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FULL PAPER

Metal-Free *O*-Selective Direct Acylation of Amino Alcohols *via* Pseudo-Intramolecular Process

Soichi Yokoyama,[a,b] Hiroshi Shibauchi,[a] Haruyasu Asahara,[a,b,c] and Nagatoshi Nishiwaki*[a,b]

Abstract: Efficient α-aryl-β-keto ester acylation of amine accompanied by the elimination of ethyl phenylacetate, was achieved owing to the pseudo-intramolecular process. The eliminated ethyl phenylacetate could be recycled by converting to an α-aryl-β-keto ester upon treatment with an acyl chloride in the presence of lithium bis(trimethylsilyl)amide, by which atom economy considerably increased. Acylation using an α-aryl-β-keto ester is highly sensitive to the bulkiness of the nucleophile, which facilitated the regioselective-acylation of the less hindered amino group in diamine without protecting the other. The transacylation of α-aryl-β-keto ester with *N*-alkylamino alcohol resulted in chemoselective *O*-acylation without protecting the amino group because the hydroxy group was attracted to the reaction site of the keto ester by forming an ammonium salt. Transacylation was demonstrated to be a practically useful tool for organic synthesis because this protocol can be conducted under mild conditions with simple manipulations in the absence of any additives such as metal catalyst and base.

Introduction

Acylation is one of the fundamental reactions for chemical conversion, and numerous methods and acylating reagents have been developed. However, it is still challenging even now to acylate an amino/a hydroxy group of polyamines/amino alcohols selectively without any modification or protection of the other sites. Among selective acylation methods, monoacylation of a polyamine possessing plural equivalent amino groups is relatively easy.[1,2] Recognition between primary and secondary amino groups in *N*-alkyl-1,2-diaminoethanes was possible by using acylimidazole,[1] 3-acyl-1,3-thiazolidine-2-thione,[3] *N*-acyl-2-amino-1,3-thiazoline,[4] *N*,*N*-diacyl-2-trifluoromethylaniline,[5] and *N*-acyl-*N*-mesyl-2-fluorolaniline,[6] although the control of the selectivity depended on the bulkiness of the *N*-alkyl group of diamine.[1] These reagents were also effective for recognition of the presence of a methyl group at the α-position.[4-6] Regioselective control for the acylation of 3,4-diaminopyridine was also achieved by using acetyl chloride or *tert*-butyl dicarbonate.[7]

Selective *N*-acylation of amino alcohols was performed by using lipase[8] and dibutyltin oxide[9] as a catalyst, and both methods were conducted under microwave irradiation. *N*-Acylation of α,β-diamino alcohol was also reported.[10] Regarding *O*-acylation of amino alcohols, only a few reports are found in the literature (Scheme 1). A combination of 2,2'-bipyridyl-6-yl carboxylate and cesium fluoride underwent *O*-acetylation of 4-(2-hydroxyethyl)aniline, however, *O*,*N*-diacetylation also occurred (eq. 1).[11] RajanBabu *et al.* demonstrated selective *O*-acylation of 2-hydroxymethylpiperidine by acetyl transfer reaction from isopropenyl acetate in the presence of $Y_5(OPr^i)_{13}O$ catalyst (eq. 2).[12] Recently, excellent methods have been developed using μ-oxo-dinuclear iron(III) salen complex (eq. 3),[13] alkoxy-bridged dinuclear cobalt complex (eq. 4),[14] $(Bu_4N)_6{\cdot}[\gamma\text{-}HGeW_{10}O_{36}]$ (eq. 5)[15] and *N*-heterocyclic carbine (eq. 6),[16] by which *O*-acylation of versatile amino alcohols was achieved. However, these methods require special reagents or metal catalysts, which prompted us to study the transacylation as a general and metal-free protocol for the selective acylation.

Meanwhile, we previously disclosed several efficient reactions, that proceed in a similar manner to an intramolecular reaction, even in the absence of additives.[17-19] Of these reactions, transacylation is illustrated in Scheme 2. The enolic hydroxy group of α-aryl-β-keto ester **1** is highly acidic and attracts the nearby amine **2** due to the formation of an ammonium enolate **3**. When the amine is liberated from the ammonium salt **3** under equilibrium conditions, the nucleophilic amine **2** is located close to the electrophilic keto ester **1**, which is called an 'intimate pair.' The nearness facilitates an efficient reaction to produce amide **4** and the deacylated product **5**.[18] This reaction proceeds in an intramolecular reaction although it is actually intermolecular reaction. It is a "pseudo-intramolecular reaction." The ^{1}H NMR monitoring study demonstrated that the rate of the transacylation is not affected by the polarity of the solvent, which is one of the features of intramolecular reactions.[19] Although the transacylation is expected to be a useful tool for elaborate synthesis, this reaction faces several drawbacks. As the diversity of commercially available β-keto esters is low, limited acyl groups can be introduced. Furthermore, compound **5** formed during the transacylation, is wasted, which considerably diminishes the atom economy of this protocol. In this work, the acylation of waste compound **5** by acyl chloride **6** or acid anhydride **8** was

[a] Dr. S. Yokoyama, Mr. H. Shibauchi, Dr. H. Asahara, Prof. Dr. N. Nishiwaki
School of Environmental Science and Engineering
Kochi University of Technology
Tosayamada, Kami, Kochi 782-8502, Japan
E-mail: nishiwaki.nagatoshi@kochi-tech.ac.jp
Homepage: http://www.env.kochi-tech.ac.jp/naga/nishiwaki-lab.html
[b] Dr. S. Yokoyama, Dr. H. Asahara, Prof. Dr. N. Nishiwaki
Research Center for Material Science and Engineering
Kochi University of Technology
[c] Dr. H. Asahara
Division of Applied Chemistry, Graduate School of Engineering
Osaka University
Yamadaoka 2-1, Suita, Osaka 565-0871, japan

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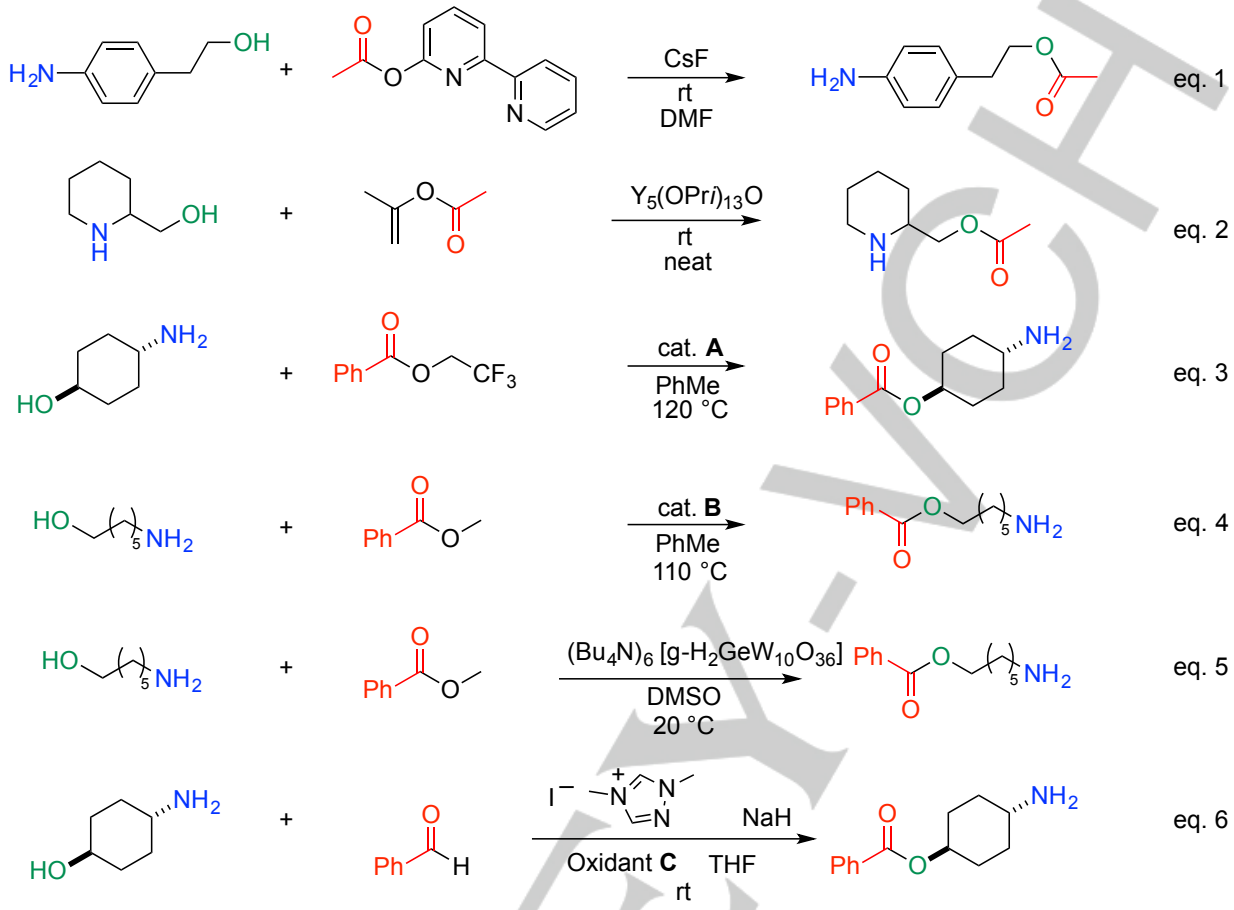
studied[20] to prepare α-aryl-β-keto ester **1**, which addresses the above problems.



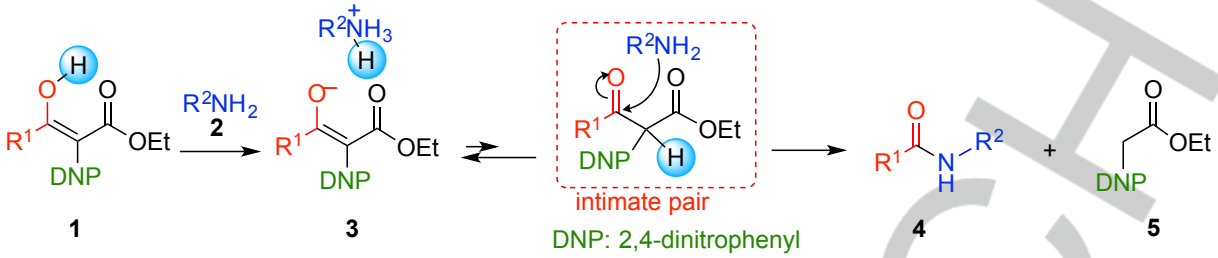
Scheme 1. Reported *O*-selective acylation of amino alcohols without protecting the amino group.

In addition to high efficiency, high sensitivity to the steric bulk is a unique feature of transacylation. Because versatile α-aryl-β-keto esters **1** could be prepared by the acylation of **5**, the influence of the steric factor on this reaction was determined systematically, and the regio-/chemoselective acylations of diamines and amino alcohols were also investigated.

Results and Discussion

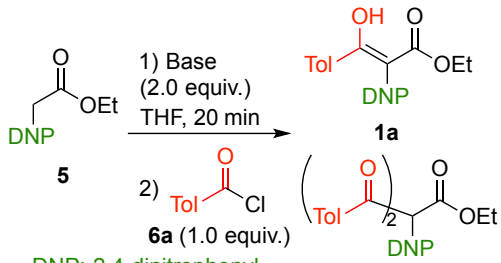
We firstly screened the bases for the acylation of 2,4-dinitrophenylacetate **5** by *p*-toluoyl chloride **6a** (Table 1). When sodium hydride was used, acylation proceeded to generate a 44% yield of target material **1a** together with doubly acylated product **7a** (Entry 1). Bulky bases were used to suppress excess acylation. While potassium *t*-butoxide exhibited a similar reactivity to sodium hydride, lithium bis(trimethylsilyl)amide (LiHMDS) could generate a 57% yield of **1a** in without any detectable **7a** (Entries 2 and 3). Furthermore, conducting the

reaction at 0 °C with longer reaction time enhanced the yield of **1a** up to 90% (Entries 4–7).



Scheme 2. Transacylation of **1** with amine by pseudo-intramolecular reaction

Table 1. Assessment of bases and temperatures for the synthesis of α-aryl-β-keto ester **1a**.

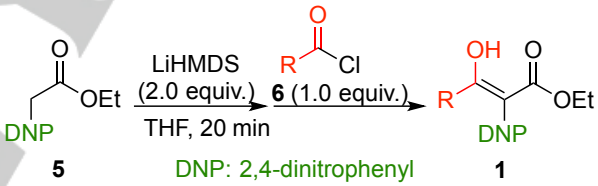


Entry	Base	Temp. (°C)	Time (h)	Yield (%)[a] 1a	7a	5
1	NaH	rt	3	44	12	24
2	*t*-BuOK	rt	3	39	9	39
3	LiHMDS	rt	3	57	0	21
4	LiHMDS	-78	3	7	0	83
5	LiHMDS	0	3	61	0	11
6	LiHMDS	0	6	74	0	7
7	LiHMDS	0	24	90	0	4

[a] Determined by ^{1}H NMR

Under the optimized conditions, various acid chlorides **6** were employed for the acylation of **2** (Table 2). Aroyl chlorides **6a** and **6b** efficiently reacted with **5** to generate the corresponding keto esters **1a** and **1b**, respectively (Entries 1 and 2). In contrast, the yields of keto esters **1c**–**g** were lower in the presence of the more reactive aliphatic acid chlorides **6c**–**g** (Entries 3–7). These results were presumably due to the high reactivity of products **1c**–**g**, which undergo competitive deacylation resulting in the recovery of starting material **5**. It was also possible to introduce a functionalized acyl group (Entries 8–11). While the acryloyl group caused side reactions, the cinnamoyl and ethoxymalonyl groups persisted under the experimental conditions and generated keto esters **1i**–**k** (Entries 8–11, respectively). Both the acyl and aroyl groups were efficiently transferred upon treatment of the obtained α-aryl-β-keto esters **1a**, **1c**, **1d**, and **1j** and two disadvantages of transacylation with propylamine, i.e., the low diversity of **1** and generation of **5**, were successfully overcome (Table S1).

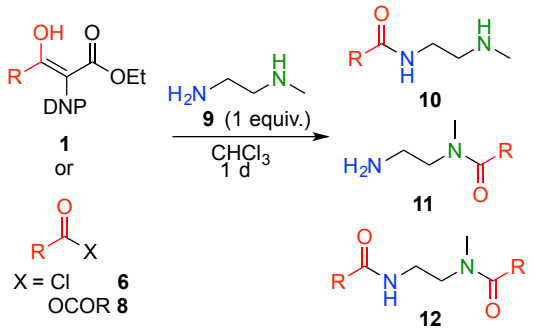
Table 2. Assessment of the substituent of acid chloride for the synthesis of α-aryl-β-keto ester **1**.



Entry	R		Yield of **1** (%)[a]	Recovery of **5** (%)[a]
1	*p*-Tol	**a**	90	trace
2	Ph	**b**	84	9
3	Me	**c**	42	33
4	Et	**d**	42	36
5	*i*-Pr	**e**	40	35
6	*t*-Bu	**f**	0	88
7	*c*-Hex	**g**	25	68
8	H_2C=CH-	**h**	trace	—
9	PhC=CH-	**i**	38	57
10	EtO-$COCH_2$-	**j**	10	76
11	$ClCH_2$-	**k**	44	24

[a] Determined by ^{1}H NMR

Table 3. Transacylation of α-aryl-β-keto ester **1**, acid chloride **6**, or acid anhydride **8** with *N*-methylethylenediamine **9**.[21]

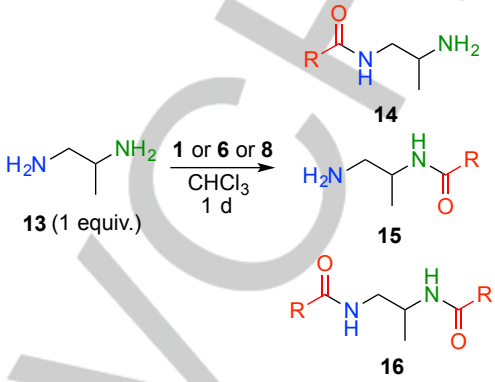


Entry	Reagent		Temp.	Yield (%)[a]		
	R		(°C)	**10**	**11**	**12**
1	Me	**1c**	rt	90	0	0
2[b]	Me	**6c**	rt	17	10	36
3[b]	Me	**8c**	rt	16	8	41
4[b]	Me	**6c**	-30	30	17	25
5[b]	Me	**8c**	-30	16	6	40
6	Me	**1c**	70	96	0	0
7	Et	**1d**	rt	94	0	0
8[b]	Et	**6d**	rt	21	3	39
9[b]	Et	**8d**	rt	43	8	26
10	*p*-Tol	**1a**	rt	94	0	0
11[b]	*p*-Tol	**6a**	rt	2	2	48
12[c]	CH_2COOEt	**1j**	rt	99	0	0

[a] Determined by ^1H NMR [b] 1 equiv. of triethylamine was added. [c] *N*-Ethylethylenediamine was used as a substrate.

Transacylation using α-aryl-β-keto ester **1** is sensitive to the bulkiness of amine **2**,[18] which has the potential to facilitate regio- and chemoselective acylation; however, there has been no systematic study of this. With regard to the selective acylation of diamines without any protection, only a few reports are found.[1,3–6] For comparison, keto ester **1**, acid halides **6**, and acid anhydrides **8** underwent the reaction with *N*-methylethylenediamine **9** (Table 3). The transacylation of **1c** with **9** resulted in exclusive acylation at the primary amino group without any protection of the secondary amino group, even in the absence of a base (Entry 1). However, acid chloride **6c** and acid anhydride **8c** could not recognize the two amino groups of **9**, and double acylation also occurred, which could not be suppressed at -30 °C (Entries 2–5). During transacylation using **1c**, high selectivity was maintained and only **10** was generated, even at 70 °C (Entry 6). Furthermore, propanoyl and toluoyl groups were also efficiently transferred to the primary amino group of **9** by transacylation (Entries 7 and 10).

Table 4. Evaluation of recognition ability of the transacylation using 1,2-diaminopropane **13**.

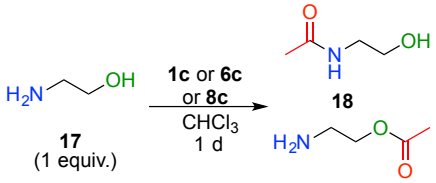


Entry	Reagent		Temp.	Yield (%)[a]		
	R		(°C)	**14**	**15**	**16**
1[b]	Me	**6c**	rt	6	6	42
2[b]	Me	**8a**	rt	17	3	24
3[b]	Me	**8a**	-30	37	24	18
4	Me	**1c**	rt	99	0	0
5	Et	**1d**	rt	99	0	0
6	*p*-Tol	**1a**	rt	99	0	0
7	CH_2COOEt	**1j**	rt	99	0	0
8	Me	**1c**	70	73	20	0
9	*p*-Tol	**1a**	70	82	12	0

[a] Determined by ^1H NMR [b] 1 equiv. of triethylamine was added.

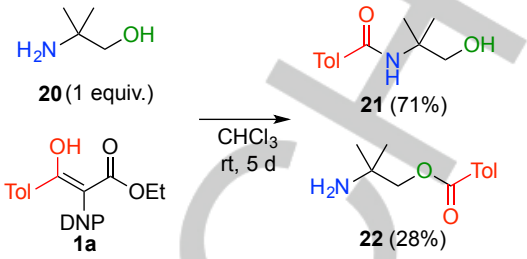
Next, recognizing the ability of these acylating agents, the existence of the methyl group at α-position in the diamine was evaluated using 1,2-propanediamine (**13**) as a substrate. When acid chloride **6c** or acid anhydride **8c** was used, a mixture of **14**, **15**, and diacylated compound **16** was obtained,[21] indicating that the presence of α-methyl group was not recognized (Entries 1–3 in Table 4 and Entries 1–5 in Table S2). To the contrary, the transacylation recognized subtle difference of two amino groups in **13** to generate *N*-(2-amino-1-propyl)acetamide (**14c**) exclusively (Entry 4 in Table 4). The reaction using **1d** and **1a** also generated quantitative yields of the corresponding compounds **14d** and **14a**, respectively (Entries 5 and 6 in Table 4). High regioselectivity was still observed when the reaction was conducted at 70 °C (Entries 8 and 9). α-Aryl-β-keto ester **1** was confirmed to serve as an acylating agent for the regioselective acylation of diamines without the necessity for any modification of the similar, but somewhat bulkier, amino group.

Table 5. Transacylation using amino alcohol **17**.



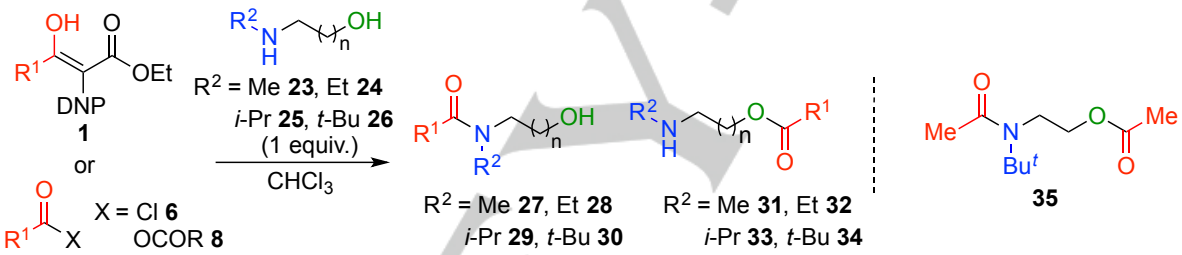
Entry	Acylating Reagent	Yield (%)[a]	
		18	**19**
1[b]	**6c**	82	15
2[b]	**8c**	99	0
3	**1c**	99	0

[a] Determined by ^{1}H NMR [b] 1 equiv. of triethylamine was added.



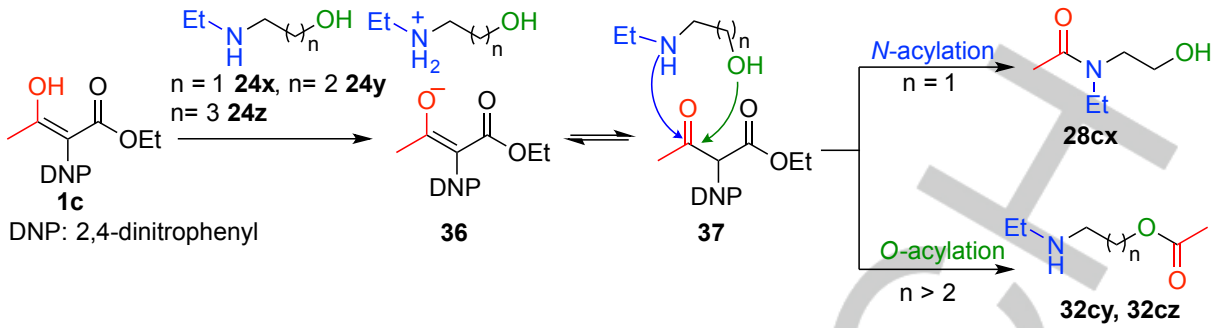
Scheme 3. Transacylation of **1a** with 2,2-dimethyl-2-aminoethanol **20**.

Table 6. Chemoselective acylation of *N*-alkyl-ethanolamines **23-26**.



Entry	Acylating reagent		Amino alcohol			Temp.	Time	Yield of product (%)[a]			
	R^1		R^2	n		(°C)	(d)	*N*-Acylated product		*O*-Acylated product	
1[b,c]	Me	**6c**	*t*-Bu	1	**26**	rt	1	**30**	35	**34**	31
2[b,d]	Me	**6c**	*t*-Bu	1	**26**	-30	1	**30**	23	**34**	37
3[b]	Me	**6c**	Et	1	**24**	rt	1	**28**	49	**28**	29
4[b]	Me	**8c**	Et	1	**24**	rt	1	**28**	40	**28**	60
5	Me	**1c**	Me	1	**23**	rt	4	**27**	96	**31**	0
6	Me	**1c**	Et	1	**24x**	rt	5	**28cx**	95	**32cx**	0
7	Me	**1c**	*i*-Pr	1	**25**	rt	5	**29**	34	**33**	66
8	Me	**1c**	*t*-Bu	1	**26**	rt	4	**30**	0	**34**	94
9	Me	**1c**	Et	2	**24y**	rt	6	**28cy**	9	**32cy**	88
10	Me	**1c**	Et	3	**24z**	rt	6	**28cz**	19	**32cz**	75
11	*p*-Tol	**1a**	Et	1	**24x**	rt	1	**28ax**	0	**32ax**	92
12	*p*-Tol	**1a**	Et	2	**24y**	rt	7	**28ay**	8	**32ay**	86
13	*p*-Tol	**1a**	Et	3	**24z**	rt	7	**28az**	8	**32az**	84

[a] Determined by ^{1}H NMR. [b] 1 equiv. of triethylamine was added. [c] **35** was obtained in 16% yield. [d] **35** was obtained in 6% yield.



Scheme 4. A plausible mechanism of the *O*-acylation of 2-(ethylamino)ethanol **24**.

When amino alcohol **17** reacted with acetyl chloride **6c**, both the amino and hydroxy groups were acylated, even at -30 °C (Entry 1 in Table 5 and Entry 1 in Table S3). Although acid anhydride **8c** only underwent *N*-acylation, triethylamine was required to capture the acid generated during the reaction (Entry 2 in Table 5 and Entries 4–8 in Table S3). However, transacylation using α-aryl-β-keto ester **1c** required neither protection of the hydroxy group, nor the addition of a base, which solely generated *N*-acylated product **18**[21] entirely (Entry 3 in Table 5).

The chemoselective acylation of a hydroxy group in an amino alcohol usually requires protection of the amino group or use of metal catalyst as shown in Scheme 1. Hence, it is more challenging to acylate a hydroxy group directly without any contrivance under catalyst free conditions. To achieve the selective *O*-acylation, a substituent was introduced at the α-position of the amino group, however, no positive effect was observed, even though a bulky substituent was introduced, such as a phenyl or benzyl group (Table S4). The two methyl groups of **20** prevented *N*-acylation to some extent and generated a small amount of *O*-acylated product **22**, but the chemoselectivity was not satisfactorily controlled (Scheme 3 and Entries 3 and 4 in Table S5). Hence, *N*-substituted amino alcohols **23**–**26** were employed. When acetyl chloride **6c** or acetic anhydride **8c** was used, both *N*- and *O*-acylation proceeded (Entries 1–4 in Table 6). In contrast, transacylation using **1c** facilitated *O*-acetylation (Entries 5–8 in Table 6), and chemoselective acylation was completely achieved when the *t*-butyl group was introduced into the amino group (Entry 8 in Table 6). When aroylation occurred, the introduction of a *N*-substituent larger than ethyl group was suitable for selective *O*-acylation (Entries 1–4 in Table S6).

Interestingly, the chemoselectivity was considerably affected by the distance between an amino and a hydroxy group of **24** (Entries 6 and 9–13 in Table 6 and Entries 9–14 in Table S6). While 2-(ethylamino)ethanol **24x** only underwent *N*-acetylation (Entry 6 in Table 6), 3-(ethylamino)propanol **24y** and 4-(ethylamino)butanol **24z** generated *O*-acetylated **32cy** and **32cz** as main products (Entries 7 and 8 in Table 6). A similar tendency was observed during aroylation using **1a**, which efficiently generated the corresponding *O*-toluoyl esters **32ax**–**32az** (Entries 11–13 in Table 6 and Entries 12–14 in Table S6). It should be emphasized that interconversion between products **28** and **32** was not observed at all even though a solution of each isolated product in $CDCl_3$ was monitored for more than 1 d (Figures S1–S4).

Table 7. List of reaction order *n* and rate constant *k*

$[A]_0$ (mM)[a]	*n*	*k* (M^{-1} sec^{-1})
200	2.0	2.6×10^{-4}
41	1.5	8.6×10^{-5}
8.9	1.4	1.4×10^{-5}

[a] $[A]_0$ is the initial concentration of ammonium enolate derived from **1a** and **24x**.

In our previous work, we monitored the transacylation between **1c** and propylamine by ^1H NMR with different concentration of the reaction mixture.[19] Although the reaction rate varied depending on the concentration, it became almost same in highly diluted solutions, and the reaction order was lower than second order. These results imply that not only a first order reaction but also a second order reaction proceed in the present system. So, the reaction of **1a** and **24x** was also monitored in the same way, and results are shown in Table 7 and Figure S5. As the concentration of the reaction mixture decreased, reaction order and reaction rate decreased, which is a similar tendency to the previous work.

A plausible mechanism for the chemoselectivity by the length of the alkyl spacer is illustrated in Scheme 4. Transacylation was initiated by the formation of ammonium enolate **36**, from which an amine was liberated to provide intimate pair **37**.[18] Since the quantitative formation of ammonium salt **36** was confirmed just after addition of the amino alcohol **24x** to a solution of keto ester **1**, the higher reaction order is caused by the intermolecular reaction between two intimate pairs (Figure 1). When 2-(ethylamino)ethanol **24x** was used, the hydroxy group of intimate pair **37x** was located too far from the reaction site to attack the electrophilic carbonyl carbon due to the short alkyl chain, thus, *N*-acylation proceeded to exclusively generate **28cx**. However, 3-(ethylamino)propanol **24y** and 4-(ethylamino)butanol **24z** have a long enough alkyl spacer enough to locate the hydroxy group near the electrophilic carbonyl carbon, which facilitates the *O*-acylation which predominantly generates **32cy** and **32cz**.

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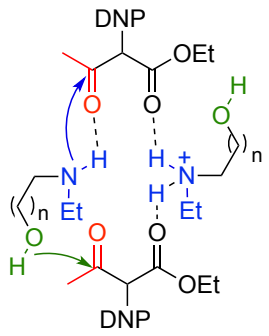

Figure 1. Intermolecular reaction between two intimate pairs.

Conclusions

A method for recycling ethyl phenylacetate **5** generated by transacylation was developed. The quantitative acylation of ethyl phenylacetate **5** was achieved upon treatment with LiHMDS as a base, generating α-aryl-β-keto esters **1** by acid chloride **6**, by which the atom economy was considerably improved. The obtained α-aryl-β-keto esters **1** underwent transacylation with alkylamine **2**, quantitatively generating amides **4**. This protocol facilitates regioselective acylation by the recognition of the different environments of the two amino groups in diamines **9** and **13**, which is not conducted by alternative acylating agents such as acid chloride **6** and acid anhydride **8**. Furthermore, the reactions of *N*-alkylated aminoalcohols **23**–**26** with α-aryl-β-keto esters **1** achieve chemoselective *O*-acylation as the hydroxy group approached the carbonyl carbon of the keto ester caused by the pseudo-intramolecular process.

This method can be conducted with simple experimental manipulations under mild conditions without necessity to use specific base and/or metal catalyst agents. These features are advantageous compared with conventional reagents for the selective acylation. Hence, this protocol will be an environmentally benign tool for the synthesis of polyfunctionalized compounds.

Experimental Section

General

The melting points were determined on SRS-Optimelt Automated Melting Point System, and were uncorrected. All the reagents and solvents were commercially available and used as received. The ^{1}H NMR spectra were measured on a Bruker Ascend-400 at 400 MHz with tetramethylsilane as an internal standard. The ^{13}C NMR spectra were measured on a Bruker Ascend-400 at 100 MHz, and assignments of ^{13}C NMR spectra were performed by DEPT experiments. The high-resolution mass spectra were measured on an AB SCIEX Triple TOF 4600. The IR spectra were recorded on a JASCO FT/IR-4200 spectrometer.

General procedure for preparation of compound 1 from phenylacetate 5

To a solution of α-(2,4-dinitrophenyl)ethyl acetate **5** (0.254 g, 1.0 mmol) in THF (5 mL), was slowly added 1.1 M lithium bis(trimethylsilyl)amide (1.8 mL, 2.0 mmol) in THF over 10 min at 0 °C under nitrogen. After stirring the mixture for 20 min at 0 °C, *p*-toluoyl chloride (0.13 mL, 1.0 mmol) was added, and stirred for further 1 d with keeping the temperature. The reaction was quenched with addition of 3 M HCl (2.0 mL, 6.0 mmol), and extracted with ethyl acetate (20 mL × 3). The organic layer was dried over $MgSO_4$, filtered and evaporated in vacuo. The product was purified with column chromatography on silica gel (dichloromethane as an eluent) to afford yellow solid **1a** (0.268 g, 0.72 mmol, 72%). When other acid chlorides were used, experiments were conducted in the same way.

Ethyl 3-hydroxy-3-(4-methylphenyl)-2-(2,4-dinitrophenyl)propenoate (1a). Yield 0.335 g, 0.90 mmol, 90% (enol form/keto form = 73/27); yellow solid; mp 99–100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) enol form: δ 1.17 (dd, *J* = 7.2, 7.2 Hz, 3H), 2.30 (s, 3H), 4.09 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.29 (dq, *J* = 7.2, 10.8 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 8.11 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.80 (d, *J* = 2.4 Hz, 1H), 13.57 (s, 1H); keto form: δ 1.24 (t, *J* = 7.2 Hz, 3H), 2.42 (s, 3H), 4.27 (q, *J* = 7.2 Hz, 2H), 6.43 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 2H), 8.44 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.88 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) enol form: δ 13.7 (CH_3), 21.5 (CH_3), 61.9 (CH_2), 100.0 (C), 119.9 (CH), 126.4 (CH), 129.0 (CH), 129.1 (CH), 130.7 (C), 136.4 (CH), 137.7 (C), 145.7 (C), 146.5 (C), 149.8 (C), 170.3 (C), 173.2 (C); keto form: δ 14.0 (CH_3), 21.8 (CH_3), 55.4 (CH), 62.8 (CH_2), 120.5 (CH), 127.2 (CH), 129.0 (CH), 129.8 (CH), 132.7 (C), 133.7 (CH), 135.0 (C), 141.6 (C), 147.5 (C), 148.9 (C), 167.0 (C), 190.9 (C); IR (ATR/cm^{-1}) 1337, 1537, 1605, 1643; HRMS (ESI/TOF) *m/z* Calcd. for $C_{18}H_{16}N_2O_7Na$ $[M+Na]^+$ 395.0850, Found 395.0865.

2-Ethoxycarbonyl-1,3-bis(4-methylphenyl)-2-(2,4-dinitrophenyl)-1,3-propanedione (7a). Yield 0.162 g, 0.33 mmol, 33%; white solid; mp 159–160 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.2 Hz, 3H), 2.27 (s, 3H), 2.45 (s, 3H), 4.05 (q, *J* = 7.2 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 8.10 (d, *J* = 8.4 Hz, 2H), 8.19 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.94 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (CH_3), 21.4 (CH_3), 21.8 (CH_3), 61.6 (CH_2), 119.7 (C), 120.1 (CH), 126.2 (C), 127.2 (CH), 129.2 (CH), 129.35 (CH), 129.41 (CH), 130.5 (CH), 131.2 (C), 136.3 (CH), 138.8 (C), 141.3 (C), 144.9 (C), 147.2 (C), 149.2 (C), 156.9 (C), 163.0 (C), 164.4 (C); IR (ATR/cm^{-1}) 1342, 1357, 1510, 1534, 1611, 1624, 1735; HRMS (ESI/TOF) *m/z* Calcd. for $C_{26}H_{22}N_2O_8Na$ $[M+Na]^+$ 513.1268, Found 513.1263.

Ethyl 3-hydroxy-2-(2,4-dinitrophenyl)-3-phenylpropenoate (1b).[22] Yield 0.301 g, 0.84 mmol, 84% (enol form/keto form = 75/25); yellow solid, mp 133–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) wnol form: δ 1.18 (dd, *J* = 7.2, 7.2 Hz, 3H), 4.10 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.29 (dq, *J* = 7.2, 10.8 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.22–7.36 (m, 5H), 8.10 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.80 (d, *J* = 2.4 Hz, 1H), 13.57 (s, 1H); keto form: δ 1.24 (t, *J* = 7.2 Hz, 3H), 4.32 (q, *J* = 7.2 Hz, 2H), 6.46 (s, 1H), 7.48–7.52 (m, 2H), 7.61–7.65 (m, 2H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.94–7.96 (m, 1H), 8.46 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.90 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) enol form: δ 13.7 (CH_3), 62.0 (CH_2), 100.5 (C), 119.9 (CH), 126.3 (CH), 128.4 (CH), 128.9 (CH), 130.9 (CH), 133.6 (C), 136.3 (CH), 137.4 (C), 146.6 (C), 149.8 (C), 170.2 (C), 172.9 (C); keto form: δ 13.9 (CH_3), 55.5 (CH), 62.8 (CH_2), 120.5 (CH), 127.2 (CH), 128.8 (CH), 129.1 (CH), 133.6 (CH), 134.4 (CH), 134.8 (C), 135.2 (C), 147.5 (C), 148.8 (C), 166.9 (C), 191.3 (C); IR (ATR/cm^{-1}) 1337, 1537, 1620, 1730, 1745; HRMS (ESI/TOF) *m/z* Calcd. for $C_{17}H_{18}N_6O_7$ $[M+NH_4]^+$ 376.1139, Found 376.1152.

Ethyl 3-hydroxy-2-(2,4-dinitrophenyl)-2-butenoate (1c).[18] Yield 0.124 g, 0.42 mmol, 42% (enol form/keto form = 93/7); yellow needles; mp 93–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) enol form: δ 1.13 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.92 (s, 3H), 4.05 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.22 (dq, *J* = 7.2, 10.8 Hz, 1H),7.53 (d, *J* = 8.4 Hz, 1H), 8.43 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.84 (d, *J* = 2.4 Hz, 1H), 13.14 (s, 1H); keto form: δ 1.29 (t, *J* = 7.2 Hz, 3H), 2.48 (s, 3H), 4.29 (q, *J* = 7.2 Hz, 2H), 5.42 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 8.48 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.89 (d, *J* = 2.4 Hz, 1H);^{13}C NMR (100 MHz, $CDCl_3$) enol form: δ 13.8 (CH_3), 20.0 (CH_3), 61.5 (CH_2), 99.8 (C), 120.1 (CH), 126.7 (CH), 135.3 (CH), 136.6 (C), 147.2 (C), 149.7 (C), 170.0 (C), 174.3 (C); keto form: δ 13.9 (CH_3), 30.2 (CH_3), 61.0 (CH), 62.8 (CH_2), 120.4 (CH), 127.2 (CH), 134.0 (CH), 134.7 (C), 147.2 (C), 149.7 (C), 166.5 (C), 198.1 (C); IR (ATR/cm^{-1}) 1337, 1537, 1643; HRMS (ESI/TOF) *m/z* Calcd. for $C_{12}H_{12}N_2O_7Na$ [M+Na]$^+$ 319.0537, Found 319.0543.

Ethyl 3-hydroxy-2-(2,4-dinitrophenyl)-2-pentenoate (1d). Yield 0.105 g, 0.34 mmol, 34% (enol form/keto form = 85/15); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) enol form: δ 1.11 (dd, *J* = 7.6, 7.6 Hz, 3H), 1.12 (dd, *J* = 7.2, 7.2 Hz, 3H), 2.13 (dq, *J* = 2.8, 7.6 Hz, 1H), 2.14 (dq, *J* = 2.8, 7.6 Hz, 1H), 4.05 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.23 (dq, *J* = 7.2, 10.8 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 8.42 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.83 (d, *J* = 2.4 Hz, 1H), 13.18 (s, 1H); keto form: δ 1.14 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.72 (dq, *J* = 4.0, 7.2 Hz, 1H), 2.85 (dq, *J* = 4.0, 7.2 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 5.46 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 1H), 8.47 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.86 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) enol form: δ 10.7 (CH_3), 13.8 (CH_3), 26.7 (CH_2), 61.5 (CH_2), 98.9 (C), 120.1 (CH), 126.7 (CH), 135.2 (CH), 136.6 (C), 147.2 (C), 149.8 (C), 170.2 (C), 178.2 (C); keto form: δ 7.7 (CH_3), 13.9 (CH_3), 36.5 (CH_2), 59.8 (CH), 62.8 (CH_2), 120.3 (CH), 127.0 (CH), 133.9 (CH), 134.6 (C), 147.5 (C), 149.0 (C), 166.6 (C), 201.1 (C); IR (ATR/cm^{-1}) 1337, 1537, 1643, 1651, 1730, 1746; HRMS (ESI/TOF) *m/z* Calcd. for $C_{13}H_{14}N_2O_7Na$ [M+Na]$^+$ 333.0693, Found 333.0683.

Ethyl 3-hydroxy-4-methyl-2-(2,4-dinitrophenyl)-2-pentenoate (1e). Yield 0.117 g, 0.36 mmol, 36% (enol form/keto form = 91/9); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) enol form: δ 1.05 (d, *J* = 6.8 Hz, 3H), 1.11 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H), 2.31 (qq, *J* = 6.8, 6.8 Hz, 1H), 4.03 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.22 (dq, *J* = 7.2, 10.8 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 8.42 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.81 (d, *J* = 2.4 Hz, 1H), 13.19 (s, 1H); keto form: δ 1.16 (d, *J* = 6.8 Hz, 3H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.95 (qq, *J* = 6.8, 6.8 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 5.69 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 8.45 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.84 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) enol form: δ 13.8 (CH_3), 19.3 (CH_3), 31.9 (CH), 61.4 (CH_2), 97.8 (C), 120.0 (CH), 126.7 (CH), 135.2 (CH), 136.6 (C), 147.2 (C), 149.8 (C), 170.4 (C), 181.2 (C); keto form: δ 13.9 (CH_3), 18.1 (CH_3), 18.3 (CH_3), 41.4 (CH), 58.0 (CH), 62.7 (CH_2), 120.3 (CH), 127.0 (CH), 133.7 (CH), 134.6 (C), 147.4 (C), 149.1 (C), 166.7 (C), 204.6 (C); IR (ATR/cm^{-1}) 1337, 1537, 1599, 1643, 1649, 1730; HRMS (ESI/TOF) *m/z* Calcd. for $C_{14}H_{16}N_2O_7Na$ [M+Na]$^+$ 347.0850, Found 347.0838.

Ethyl 3-cyclohexyl-3-hydroxy-2-(2,4-dinitrophenyl)propenoate (1g). Yield 0.084 g, 0.23 mmol, 23% (enol form/keto form = 90/10); yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) enol form δ 0.95–1.08 (m, 2H), 1.11 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.56–1.62 (m, 4H), 1.65–1.71 (m, 4H), 1.92–1.97 (m, 1H), 4.03 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.21 (dq, *J* = 7.2, 10.8 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 8.42 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.83 (d, *J* = 2.4 Hz, 1H), 13.25 (s, 1H); keto form δ 0.95–1.08 (m, 2H), 1.17–1.21 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.65–1.78 (m, 4H), 2.63–2.70 (m, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 5.67 (s, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 8.45 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.84 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) enol form δ 13.8 (CH_3), 25.4 (CH_2), 25.5 (CH_2), 25.5 (CH_2), 29.1 (CH_2), 29.4 (CH_2), 42.3 (CH), 61.4 (CH_2), 97.9 (C), 120.1 (CH), 126.6 (CH), 135.1 (CH), 136.7 (C), 147.2 (C), 149.9 (C), 170.4 (C), 180.7 (C); keto form δ 14.0 (CH_3), 25.6 (CH_2), 28.3 (CH_2), 28.7 (CH_2), 51.2 (CH), 58.0 (CH), 62.7 (CH_2), 120.3 (CH), 127.0 (CH), 133.7 (CH), 134.4 (C), 147.2 (C), 149.9 (C), 166.7 (C), 203.7 (C); IR (ATR/cm^{-1}) 1337, 1537, 1599, 1643, 1649; HRMS (ESI/TOF) *m/z* Calcd. for $C_{17}H_{20}N_2O_7Na$ [M+Na]$^+$ 387.1163, Found 387.1162.

Ethyl 3-hydroxy-2-(2,4-dinitrophenyl)-5-phenyl-2,4-pentadienoate (1i).[23] Yield 0.146 g, 0.38 mmol, 38%; yellow solid, mp 53–55 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (dd, *J* = 7.2, 7.2 Hz, 3H), 4.09 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.27 (dq, *J* = 7.2, 10.8 Hz, 1H), 6.28 (dd, *J* = 0.8, 15.6 Hz, 1H), 7.30–7.41 (m, 5H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 15.6 Hz, 1H), 8.46 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.90 (d, *J* = 2.4 Hz, 1H), 13.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 13.7 (CH_3), 61.7 (CH_2), 100.5 (C), 118.2 (CH), 120.3 (CH), 126.6 (CH), 127.9 (CH), 128.8 (H), 130.0 (CH), 134.8 (C), 136.1 (CH), 140.1 (CH), 147.2 (C), 149.7 (C), 167.4 (C), 170.2 (C), one signal was not observed because of the overlapping; IR (ATR/cm^{-1}) 1340, 1530, 1582, 1600, 1629, 1646; HRMS (ESI/TOF) *m/z* Calcd. for $C_{19}H_{16}N_2O_7Na$ [M+Na]$^+$ 407.0850, Found 407.0842.

Diethyl 3-hydroxy-2-(2,4-Dinitrophenyl)-2-pentenedioate (1j).[18] Yield 0.063 g, 0.17 mmol, 17%; yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (dd, *J* = 7.2, 7.2 Hz, 3H), 1.25 (dd, *J* = 7.2, 7.2 Hz, 3H), 3.07 (d, *J* = 15.2 Hz, 1H), 3.21 (d, *J* = 15.2 Hz, 1H), 4.01–4.29 (m, 4H), 7.70 (d, *J* = 8.4 Hz, 1H), 8.44 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.88 (d, *J* = 2.4 Hz, 1H), 13.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (CH_3), 14.0 (CH_3), 39.5 (CH_2), 61.9 (CH_2), 61.9 (CH_2), 102.4 (C), 120.2 (CH), 127.1 (CH), 135.1 (CH), 135.6 (C), 147.6 (C), 149.5 (C), 167.5 (C), 168.2 (C), 169.9 (C); IR (ATR/cm^{-1}) 1337, 1537, 1643, 1651, 1659, 1730, 1738, 1742; HRMS (ESI/TOF) *m/z* Calcd. for $C_{15}H_{16}N_2O_9Na$ [M+Na]$^+$ 391.0748, Found 391.0748.

Ethyl 4-chloro-3-hydroxy-2-(2,4-dinitrophenyl)-2-butenoate (1k). Yield: 0.135 g, 0.41 mmol, 41%; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (dd, *J* = 7.2, 7.2 Hz, 3H), 3.77 (d, *J* = 12.0 Hz, 1H), 3.98 (d, *J* = 12.0 Hz, 1H), 4.08 (dq, *J* = 7.2, 10.8 Hz, 1H), 4.28 (dq, *J* = 7.2, 10.8 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 8.50 (dd, *J* = 2.4, 8.4 Hz, 1H), 8.92 (d, *J* = 2.4 Hz, 1H), 12.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (CH_3), 40.8 (CH_2), 62.3 (CH_2), 102.3 (C), 120.3 (CH), 127.3 (CH), 134.7 (CH), 134.7 (C), 147.8 (C), 149.4 (C), 168.2 (C), 169.7 (C); IR (ATR/cm^{-1}) 1337, 1537, 1599, 1643, 1694, 1730; HRMS (ESI/TOF) *m/z* Calcd. for $C_{12}H_{11}ClN_2O_7Na$ [M+Na]$^+$ 353.0147, Found 353.0157.

General procedure of the transacylation of α-aryl-β-keto ester with diamine or amino alcohol

To a solution of α-(2,4-dinitrophenyl)-β-keto ester **1a** (186 mg, 0.5 mmol) in $CHCl_3$ (2.0 mL), was added 1,2-diaminopropane **13** (43 μL, 0.5 mmol), and the resultant solution was stirred for 1 day at room temperature. After the solvent was removed under the reduced pressure, the mixture was treated with column chromatography on silica gel to afford deacylated ester **5** (121 mg, 0.476 mmol, 96%, eluted with dichloromethane) and compound **14a** (64.9 mg, 0.495 mmol, 99%, eluted with methanol). When other keto esters, diamines, and amino alcohols were used, reactions were conducted in a similar way.

***N*-[(2-Hydroxy-1,1-dimethyl)ethyl]-4-methylbenzamide (21).**[21] Yield: 74 mg, 0.355 mmol, 71%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (s, 6H), 2.38 (s, 3H), 3.68 (s, 2H), 3.80–4.05 (br, 1H), 6.04–6.25 (br, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (CH_3), 24.7 (CH_3), 56.4 (C), 70.7 (CH_2), 126.9 (CH), 129.2 (CH), 131.9 (C), 142.1 (C), 168.4 (C); IR (ATR/cm^{-1}) 1057, 1454, 1504,

1537, 1632, 1643, 3379; HRMS (ESI/TOF) *m/z* Calcd. for $C_{12}H_{17}NO_2Na$ $[M+Na]^+$ 230.1152, Found 230.1159.

2-Amino-2-methylpropyl 4-methylbenzoate (22). Yield: 29 mg, 0.14 mmol, 28%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 6H), 2.35 (s, 3H), 3.66–4.00 (br, 2H), 4.25 (s, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 24.3 (CH_3), 52.8 (C), 70.3 (CH_2), 126.5 (CH), 129.1 (CH), 129.9 (C), 144.1 (C), 166.2 (C); IR (ATR/cm^{-1}) 1105, 1267, 1612, 1713, 1730; HRMS (ESI/TOF) *m/z* Calcd. for $C_{12}H_{18}NO_2$ $[M+H]^+$ 208.1332, Found 208.1339.

***N*-(2-Hydroxyethyl)-*N*-methylethanamide (27).**[21] Yield: 55 mg, 0.465 mmol, 93%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (s, 3H), 2.31-2.54 (br, 1H), 3.08 (s, 3H), 3.56 (t, *J* = 5.2 Hz, 2H), 3.79 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8 (CH_3), 37.6 (CH_3), 51.3 (CH_2), 61.7 (CH_2), 172.8 (C); IR (ATR /cm^{-1}) 1020, 1052, 1402, 1623, 3380; HRMS (ESI/TOF) *m/z* Calcd. for $C_5H_{11}NO_2Na$ $[M+Na]^+$ 140.0682, Found 140.0676.

***N*-Ethyl-*N*-(2-hydroxyethyl)ethanamide (28cx)**[21] Yield: 61 mg, 0.465 mmol, 93%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, *J* = 7.2 Hz, 3H), 2.13 (s, 3H), 3.37 (q, *J* = 7.2 Hz, 2H), 3.52 (t, *J* = 4.8 Hz, 2H), 3.54–3.62 (br, 1H), 3.77 (t, *J* = 4.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 21.3 (CH_3), 45.0 (CH_2), 49.4 (CH_2), 62.6 (CH_2), 172.6 (C); IR (ATR/cm^{-1}) 1059, 1467, 1624, 3414; HRMS (ESI/TOF) *m/z* Calcd. for $C_6H_{14}NO_2$ $[M+H]^+$ 132.1019, Found 132.1024.

***N*-(2-Hydroxyethyl)-*N*-(2-propyl)ethanamide (29).**[21] Yield: 48 mg, 0.33 mmol, 66%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, *J* = 6.4 Hz, 6H), 2.17 (s, 3H), 3.29–3.42 (br, 1H), 3.45 (t, *J* = 4.0 Hz, 2H), 3.74 (t, *J* = 4.0 Hz, 2H), 4.04 (sep, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (CH_3), 21.8 (CH_3), 43.9 (CH_2), 49.8 (CH), 64.4 (CH_2), 173.0 (C); IR (ATR/cm^{-1}) 1052, 1197, 1347, 1420, 1616, 3380; HRMS (ESI/TOF) *m/z* Calcd. for $C_7H_{16}NO_2$ $[M+H]^+$ 146.1196, Found 146.1182.

3-Aza-4-methyl-1-pentyl ethanoate (33).[24] Yield: 25 mg, 0.170 mmol, 34%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (d, *J* = 6.0 Hz, 6H), 1.44–1.64 (br, 1H), 2.07 (s, 3H), 2.83 (sep, *J* = 6.0 Hz, 1H), 2.85 (t, *J* = 5.2 Hz, 2H), 4.17 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9 (CH_3), 22.9 (CH_3), 45.7 (CH_2), 48.4 (CH_2), 64.5 (CH_2), 171.0 (C); IR (ATR/cm^{-1}) 1046, 1244, 1369, 1740; HRMS (ESI/TOF) *m/z* Calcd. for $C_7H_{15}NO_2Na$ $[M+Na]^+$ 168.0995, Found 168.0988.

3-Aza-4,4-dimethyl-1-pentyl acetate (34).[21] Yield: 75 mg, 0.47 mmol, 94%; Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (s, 9H), 2.06 (s, 3H), 2.15–2.32 (br, 1H), 2.82 (t, *J* = 5.6 Hz, 2H), 4.16 (t, *J* = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9 (CH_3), 28.8 (CH_3), 41.2 (CH_2), 50.6 (C), 64.9 (CH_2), 171.0 (C); IR (ATR/cm^{-1}) 1070, 1233, 1713, 1730, 1746; HRMS (ESI/TOF) *m/z* Calcd. for $C_8H_{18}NO_2$ $[M+H]^+$ 160.1332, Found 160.1327.

4-Aza-1-hexyletanoate (32cy).[25] Yield: 64 mg, 0.44 mmol, 88%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (t, *J* = 7.2 Hz, 3H), 2.06 (s, 3H), 2.27 (tt, *J* = 6.0, 8.0 Hz, 2H), 3.03 (t, *J* = 8.0 Hz, 2H), 3.07 (q, *J* = 7.2 Hz, 2H), 4.19 (t, *J* = 6.0 Hz, 2H), 5.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.2 (CH_3), 20.8 (CH_3), 25.5 (CH_2), 43.0 (CH_2), 44.5 (CH_2), 61.2 (CH_2), 170.9 (C); IR (ATR/cm^{-1}) 1048, 1245, 1740, 3378; HRMS (ESI/TOF) *m/z* Calcd. for $C_7H_{16}NO_2$ $[M+H]^+$ 146.1176, Found 146.1181.

5-Aza-1-heptyl ethanoate (32cz). Yield: 74 mg, 0.465 mmol, 93%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, *J* = 7.2 Hz, 3H), 1.57 (tt, *J* = 6.4, 7.2 Hz, 2H), 1.68 (tt, *J* = 7.2, 7.2 Hz, 2H), 2.04 (s, 3H), 2.25–2.34 (br, 1H), 2.65 (t, *J* = 7.2 Hz, 2H), 2.67 (q, *J* = 7.2 Hz, 2H), 4.07 (t, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0 (CH_3), 20.9 (CH_3), 26.3 (CH_2), 26.5 (CH_2), 44.0 (CH_2), 49.1 (CH_2), 64.3 (CH_2), 171.1 (C); IR (ATR/cm^{-1}) 1046, 1240, 1734, 3309; HRMS (ESI/TOF) *m/z* Calcd. for $C_8H_{18}NO_2$ $[M+H]^+$ 160.1332, Found 160.1337.

3-Aza-1-pentyl 4-methylbenzoate (32ax).[26] Yield: 95 mg, 0.460 mmol, 92%; yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (t, *J* = 7.2 Hz, 3H), 2.37 (s, 3H), 3.10 (q, *J* = 7.2 Hz, 2H), 3.31 (t, *J* = 5.2 Hz, 2H), 4.66 (t, *J* = 5.2 Hz, 2H), 5.90–6.42 (br, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.98 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6 (CH_3), 21.6 (CH_3), 43.1 (CH_2), 45.9 (CH_2), 60.3 (CH_2), 126.4 (C), 129.2 (CH), 130.0 (CH), 144.2 (C), 166.3 (C); IR (ATR/cm^{-1}) 1107, 1269, 1454, 1613, 1713; HRMS (ESI/TOF) *m/z* Calcd. for $C_{12}H_{18}NO_2$ $[M+H]^+$ 208.1332, Found 208.1338.

4-Aza-1-hexyl 4-methylbenzoate (32ay). Yield: 104 mg, 0.470 mmol, 94%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (t, *J* = 7.2 Hz, 3H), 2.30 (tt, *J* = 6.4, 7.2 Hz, 2H), 2.39 (s, 3H), 3.00 (q, *J* = 7.2 Hz, 2H), 3.05 (t, *J* = 7.2 Hz, 2H), 4.44 (t, *J* = 6.4 Hz, 2H), 5.48–5.68 (br, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.8 (CH_3), 21.6 (CH_3), 26.2 (CH_2), 43.1 (CH_2), 44.8 (CH_2), 61.8 (CH_2), 127.0 (C), 129.1 (CH), 129.6 (CH), 143.9 (C), 166.6 (C); IR (ATR/cm^{-1}) 1107, 1271, 1537, 1612, 1713; HRMS (ESI/TOF) *m/z* Calcd. for $C_{13}H_{20}NO_2$ $[M+H]^+$ 222.1489, Found 222.1498.

5-Aza-1-heptyl 4-methylbenzoate (32az). Yield: 112 mg, 0.475 mmol, 95%; brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (t, *J* = 7.2 Hz, 3H), 1.86 (tt, *J* = 6.4, 7.2 Hz, 2H), 2.05 (tt, *J* = 7.2, 7.2 Hz, 2H), 2.38 (s, 3H), 2.99 (t, *J* = 7.2 Hz, 2H), 3.02 (q, *J* = 7.2 Hz, 2H), 3.06–3.99 (br, 1H), 4.29 (t, *J* = 6.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.1 (CH_3), 21.6 (CH_3), 22.8 (CH_2), 26.2 (CH_2), 42.7 (CH_2), 46.8 (CH_2), 63.6 (CH_2), 127.3 (C), 129.1 (CH), 129.6 (CH), 143.7 (C), 166.5 (C); IR (ATR/cm^{-1}) 1109, 1273, 1454, 1612, 1713; HRMS (ESI/TOF) *m/z* Calcd. for $C_{14}H_{22}NO_2$ $[M+H]^+$ 236.1645, Found 236.1654.

3-Aza-4-methyl-1-pentyl 4-methylbenzoate (38).[27] Yield: 109 mg, 0.495 mmol, 99%; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.0 Hz, 6H), 2.39 (s, 3H), 2.80–2.87 (br, 1H), 2.92 (sep, *J* = 6.0 Hz, 1H), 3.01 (t, *J* = 5.6 Hz, 2H), 4.42 (t, *J* = 5.6 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 22.6 (CH_3), 45.6 (CH), 48.5 (CH_2), 64.4 (CH_2), 127.4 (C), 129.1 (CH), 129.6 (CH), 143.7 (C), 166.6 (C); IR (ATR/cm^{-1}) 1109, 1267, 1504, 1556, 1713; HRMS (ESI/TOF) *m/z* Calcd. for $C_{13}H_{20}NO_2$ $[M+H]^+$ 222.1489, Found 222.1497.

3-Aza-4,4-dimethyl-1-pentyl 4-methylbenzoate (39).[27] Yield: 116 mg, 0.495 mmol, 99%; yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (s, 9H), 2.10–2.31 (br, 1H), 2.39 (s, 3H), 2.95 (t, *J* = 5.6 Hz, 2H), 4.40 (t, *J* = 5.6 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 28.9 (CH_3), 41.4 (CH_2), 50.5 (C), 65.3 (CH_2), 127.5 (C), 129.1 (CH), 129.6 (CH), 143.6 (C), 166.6 (C); IR (ATR/cm^{-1}) 1101, 1269, 1537, 1632, 1713, 1728; HRMS (ESI/TOF) *m/z* Calcd. for $C_{14}H_{22}NO_2$ $[M+H]^+$ 236.1645, Found 236.1656.

Keywords: Chemoselectivity • Regioselectivity • Acylation • Amino alcohols • Steric hindrance

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[27] This compound appears in only Supporting Information.

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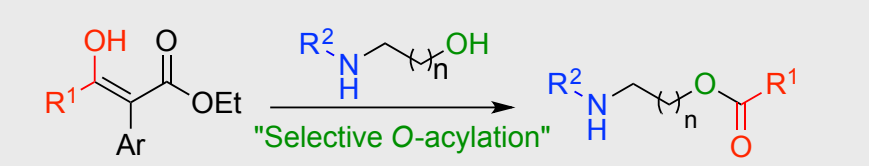

Key Topic*

*Author(s), Corresponding Author(s)**

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Title

Acylation using an α-aryl-β-keto ester facilitated the regioselective-acylation of the less hindered amino group in diamine without protecting the other. The transacylation using *N*-alkylamino alcohol resulted in chemoselective *O*-acylation without protecting the amino group in the absence of metal catalyst. These reactions proceed efficiently because of the pseudo-intramolecular process.

*Selective Acylation