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Transacylation of α-Aryl-β-keto Esters

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The acyl group of an α-aryl-β-keto ester was readily transferred to *N*-, *O*-, and *S*-nucleophiles. The transacylation from arylated diethyl 3-oxoglutarate to amines led to unsymmetrical malonic acid amide esters in high yields. The present reaction proceeded under mild conditions without formation of detectable byproducts. Only simple experimental manipulations were required. This reaction was also found to be sensitive to steric factors, which enabled the chemoselective monoacylation of diamines and amino alcohols without any modifications such as protection.

Introduction

In our previous work, we have shown that *cine*-substitution readily proceeds in the reaction of 1-methyl-3,6,8-trinitro-2-quinolone (**1**) with 1,3-dicarbonyl compounds in the presence of triethylamine.[1] The attack of the nucleophile at the 4 position and the subsequent elimination of nitrous acid resulted in regioselective functionalization; namely, β-diketone, β-keto ester, and β-diester functions were introduced. During our subsequent studies of *cine*-substituted quinolones **2**, we found that keto esters **2b** and **2c** showed reactivity different from diketone **2a**. Diketone **2a** could be isolated with column chromatography on silica gel, and conversion from **2a** to pyrazolylquinolone **3** was easily performed upon treatment with methylhydrazine. On the other hand, keto esters **2b** and **2c** afforded only deacylated product, quinolylacetic acid **4**, under the same conditions. These results demonstrated that the acyl group of β-keto esters appeared to be activated with a quinolyl group and prompted us to exploit this observation for new methodology. We realized that transfer of the activated acyl group from α-aryl-β-keto esters to nucleophiles could be employed as a new acylating procedure. 2-Arylated 3-oxogulutarate seems especially suitable for the preparation of unsymmetrical malonic acid derivatives. Dicarboxylic acids and their derivatives are important synthetic intermediates in the synthesis of various kinds of polyfunctionalized systems.[2] Among them, unsymmetrical acid derivatives are valuable tools for elaborate molecular design.[3,4] While succinic (or adipic) acid amide esters are easily prepared by aminolysis of corresponding acid anhydrides,[2] synthesis of unsymmetrical derivatives of malonic acid cannot be performed in a similar way because malonic anhydride is not commonly used. Hence, they are generally prepared by aminolysis of diethyl malonate or by chemical conversion from malonic acid.[4] These methods require selective chemical transformation of one of the two equivalent carbonyl groups, which sometimes accompanies troublesome manipulations such as separation of amide ester and diamide. From this viewpoint, development of alternative procedures for the preparation of unsymmetrical malonic acid derivatives could be useful. In the present paper, we would like to describe new methodology for acylation chemistry, which proceeds via the transacylation of α-aryl-β-keto esters.

Results and Discussion

Preparation of α-Aryl-β-keto Esters. While it is known that α-aryl-β-diketones are easily prepared,[5,6] the number of reports dealing with preparation of α-aryl-β-keto esters are markedly few.[7,8] We actually attempted to introduce a phenyl group at the α position of ethyl

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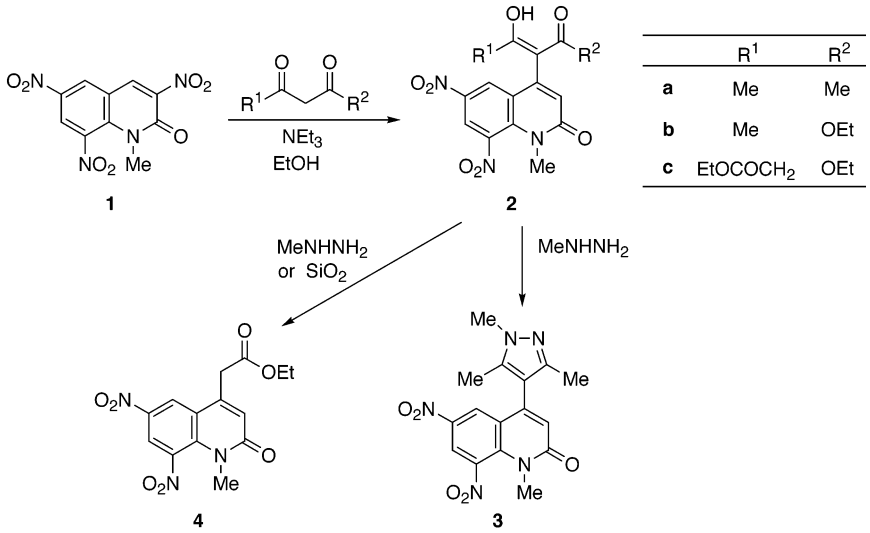
SCHEME 1. Chemical Transformation of Nitroquinolones



	R^1	R^2
a	Me	Me
b	Me	OEt
c	$EtOCOCH_2$	OEt

acetoacetate (**EAA**−**H**) with iodobenzene in the presence of copper iodide under the same conditions used for β-diketones;[5] however, phenylacetic acid was isolated in 34% yield instead of the desired product **EAA**−**Ph**. The phenylation of **EAA**−**H** surely proceeded at the α position to afford **EAA**−**Ph**, however, its deacetylation successively occurred. This fact means that the acetyl group was activated with a phenyl group similar to a quinolyl group. Although deacylation of α-aryl-β-diketones[9] or α-aryl-β-keto esters[10] is sometimes observed, this reactivity has not been used for acylation. In the present work, we employ a 2,4-dinitrophenyl (DNP) group as the activating group.

The introduction of a DNP group to **EAA**−**H** was easily achieved by the nucleophilic substitution of 1-chloro-2,4-dinitrobenzene (**DNP**−**Cl**) with sodium enolate (**EAA**−**Na**), which was prepared from **EAA**−**H** and sodium hydride. In the arylation of diethyl 3-oxoglutarate (**DEOG**−**H**), the reaction mixture was complicated under the same conditions due to the presence of one more active methylene group. The use of a milder base such as potassium carbonate and sodium ethoxide improved the yield of **DEOG**−**DNP** to 22 and 62%, respectively. Triethylamine was found to be the most suitable base for this reaction because the formation of byproducts was not observed. As a result of the survey of reaction conditions, stirring reagents at room temperature in the presence of 10 equiv of triethylamine effectively improved the isolated yield of **DEOG**−**DNP** up to 86%.

It was confirmed by ^{1}H NMR spectra that both **EAA**−**DNP** and **DEOG**−**DNP** existed in the enol form.[8,11] The methylene hydrogens of the ethoxy group were unequivalently observed in both cases, which indicated that these arylated keto esters have rigid structures. Since **DEOG**−**DNP** showed a pair of signals having a large coupling constant (15.5 Hz) at 3.11 and 3.23 ppm, the position of the double bond was indicated between the 2 and 3 positions and not between the 3 and 4 positions.

Transacylation from α-Aryl-β-keto Esters to Nucleophiles. To a solution of **EAA**−**DNP** in chloroform, stoichiometric propylamine **5a** was added and the mixture was stirred at room temperature for 1 day. After removal of the solvent, the residue was purified by column chromatography on silica gel to isolate transacylated products, *N*-propylacetamide **6a** and ethyl 2,4-dinitrophenylacetate **7**, in 95 and 92% yields, respectively. Ethanol and acetonitrile were also usable as solvents for this reaction. Since treatment of **EAA**−**H** with **5a** under the same conditions caused no change, the aryl group at the α position was found to be necessary for this transacylation reaction to occur. The reaction was monitored with ^{1}H NMR using chloroform-*d* as the solvent. When propylamine **5a** was added to a solution of **EAA**−**DNP**, the signal of the enol hydroxyl group immediately disappeared and signals of the propyl group were observed in a lower field than those of **5a**. This indicated that **EAA**−**DNP** was converted to ammonium enolate **8a**. Then signals of **6a** and **7** gradually increased as those of **8a** decreased, and 90% of **8a** was consumed within 4 h at room temperature (Figure 1). It is noteworthy that the reaction quantitatively proceeded without formation of any byproduct detectable (Table 1, run 1). Unsymmetrical malonic acid amide ester **9a** was also quantitatively obtained according to our expectation upon treatment of **DEOG**−**DNP** with **5a** in the same way.

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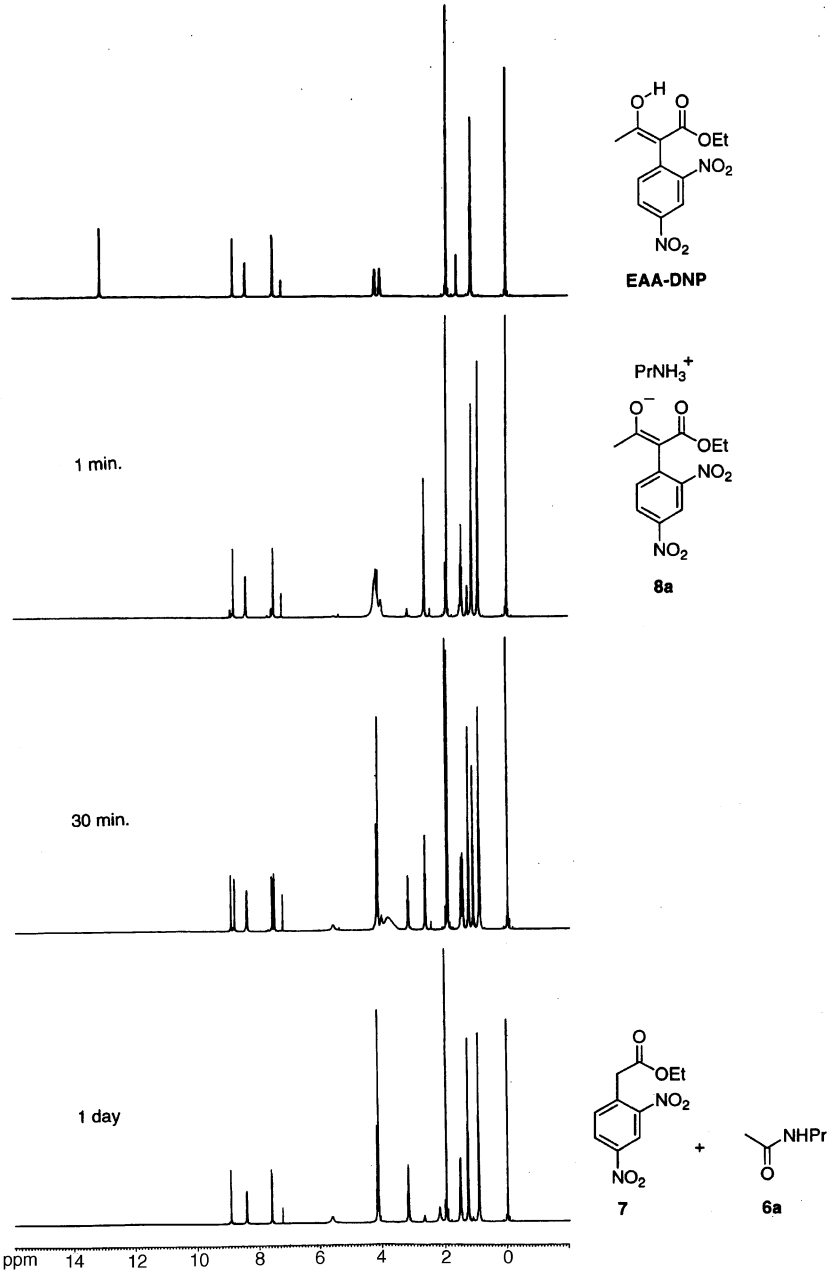
CHART 1. Monitoring the Transacylation by ^{1}H NMR



The present transacylation was applicable to other amines with observation of a different reaction rate caused by steric bulk of amines (Table 1, runs 2−3). When **EAA**−**DNP** was treated with isopropylamine **5b**, the transacylation effectively proceeded to afford corresponding products **6b** and **7**, which required 15 h for 90% conversion. In the case of *tert*-butylamine **5c**, the formation of ammonium enolate **8c** was confirmed with ^{1}H NMR; however, the subsequent transacylation did not occur even at 140 °C in a sealed tube. **DEOG**−**DNP** afforded a similar tendency in a series of reactions with **5a**−**c**. Since **DEOG**−**DNP** was more reactive than **EAA**−**DNP** due to the presence of an electron-withdrawing ethoxycarbonyl group, the transacylation to **5c** did occur, providing amide ester **9c** quantitatively under reflux conditions (Table 1, runs 4−8).

Competitive reactions were conducted in order to evaluate the effect of the amines on the rate of the transacylation. The ratios of **A**/**B** corresponded to those of the integrals in the ^{1}H NMR since the reactions were completed with no byproduct (Table 2). This reaction precisely recognized the presence of a methyl group at the α position of the amino group (runs 1−4), and the different position of a methyl group between the α and the *β* positions was effectively distinguished (runs 7 and 8). The presence of a methyl group at the *β* position was also recognized although the selectivity was lowered (runs 5 and 6). In the case of a combination of secondary and tertiary amines, high selectivity was achieved even at elevated temperature (run 9).

The sensitivity of this reaction to steric bulk enabled the selective acylation of 1,2-diaminopropane **5g** (Table

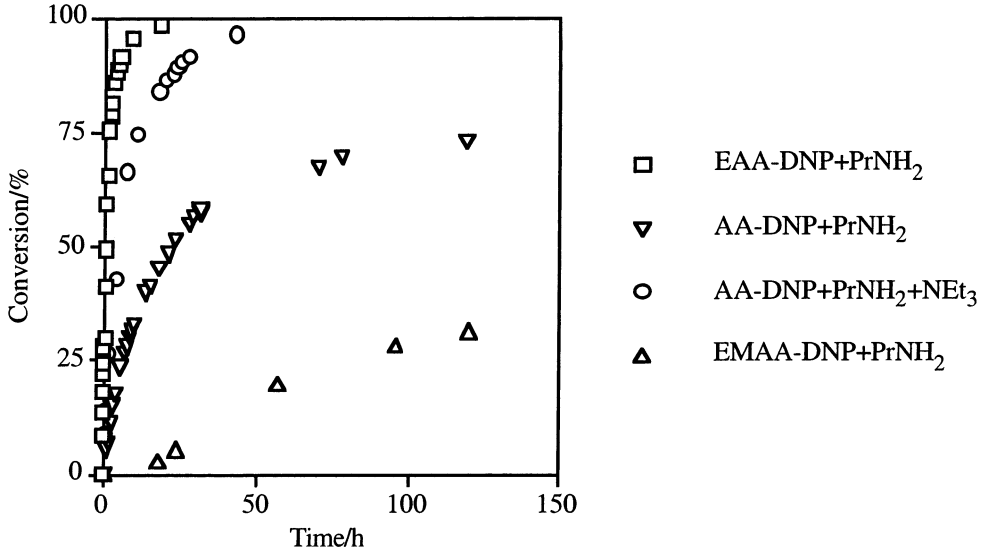
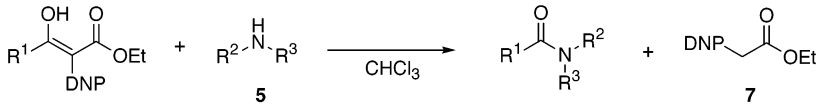
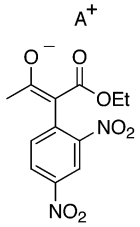


FIGURE 1. Different reactivity depending on 1,3-dicarbonyl compounds.

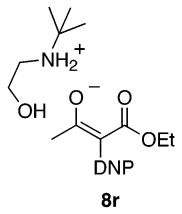
TABLE 1. Transacylation from α-Aryl-β-keto Esters to Amines



run	R^1	R^2	R^3	temp/°C	time/d	additive	product	yield/%
1	Me	Pr	H	rt	1		**6a**	quant.
2	Me	*i*-Pr	H	rt	1		**6b**	98
3	Me	*t*-Bu	H	140	1		**6c**	0
4	CH_2COOEt	Pr	H	rt	1		**9a**	quant.
5	CH_2COOEt	*i*-Pr	H	rt	1		**9b**	49
6	CH_2COOEt	*i*-Pr	H	61	1		**9b**	quant.
7	CH_2COOEt	*t*-Bu	H	61	1		**9c**	48
8	CH_2COOEt	*t*-Bu	H	61	7		**9c**	quant.
9	Me	Et	Et	rt	1		**6h**	0
10	Me	Et	Et	80	2		**6h**	quant.
11	Me	$-(CH_2)_4-$		rt	1		**6i**	quant.
12	Me	$-(CH_2)_2-O-(CH_2)_2-$		rt	1		**6j**	90
13	CH_2COOEt	Et	Et	61	7		**9h**	quant.
14	CH_2COOEt	$-(CH_2)_4-$		61	1		**9i**	quant.
15	Me	Ph	H	rt	1		**6l**	0
16	Me	Ph	H	80	1	NEt_3	**6l**	77
17	Me	*p*-$MeOC_6H_4$	H	80	2		**6n**	quant.
18	CH_2COOEt	Ph	H	61	1		**9l**	trace
19	CH_2COOEt	Ph	H	61	7	NEt_3	**9l**	quant.
20	CH_2COOEt	*p*-$NO_2C_6H_4$	H	61	1	NEt_3	**9m**	trace
21	CH_2COOEt	*p*-$MeOC_6H_4$	H	rt	1		**9n**	62



	A
8a	$PrNH_3$
8c	*t*-$BuNH_3$
8l	$PhNH_3$
8o	$HNEt_3$



8r

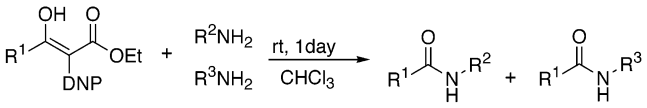
FIGURE 2. Ammonium enolate **8**.

3). Commercially available acetyl chloride and ethoxymalonyl chloride could not distinguish between the two amino groups and produced both possible monoacylated products in almost equal amounts (runs 2 and 4). On the other hand, keto esters having a DNP group reacted with equimolar **5g** to acylate the terminal amino group selectively. In both cases, the transacylation quantitatively proceeded at room temperature without protection of the internal amino group (runs 1 and 3). Furthermore, the reaction did not require the presence of base for trapping generated acids.

Secondary amines **5h**−**j** were usable for the present transacylation, and cyclic amines were acylated faster than acyclic amines (Table 1, runs 9−14). In the case of diamine **5k**, the primary amino group was predominantly acylated with no modification of the secondary amino group (Scheme 2).

In the present transacylation, the initial formation of ammonium enolate **8** seems to be an important step. To confirm this consideration, the transacylation using ethyl

TABLE 2. Competitive Transacylation Sensitive to Steric Bulk of Amines

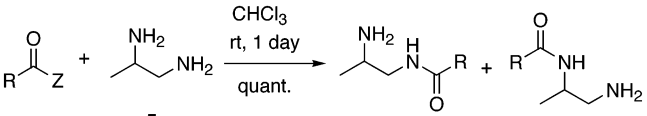


A B

run	R^1	R^2		R^3		A/B
1	Me	*n*-Pr	**5a**	*i*-Pr	**5b**	88/12
2	CH_2COOEt	*n*-Pr	**5a**	*i*-Pr	**5b**	94/6
3	Me	*n*-Bu	**5d**	*s*-Bu	**5e**	95/5
4	CH_2COOEt	*n*-Bu	**5d**	*s*-Bu	**5e**	96/4
5	Me	*n*-Bu	**5d**	*i*-Bu	**5f**	58/42
6	CH_2COOEt	*n*-Bu	**5d**	*i*-Bu	**5f**	60/40
7	Me	*i*-Bu	**5f**	*s*-Bu	**5e**	82/18
8	CH_2COOEt	*i*-Bu	**5f**	*s*-Bu	**5e**	96/4
9[a]	CH_2COOEt	*s*-Bu	**5e**	*t*-Bu	**5c**	98/2

[a] At 61 °C.

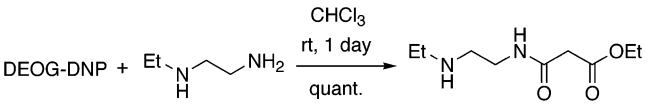
TABLE 3. Selective Acylation of 1,2-Propanediamine



run	R	Z	A/B
1	Me	CH(DNP)COOEt	100/0
2[a]	Me	Cl	55/45
3	CH_2COOEt	CH(DNP)COOEt	100/0
4[a]	CH_2COOEt	Cl	50/50

[a] In the presence of 1 equiv of triethylamine.

SCHEME 2. Selective Acylation of *N*-ethyl-1,2-diaminoethane (5k)



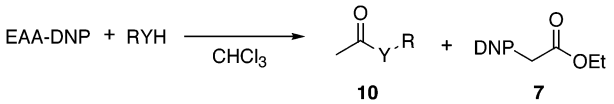
5k 9k

α-(2,4-dinitrophenyl)-α-methylacetoacetate (**EMAA−DNP**) was studied. As this compound exists in the keto form only, it does not have the acidic enol group. The transacylation from **EMAA−DNP** to propylamine **5a** proceeded, giving transacylated products; however, the reaction rate was much slower (39% conversion after 170 h) than that of **EAA−DNP** (90% conversion after 4 h) (Figure 1). The large difference of reaction rate cannot be clearly explained by only steric hindrance of the methyl group adjacent to the reaction site, and the absence of the acidic enol group in **EMAA−DNP** is thought to be an important cause for this deceleration. The experiment using ^{1}H NMR showed that treatment of **EAA−DNP** with aniline **5l** caused no change such as formation of anilinium enolate **8l** because of low basicity of **5l**. The transacylation did not occur even when this solution was heated. This disadvantage was overcome by adding triethylamine to the reaction mixture for conversion of **EAA−DNP** into triethylammonium enolate **8o** though heated conditions and longer reaction times were required for the transacylation (Table 1, runs 15−16). In reactions of **DEOG−DNP** with aniline derivatives,

EMAA-DNP **AA-DNP**

FIGURE 3. Other 2-arylated 1,3-dicarbonyl compounds.

TABLE 4. Transacylation to Alcohols and Thiol



10 7

run	R	Y	product	temp/ °C	time/ d	additive	yield/ %
1	Et	O	**10p**	80	7	NEt_3	63
2	Et	S	**10q**	rt	10	NEt_3	44
3	Et	S	**10q**	80	7	NEt_3	74
4	*t*-Bu$(CH_2)_2$	O	**10r**	80	0.3		quant.
5	$NH_2CMe_2CH_2$	O	**10s**	80	7		80

remarkable substituent effects were observed (Table 1, runs 18−21). While *p*-nitroaniline **5m** was recovered, even though the mixture was heated with triethylamine, *p*-methoxyaniline **5n** effectively reacted to furnish amide ester **9n** at room temperature in the absence of triethylamine.

Less nucleophilic and less basic ethanol and ethanethiol also were reacted with **EAA−DNP**. The transacylation similarly proceeded to give corresponding products; however, it required more severe conditions (Table 4). These results prompted us to study the reaction using amino alcohols having a sterically hindered amino group. O-Acylation proceeded without protection of the amino group, and it is noteworthy that the reaction rate was much faster than that of ethanol in the presence of triethylamine. The formation of ammonium enolate **8r** is considered to realize the easy approach of the hydroxyl group to the EAA moiety.

Application of the transacylation to α-aryl-*β*-diketone was also studied (Figure 1). When acetylacetone, having a DNP group (**AA−DNP**), was treated with propylamine **5a** under the same conditions used for **EAA−DNP**, the acetyl group was similarly transferred from **AA−DNP** to **5a**, despite a quite slow reaction rate (75% conversion after 120 h). This problem was dissolved by adding triethylamine; namely, the conversion was improved to 97% after 42 h. Thus α-arylated *β*-diketones also can be used as acylating agents by the transacylation.

A Plausible Mechanism. On the basis of the above experimental facts, a plausible mechanism of the present reaction was provided. The EAA and DNP moieties are distorted through about 60° because of their steric repulsion.[11] When a sterically hindered substituent is introduced at the α position of the carbonyl group, only the keto form is destabilized[12] to give the stable enol form consequently. Actually, only signals of enol forms were observed in the ^{1}H NMR of **EAA−DNP** and **DEOG−DNP**. In addition, introduction of a DNP group into **EAA−H** increases the acidity with approximately 7 orders of magnitude, which means that **EAA−DNP** is a stronger acid than acetic acid.[11,13] Hence, α-aryl-*β*-keto

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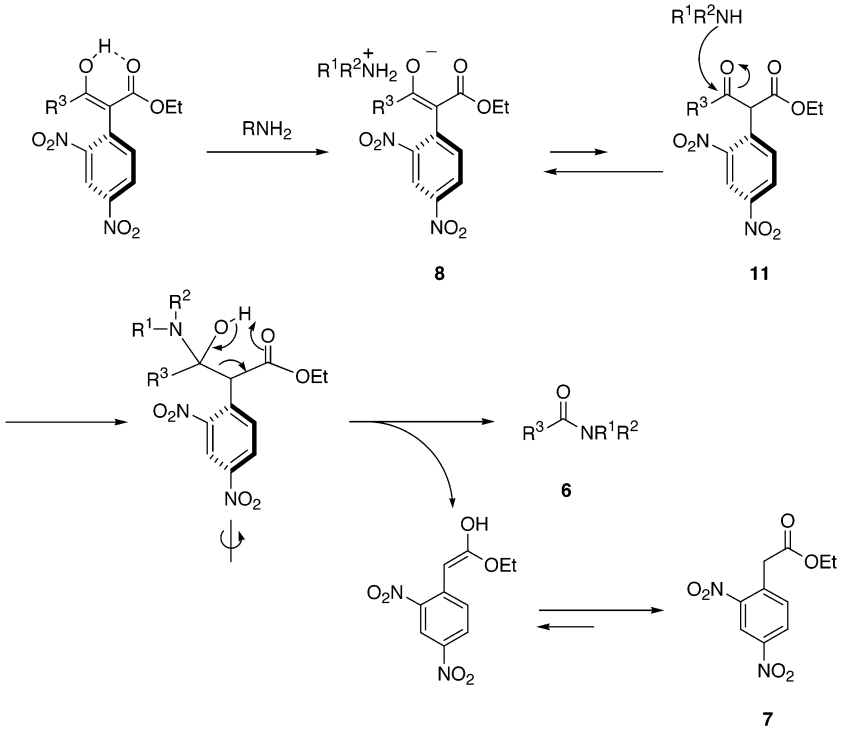
SCHEME 3. A Plausible Mechanism for the Transacylation



esters were immediately converted to corresponding ammonium enolates **8** accompanied by fission of an intramolecular hydrogen bond just after addition of amines. When the keto form **11** is produced under equilibrium, both nucleophile and electrophile (amine and **11**) are in close proximity. This intimate-pair effect realizes the quantitative transacylation under mild conditions. During the nucleophilic substitution of **11** with amine, the benzene ring rotates to attain coplanarity with adjacent carbonyl group, which assists the elimination of transacylated products.

In cases of less basic nucleophiles such as anilines and ethanol, addition of triethylamine was necessary for conversion of **EAA**−**DNP** to ammonium enolate **8**. However, longer reaction time and higher reaction temperature were required due to the intermolecular process without the intimate-pair effect. The reaction was quite slow in the case of aniline, even though the mixture is heated with triethylamine. On the other hand, the reaction with *p*-methoxyaniline effectively proceeded at room temperature in the absence of triethylamine. The *O*-acylation of *N*-*tert*-butylethanol was rather fast since formation of the intimate pair was possible. The transacylation of **EMAA**−**DNP**, having no acidic proton, was remarkably slow, which also supported this mechanism though the steric hindrance of a methyl group should be taken into consideration.

In the case of β-diketone, introduction of a DNP group stabilizes the enol form to excess. The estimated difference of heat of formation[14] between the keto and the enol forms for **EAA**−**DNP** was 35.77 kJ/mol and that for **AA**−**DNP** was 39.16 kJ/mol. Since the excessively stabilized enol form cannot easily be converted to the keto form, the transacylation using **AA**−**DNP** is considered to be slower than that of α-aryl-β-keto ester. Furthermore, the distorted benzene ring at the α position and a nitro group on the benzene ring prevent the approach of sterically hindered nucleophiles to the keto ester moiety. This congestion around the keto ester enabled the selective acylation distinguishing the steric bulk of nucleophiles.

Conclusions

The transacylation from α-aryl-β-keto esters to amines could be performed conveniently at ambient conditions without an inert atmosphere. In studied reactions, no byproducts were detected and separation of amide and deacylated product was quite easy. Steric factors were important for selectivity of the reaction. For example, the selective acylation of an unsymmetrical diamine or amino alcohol was achieved in a single step without any protection. Hence, the present transacylation provided a new methodology for acylation chemistry such as a convenient synthesis of malonic acid amide esters, which was demonstrated.

The number of reports dealing with an α-aryl-β-keto ester[15] is considerably fewer than reports dealing with an α-aryl-β-diketone.[16] The facility of the retro-Claisen-type deacylation described in this report might be the

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cause for difficulties in the preparation of α-aryl-β-keto ester compared with α-aryl-β-diketone.

Experimental Section

General Methods. All chemicals were commercially available and were used as received without further purification. Tetrahydrofuran (THF) was dried with sodium and distilled before use. Other solvents were used without drying and purification. All of the reactions were carried out under ambient atmosphere. Each transacylated product was isolated with column chromatography on silica gel (isolated yield was 90−95%), and its structure was determined with comparison of spectral data with those of authentic sample, which was commercially available or prepared by acylation of amines (or alcohols) with commercial acetyl chloride or ethoxymalonyl chloride. The yields of **6** and **9** were determined with ^{1}H NMR of the reaction mixture. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded in $CDCl_3$ at 400 and at 100 MHz, respectively, with TMS as internal standard. ^{13}C NMR assignments (s, d, t, and q) were made from DEPT experiments. Column chromatography was performed using Merck silica gel 60.

Preparation of EAA−DNP. Preparation of **EAA−DNP** was conducted by using a procedure modified from the known method.[8] To a solution of **EAA−H** (1.30 g, 10 mmol) in THF (10 mL), sodium hydride (60 wt %, 0.80 g, 20 mmol) was gradually added, and the mixture was stirred at room temperature for 15 min. Then 1-chloro-2,4-dinitrobenzene (**DNP−Cl**, 2.02 g, 10 mmol) was added, and the resultant reddish solution was stirred for 1 day. After addition of 3 M hydrochloric acid (10 mL), generated sodium chloride was filtered off, and the filtrate was concentrated. The extraction of the residue with hot hexane (30 mL × 3) followed by concentration afforded **EAA−DNP** (2.70 g, 9.1 mmol, 91%). Further purification was performed with recrystallization from hexane. **EMAA−DNP** and **AA−DNP** were also prepared with the same procedure.

Ethyl α-(2,4-Dinitrophenyl)-α-methylacetoacetate (EMAA−DNP). Yellow plates. Mp 88−89 °C. IR (Nujol/cm^{-1}) 1722, 1701, 1531, 1342; ^{1}H NMR δ = 1.17 (dd, J = 7.2, 7.2 Hz, 3H), 1.98 (s, 3H), 2.59 (s, 3H), 4.12 (dq, J = 10.7, 7.2 Hz, 1H), 4.21 (dq, J = 10.7, 7.2 Hz, 1H), 7.70 (d, J = 8.7 Hz, 1H), 8.50 (dd, J = 8.7, 2.5 Hz, 1H), 8.99 (d, J = 2.5 Hz, 1H); ^{13}C NMR δ = 13.8 (q), 23.2 (q), 27.8 (q), 62.5 (t), 64.2 (s), 121.1 (d), 127.5 (d), 130.7 (d), 142.0 (s), 147.1 (s), 148.2 (s), 169.7 (s), 203.1 (s). Anal. Calcd for $C_{13}H_{14}N_2O_7$: C, 50.33; H, 4.55; N, 9.03. Found: C, 50.63; H, 4.55; N, 9.17.

Preparation of Diethyl 2-(2,4-Dinitrophenyl)-3-hydroxy-2-pentenedioate (DEOG−DNP). To a solution of diethyl 3-oxogulutarate (**DEOG−H**, 1.82 mL, 10 mmol) and **DNP−Cl** (4.05 g, 20 mmol) in ethanol (100 mL) was added triethylamine (14 mL, 100 mmol). The resultant reddish solution was stirred at room temperature for 7 days. After addition of 1 M hydrochloric acid (100 mL, 100 mmol), the mixture was extracted with benzene (50 mL × 3). The organic layer was dried over magnesium sulfate and concentrated solvent under reduced pressure to give crude oil. The residue was treated with column chromatography on silica gel to give **DEOG−DNP** (eluted with benzene-chloroform 1/1, 3.17 g, 8.6 mmol, 86%) as a yellow oil. TLC (SiO_2, $CHCl_3$, UV) R_f value = 0.58; IR (Nujol/cm^{-1}) 1722, 1701, 1531, 1342; ^{1}H NMR δ = 1.15 (dd, J = 7.1, 7.1 Hz, 3H), 1.27 (dd, J = 7.1, 7.1 Hz, 3H), 3.11 (d, J = 15.5 Hz, 1H), 3.23 (d, J = 15.5 Hz, 1H), 4.0−4.3 (m, 4H), 7.74 (d, J = 8.4 Hz, 1H), 8.47 (dd, J = 8.4, 2.3 Hz, 1H), 8.90 (d, J = 2.3 Hz, 1H), 13.06 (s, 1H); ^{13}C NMR δ = 13.8 (q), 14.1 (q), 39.5 (t), 61.8 (t), 62.0 (t), 102.5 (s), 120.3 (d), 127.3 (d), 135.2 (d), 135.7 (s), 147.6 (s), 149.5 (s), 167.6 (s), 168.2 (s), 170.0 (s). Anal. Calcd for $C_{15}H_{16}N_2O_9$: C, 48.92; H, 4.38; N, 7.61. Found: C, 49.13; H, 4.37; N, 7.45.

The Typical Procedure for the Transacylation. To a solution of **EAA−DNP** (296 mg, 1 mmol) in chloroform (10 mL), propylamine **5a** (82 μL, 1 mmol) was added. The resultant solution was stirred at room temperature for 1 day. After removal of the solvent, the residue was treated with column chromatography on silica gel to afford **7** (eluted with chloroform, 233 mg, 0.92 mmol) and *N*-propylacetamide **6a** (eluted with methanol, 77 mg, 0.95 mmol).

Ethyl (2,4-Dinitrophenyl)acetate. Yellow oil; TLC (SiO_2, $CHCl_3$, UV) R_f value = 0.40; ^{1}H NMR δ = 1.27 (t, J = 7.1 Hz, 3H), 4.16 (s, 2H), 4.19 (q, J = 7.1 Hz, 2H), 7.62 (d, J = 8.4 Hz, 1H), 8.45 (dd, J = 8.4, 2.3 Hz, 1H), 8.95 (d, J = 2.3 Hz, 1H); ^{13}C NMR δ = 14.1 (q), 39.7 (t), 61.9 (t), 120.7 (d), 127.5 (d), 134.7 (d), 136.6 (s), 147.4 (s), 148.9 (s), 168.6 (s). In the transacylation using other amines and alcohols, the experiment was conducted in a similar way.

Reaction Monitored with NMR. To a solution of **EAA−DNP** (29.6 mg, 0.1 mmol) in deuterated chloroform (0.3 mL), propylamine **5a** (8.2 μL, 0.1 mmol) was added. The sample tube was allowed to stand at room temperature, and the ^{1}H NMR spectrum was measured at intervals of either several minutes or several hours. Conversion of the reaction was determined with ratio of integrals for product and starting material since no signals were observed other than ammonium enolate **8a** and products **6a** and **7**. When other keto esters and nucleophiles were used, the experiments were similarly conducted. In cases of reactions under heated conditions, the tube was sealed after the sampling of reagents.

Competition Studies with Amines. To a solution of **EAA−DNP** (296 mg, 1 mmol) in chloroform (7 mL) was added a solution of propylamine **5a** (82 μL, 1 mmol) and isopropylamine **5b** (85 μL, 1 mmol) in chloroform (3 mL). The resultant solution was stirred at room temperature for 1 day. After removal of the solvent, the residue was allowed to measure the ^{1}H NMR spectrum. As no signal other than **6a**, **6b**, and **7** was observed, the ratio of transacylated products was determined with measuring integrals of **6a** and **6b**. When **DEOG−DNP** and other combination of amines were used, experiments were similarly carried out.

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