.42–1.30 (m, 8H), 0.89 (t, 3H, J=6.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 172.2, 150.9, 129.4, 124.7, 121.6, 34.4, 31.7, 29.1, 29.0, 25.0, 22.7, 14.1. Elemental analysis calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.36; H, 9.23.

4.3.22. Pyridin-3-yl octanoate (6v). Liquid. R_f=0.43 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3060, 2950, 2880, 1780, 1740, 1600, 1490, 1440, 1400, 1290, 1220, 1140, 1120, 1040 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.44 (d, 1H, J=4.7 Hz), 8.40 (d, 1H, J=2.6 Hz), 7.47–7.42 (m, 1H), 7.31–7.26 (m, 1H), 2.56 (t, 2H, J=7.4 Hz), 1.78–1.68 (m, 2H), 1.40–1.24 (m, 8H), 0.87 (t, 3H, J=7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 171.7, 147.4, 146.7, 143.4, 129.2, 123.8, 34.2, 31.6, 29.0, 28.8, 24.8, 22.5, 14.0. Elemental analysis calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.59; H, 8.67; N, 6.37.

4.3.23. Methyl 2,2-diphenylacetate (6w). Mp 58–59 °C. R_f=0.63 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3070, 3040, 2950, 1730, 1600, 1500, 1460, 1430, 1340, 1320, 1280, 1190, 1150, 1000, 840, 800 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.31–7.12 (m, 10H), 5.03 (s, 1H), 3.72 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 173.0, 138.7, 128.6, 127.6, 127.3, 57.1, 52.3. Elemental analysis calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.67; H, 6.25.

4.3.24. Hexyl 2,2-diphenylacetate (6x). Liquid. R_f=0.70 (CH_2Cl_2). IR (KBr) 3090, 3050, 2950, 2890, 1740, 1610, 1500, 1460, 1400, 1320, 1290, 1240, 1200, 1160, 1010, 760 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.32–7.19 (m, 10H), 5.01 (s, 1H), 4.13 (t, 2H, J=6.7 Hz), 1.61–1.54 (m, 2H), 1.30–1.20 (m, 6H), 0.85 (t, 3H, J=7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 172.6, 138.9, 128.7, 128.6, 127.3, 65.4, 57.3, 31.4, 28.6, 25.5, 22.6, 14.0. Elemental analysis calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.61; H, 7.58.

4.3.25. Phenyl 2,2-diphenylacetate (6y). Mp 67–68 °C. R_f=0.72 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3100, 3050, 1760, 1600, 1500, 1460, 1320, 1240, 1200, 1270, 1250, 1090, 960, 760, 740, 710, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.44–7.18 (m, 13H), 7.07–7.03 (m, 2H), 5.26 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 171.0, 150.8, 138.2, 129.4, 128.7, 127.5, 125.9, 121.4, 57.1. Elemental analysis calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.38; H, 5.61.

4.3.26. Pyridin-3-yl 2,2-diphenylacetate (6z). Mp 61–63 °C. R_f=0.62 (EtOAc/CH_2Cl_2=1:5, v/v). IR (KBr) 3100, 3050, 1680, 1600, 1510, 1490, 1470, 1440, 1380, 1330, 1230, 1150, 1040, 960, 760, 720 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.47 (d, 1H, J=3.6 Hz), 8.40 (d, 1H, J=2.4 Hz), 7.44–7.29 (m, 12H), 5.29 (s, 1H). ^{13}C NMR ($CDCl_3$) δ: 170.6, 147.5, 147.1, 143.3, 137.8, 129.1, 128.9, 128.6, 127.7, 123.9, 57.0. Elemental analysis calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.91; H, 5.27; N, 4.89.

4.3.27. Hexyl 2,2-dimethylcyclopropanecarboxylate (6aa). Liquid. R_f=0.78 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 2950, 2890, 1740, 1470, 1410, 1390, 1330, 1280, 1180, 1130, 1100, 1030 cm^{-1}. ^{1}H NM ($CDCl_3$) δ: 4.06 (t, 2H, J=6.8 Hz), 1.67–1.58 (m, 2H), 1.51–1.46 (m, 1H), 1.38–1.26 (m, 6H), 1.21 (s, 3H), 1.16 (s, 3H), 1.07 (t, 1H, J=5.2 Hz), 0.89 (t, 3H, J=6.9 Hz), 0.85–0.81 (m, 1H). ^{13}C NMR ($CDCl_3$) δ: 172.7, 64.3, 31.4, 28.7, 26.9, 26.8, 25.6, 22.7, 21.8, 18.7, 13.9. Elemental analysis calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.47; H, 10.31.

4.3.28. Phenyl 2,2-dimethylcyclopropanecarboxylate (6ab). Liquid. R_f=0.70 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3100, 2970, 2900, 1760, 1660, 1600, 1500, 1450, 1400, 1280, 1200, 1150, 1100, 1080 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.29 (t, 2H, J=8.2 Hz), 7.12 (t, 1H, J=7.4 Hz), 7.07–7.03 (m, 2H), 1.71–1.66 (m, 1H), 1.28 (s, 3H), 1.17 (t, 1H, J=4.7 Hz), 1.15 (s, 3H), 0.93–0.89 (m, 1H). ^{13}C NMR ($CDCl_3$) δ: 171.2, 151.2, 129.4, 125.6, 121.8, 26.9, 26.8, 24.1, 22.8, 18.8. Elemental analysis calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.81; H, 7.47.

4.3.29. Pyridin-3-yl 2,2-dimethylcyclopropanecarboxylate (6ac). Liquid. R_f=0.62 (EtOAc/CH_2Cl_2=1:5, v/v). IR (KBr) 3100, 3040, 2990, 2900, 1760, 1600, 1490, 1440, 1400, 1280, 1230, 1140, 1100, 1080, 1040, 980 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.46–8.43 (m, 2H), 7.50–7.46 (d, 1H, J=8.3 Hz), 7.33–7.29 (m, 1H), 1.78–1.74 (m, 1H), 1.30 (s, 3H), 1.25 (s, 3H), 1.23 (t, 1H, J=5.1 Hz), 1.07–1.03 (m, 1H). ^{13}C NMR ($CDCl_3$) δ: 170.9, 147.6, 146.5, 143.5, 129.4, 123.8, 26.8, 26.6, 24.8, 23.2, 18.7. Elemental analysis calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.15; H, 6.87; N, 7.34.

4.3.30. Methyl furan-2-carboxylate (6ad). Liquid. R_f=0.75 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3170, 3040, 2990, 1750, 1600, 1500, 1450, 1400, 1320, 1250, 1210, 1190, 1040, 980, 780 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.62–7.61 (m, 1H), 7.18 (d, 1H, J=3.5 Hz), 6.53–6.51 (m, 1H), 3.89 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 158.9, 146.2, 144.4, 118.0, 111.9, 51.5. Elemental analysis calcd for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.18; H, 4.86.

4.3.31. Hexyl furan-2-carboxylate (6ae). Liquid. R_f=0.61 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3150, 2950, 2870, 1730, 1580, 1480, 1400, 1300, 1230, 1170, 1110, 760 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.58–7.57 (m, 1H), 7.17 (d, 1H, J=3.5 Hz), 6.51–6.49 (m, 1H), 4.30 (t, 2H, J=6.8 Hz), 1.79–1.70 (m, 2H), 1.35–1.26 (m, 6H), 0.92–0.85 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 18.8, 146.1, 144.9, 117.6, 111.7, 65.0, 31.4, 28.6, 25.5, 22.5, 13.9. Elemental analysis calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.05; H, 7.34.

4.3.32. Phenyl furan-2-carboxylate (6af). Mp 38–40 °C. R_f=0.66 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3150, 3080, 1740, 1600, 1570, 1490, 1470, 1400, 1300, 1220, 1200, 1170, 1090, 1010, 930, 910 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.66–7.65 (m, 1H), 7.43–7.36 (m, 3H), 7.28–7.18 (m, 3H), 6.58–6.56 (m, 1H). ^{13}C NMR ($CDCl_3$) δ: 156.9, 150.2, 147.2, 144.0, 129.5, 126.1, 121.6, 119.5, 112.2. Elemental analysis calcd for $C_{11}H_{14}O_3$: C, 70.21; H, 4.29. Found: C, 70.27; H, 4.32.

4.3.33. Pyridin-3-yl furan-2-carboxylate (6ag). Liquid. R_f=0.46 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3100, 3050, 1750, 1610, 1560, 1500, 1440, 1330, 1240, 1200, 1160, 1080, 980 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.57 (d, 1H, J=2.4 Hz), 8.54 (d, 1H, J=4.7 Hz), 7.71–7.70 (m, 1H), 7.63 (d, 1H, J=8.3 Hz), 7.43 (d, 1H, J=3.6 Hz), 7.41–7.38

(m, 1H), 6.63–6.62 (m, 1H). ^{13}C NMR ($CDCl_3$) δ: 156.3, 147.6, 147.1, 143.4, 143.3, 137.0, 129.3, 124.0, 120.2, 112.4. Elemental analysis calcd for $C_{11}H_{14}O_3$: C, 63.49; H, 3.73; N, 7.40. Found: C, 63.51; H, 3.75; N, 7.44.

4.3.34. Hexyl benzoate (6ah). Liquid. R_f=0.65 (EtOAc/*n*-hexane=1:4, v/v). IR (KBr) 3050, 2990, 1730, 1470, 1190, 1120, 1090, 1040, 720 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.04 (d, 2H, J=7.1 Hz), 7.49 (t, 1H, J=7.3 Hz), 7.39 (t, 2H, J=7.7 Hz), 4.29 (t, 2H, J=7.0 Hz), 1.78–1.68 (m, 2H), 1.44–1.29 (m, 6H), 0.89 (t, 3H, J=7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 166.4, 132.6, 130.5, 129.4, 128.2, 64.9, 31.4, 28.7, 25.7, 22.5, 13.9. Elemental analysis calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.73; H, 8.82.

4.3.35. Phenyl benzoate (6ai). Mp 66–68 °C (lit.[14] mp 68–70 °C). R_f=0.71 (EtOAc/*n*-hexane=1:3, v/v). IR (KBr) 3080, 1740, 1600, 1500, 1460, 1270, 1210, 1190, 1180, 1090, 1070, 1040, 1010, 760, 720, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.20 (d, 2H, J=7.1 Hz), 7.62 (t, 1H, J=7.5 Hz), 7.49 (t, 2H, J=7.3 Hz), 7.42 (t, 2H, J=7.8 Hz), 7.28–7.19 (m, 3H). ^{13}C NMR ($CDCl_3$) δ: 165.2, 151.0, 133.6, 130.2, 129.6, 129.5, 128.6, 125.9, 121.8. Elemental analysis calcd for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.79; H, 5.14.

4.3.36. *S*-Phenyl benzothioate (6aj). Mp 61–63 °C. R_f=0.73 (CH_2Cl_2). IR (KBr) 3090, 1740, 1680, 1600, 1490, 1440, 1260, 1200, 1180, 1060, 1040, 900, 760, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.03 (d, 2H, J=7.1 Hz), 7.60 (t, 1H, J=7.3 Hz), 7.54–7.43 (m, 7H). ^{13}C NMR ($CDCl_3$) δ: 190.2, 135.1, 133.7, 130.2, 129.6, 129.3, 128.8, 128.6, 127.5. Elemental analysis calcd for $C_{13}H_{10}OS$: C, 72.87; H, 4.70; S, 14.96. Found: 72.90; H, 4.76; S, 15.00.

4.3.37. Diphenyldisulfide. Mp 56–58 °C (lit.[15] mp 58–60 °C). R_f=0.81 (CH_2Cl_2). IR (KBr) 3060, 2930, 1580, 1480, 1440, 1300, 1070, 1020, 900, 740, 690 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.71–7.47 (m, 2H), 7.29 (t, 2H, J=7.0 Hz), 7.21 (t, 1H, J=7.1 Hz). ^{13}C NMR ($CDCl_3$) δ: 137.1, 129.1, 127.6, 127.2. Elemental analysis calcd for $C_{12}H_{10}S_2$: C, 66.01; H, 4.62. Found: C, 66.04; H, 4.69.

4.3.38. *S*-2-Hydroxyethyl octanethioate (6ak). Liquid. R_f=0.56 (EtOAc/*n*-hexane=1:1, v/v). IR (KBr) 3443, 2953, 2925, 2854, 1732, 1681, 1456, 1415, 1273, 1123, 1044, 748 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.72 (t, 2H, J=11.3 Hz), 3.5 (s, 1H), 3.1 (t, 2H, J=12.9 Hz), 2.57 (t, 2H, J=15.1 Hz), 1.64 (m, 2H), 1.23 (t, 8H, J=7.7 Hz), 0.88 (t, 3H, J=13.4 Hz). ^{13}C NMR ($CDCl_3$) δ: 200.0, 61.4, 44.0, 31.5, 31.4, 28.8, 25.5, 22.5, 13.9. Elemental analysis calcd for $C_{10}H_{20}O_2S$: C, 58.78; H, 9.87. Found: C, 58.80; H, 9.91.

4.3.39. *S*-2-Hydroxyethyl benzothioate (6al). Liquid. R_f=0.61 (EtOAc/CH_2Cl_2=1:3, v/v). IR (KBr) 3450, 3350, 3100, 2950, 2900, 1670, 1600, 1460, 1410, 1300, 1210, 1180, 1170, 1150, 1020, 920 cm^{-1}. ^{1}H NMR (DMSO) δ: 7.95 (d, 2H, J=7.1 Hz), 7.54 (t, 1H, J=7.5 Hz), 7.41 (t, 2H, J=7.4 Hz), 3.84 (t, 2H, J=6.2 Hz), 3.34 (s, OH), 3.27 (t, 2H, J=6.3 Hz). ^{13}C NMR (DMSO) δ: 192.3, 136.8, 133.6, 128.6, 127.3, 61.6, 31.7. Elemental analysis calcd for $C_9H_{10}O_2S$: C, 59.32; H, 5.53; S, 17.59. Found: C, 59.34; H, 5.57; S, 17.62.

4.3.40. *N*-(4-Hydroxyphenyl)octanamide (6am). Mp 114–116 °C. R_f=0.57 (EtOAc). IR (KBr) 3311, 3194, 3144, 3069, 3041, 2949, 2923, 2866, 2849, 1651, 1588, 1545, 1515, 1450, 1379, 1245, 1184, 941, 832 cm^{-1}. ^{1}H NMR (DMSO) δ: 13.7 (s, 1H), 7.33 (t, 2H, J=11.9 Hz), 6.65 (t, 2H, J=12.0 Hz), 2.22 (t, 2H, J=14.8 Hz), 1.56 (t, 2H, J=13.5 Hz), 1.27–1.18 (m, 8H), 0.86 (t, 3H, J=13.0 Hz). ^{13}C NMR (DMSO) δ: 171.0, 153.5, 137.1(2), 121.2, 115.4, 36.7, 31.6, 29.1, 28.9, 25.7, 22.5, 14.4. Elemental analysis calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.51; H, 9.02; N, 5.97.

4.3.41. *N*-(4-Hydroxyphenyl)benzamide (6an). Mp 207–209 °C. R_f=0.48 (EtOAc/*n*-hexane=1:2, v/v). IR (KBr) 3410, 3350, 1660, 1620, 1600, 1560, 1530, 1450, 1340, 1260, 1240, 1120, 840 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 10.03 (s, NH, D_2O exchangeable), 9.26 (s, OH), 7.93 (d, 2H, J=6.8 Hz), 7.56–7.48 (m, 5H), 6.75 (d, 2H, J=8.8 Hz). ^{13}C NMR ($CDCl_3$) δ: 165.4, 154.2, 137.1, 135.6, 131.7, 131.2, 128.8, 128.0, 122.7, 115.4. Elemental analysis calcd for $C_{13}H_{11}NO_2$: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.25; H, 5.24; N, 6.60.

4.3.42. Octanoic anhydride. Liquid. R_f=0.90 (EtOAc/*n*-hexane=1:4, v/v). IR (KBr) 2954, 2927, 2855, 1818, 1749, 1463, 1411, 1375, 1273, 1260, 1040, 761, 747 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 5.03 (s, 2H), 2.45 (t, 8H, J=7.4 Hz), 2.35 (t, 1H, J=7.4 Hz), 1.71–1.61 (m, 10H), 1.31–1.29 (t, 41H, J=8.0 Hz), 0.88 (t, 15H, J=6.4 Hz). ^{13}C NMR ($CDCl_3$) δ: 169.6, 35.2, 31.6, 28.8 (2), 24.2, 22.5, 14.0. Elemental analysis calcd for $C_{16}H_{30}O_3$: C, 71.07; H, 11.18. Found: C, 71.13; H, 11.20.

4.3.43. Benzoic anhydride. Mp 40–41 °C (lit.[16] mp 38–42 °C). R_f=0.40 (EtOAc/*n*-hexane=1:4, v/v). IR (KBr) 3100, 1780, 1720, 1610, 1500, 1460, 1430, 1340, 1300, 1230, 1180, 1050, 1030, 1010, 950, 790 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 8.16 (m, 4H), 7.67 (t, 2H, J=7.5 Hz), 7.52 (t, 4H, J=7.8 Hz). ^{13}C NMR ($CDCl_3$) δ: 162.4, 147.4, 139.6, 131.2, 129.1, 128.6, 127.7, 127.6, 127.4. Elemental analysis calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39. Found: C, 80.36; H, 5.43.

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