Tetrahedron 66 (2010) 2132–2140

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Studies on the Lossen-type rearrangement of *N*-(3-phenylpropionyloxy) phthalimide and *N*-tosyloxy derivatives with several nucleophiles

Md. Chanmiya Sheikh *, Shunsuke Takagi, Asako Ogasawara, Masayuki Ohira, Ryuta Miyatake, Hitoshi Abe, Toshiaki Yoshimura, Hiroyuki Morita

Department of Applied Chemistry, Faculty of Engineering, University of Toyama, 3190 Gofuku, Toyama 930-8555, Japan

ARTICLE INFO

Article history:
Received 13 November 2009
Received in revised form
18 January 2010
Accepted 20 January 2010
Available online 28 January 2010

Keywords:
Lossen rearrangement
Cross-linking reagent
Phthalimide
Active ester

ABSTRACT

The reaction of *N*-(3-phenylpropionyloxy)phthalimide (**1a**) and *N*-tosyloxy (**5a**,**b**) derivatives with nucleophiles was examined and found to give the products via Lossen-type rearrangement. In order to obtain the scope of this reaction mechanism, further studies the reaction of several *N*-sulfonyloxyimide derivatives with various nucleophiles under similar conditions were carried out and found to afford the corresponding same types of products in high yields.

1. Introduction

It is well known that hetero-functional bi-dentate cross-linking reagents such as DSG (disuccimidyl glutarate), MBS (*m*-malei-mid-obenzoyl-*N*-hydoxysuccinimide) and their related modified linkers are useful in the area of chemical conjugation of particular biologically active molecules.[1,2] Recently, by using MBS linker we have succeeded in synthesizing the particular antigen bearing oxidized cholesterol moiety by introducing SH group in the cholesterol framework.[3] While seeking more convenient and shorter synthetic route, we have finally used the stepwise approach, however, we could not find the good conditions to obtain the target molecules.[4] Under these backgrounds, we strongly thought that the new type of non-symmetrical cross-linking reagents bearing different bi-dentate reactivities should be realized. Recently, we have succeeded to synthesize the new non-symmetrical bi-dentate cross-linking reagents having two different reactivities toward various nucleophilic groups and demonstrated their usefulness for preparation of pre-antigen.[5] In the course of these syntheses, it is necessary and important to determine the reactivities of the 'active ester' groups toward the various nucleophiles. Therefore, at first we have determined the reactivity difference of several so-called 'activated carbonyl' groups using the model compounds i.e. *N*-(3-phenylpropionyloxy)phthalimide (**1a**), *N*-(3-phenylpro-pio-nyloxy)benzotriazole (**1b**), *N*-(3-phenylpropionyloxy)benzothiazole (**1c**), and *N*-(3-phenylpropionyl)benzotriazole (**1d**).[5,6] However, in the reaction of **1b**, **1c** or **1d** with BnOH, 3-phenylpropionic acid benzyl ester (**2a**) was obtained as a sole product and in the case of **1a**, we found unexpectedly the formation of 2-benzyloxycarbonyl-*N*-(benzyloxycarbonyl)aniline (**3a**) besides the desired normal product **2a**.[7] To study the scope and limitations of the reactions, we also prepared *N*-sulfonyloxyimide derivatives and studied their reactions toward several nucleophiles. Fahmy et al.[8a] reported the Lossen-type rearrangement product in *N*-(arysulfonyloxy)phthalimides using only base catalyzed aromatic amines. However, these reaction systems have not been applied to other organic reactions. Herein, we report the full details in the reaction of **1a** and *N*-sulfonyloxyimide derivatives toward the various nucleophiles with mechanistic studies.

2. Results and discussion

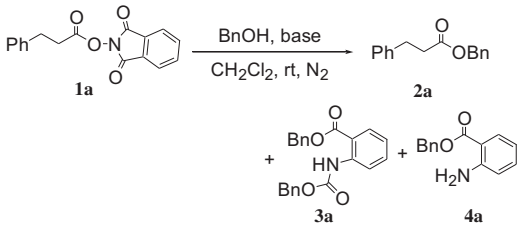
2.1. Reaction of 1a with benzyl alcohol in the presence of various bases

The active ester **1a** was prepared by the following procedure, which was reported previously.[5] In our initial experiments, we studied the reaction of **1a** with BnOH in the presence of various bases in CH_2Cl_2 at room temperature under N_2 and the corresponding ester **2a** was obtained as a sole product and unexpectedly we found the formation of **3a** in very low yield. The results are summarized in Table 1.

* Corresponding author.
E-mail address: chansheikh@yahoo.com (M. C. Sheikh).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.01.074

Table 1
Reaction of **1a** with BnOH in the presence of various bases



Entry	BnOH (equiv)	Base	Time (h)	Product[a] (% yield)		
				2a	**3a**	**4a**
1	2.0	4-DMAP	24	82	5	0
2	2.0	Et_3N	40	47	7	0
3	2.0	DBN	40	53	19	18
4	2.0	DBU	40	46	27	11

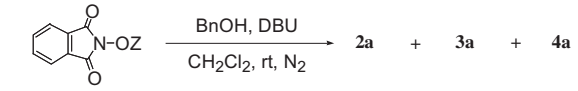
[a] Yields were not optimized.

As shown in Table 1, when the reaction was performed using, 4-DMAP or Et_3N as the base (entries 1,2), the yields of the side products, **3a** and 2-aminobenzoic acid benzyl ester (**4a**) were low. In contrast, higher yields of **3a** and **4a** were obtained when strong and more hindered base such as DBU or DBN was used (entries 3,4). About the products formation, we presumed that the reaction proceeded via the Lossen-type rearrangement.[8,9]

2.2. Reaction of 1a and *N*-tosyloxy derivatives (5a,b) with various hydroxyl compounds in the presence of DBU

In order to obtain additional examples, we studied the reaction of the corresponding tosyl ester,[10,11] *N*-tosyloxyphthalimide (**5a**), and *N*-(2-mesitylenesulfonyloxy)phthalimide (**5b**) having a better leaving group than **1a** (i.e., 3-phenylpropionate anion) with BnOH in the presence of DBU in CH_2Cl_2 at room temperature under N_2 and resulted in the greatly improved yield of the Lossen-type rearrangement product **3a**. The results are listed in Table 2.

Table 2
Reaction of **1a**, **5a** or **5b** with BnOH in the presence of DBU



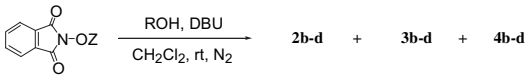
Z = -CO(CH$_2$)$_2$Ph (**1a**), -SO$_2$C$_6$H$_4$Me (**5a**), -SO$_2$C$_6$H$_2$Me$_3$ (**5b**)

Entry	Compound	BnOH (equiv)	Time (h)	Product[a] (% yield)		
				2a	**3a**	**4a**
1	**1a**	2.0	3	68	11	6
2	**1a**	2.0	12	62	21	9
3	**1a**	3.0	24	48	24	20
4	**5a**	2.0	0.5	0	91	trace
5	**5a**	2.0	24	0	93	trace
6	**5b**	2.0	0.5	0	90	trace
7	**5b**	2.0	24	0	93	trace

[a] Yields were not optimized.

As can we see in from Table 2, the rearranged product, i.e. **3a** was greatly increased and in addition, the product **4a**[12] was also increased (entries 2,3). Further, the reaction of **5a**,**b** revealed to afford the product **3a** in excellent yield (entries 4–7). For careful inspection of the products, next we studied the reaction toward several hydroxyl compounds {i.e., Bn(Me)OH, Bn(Ph)OH, and PhOH} under similar conditions. The results are shown in Table 3.

Table 3
Reaction of **1a**, **5a** or **5b** with several hydroxyl compounds in the presence of DBU

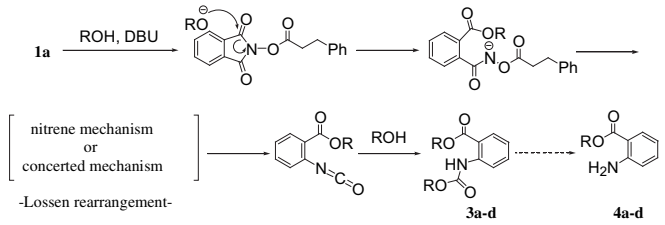


Z = -CO(CH$_2$)$_2$Ph (**1a**), -SO$_2$C$_6$H$_4$Me (**5a**), -SO$_2$C$_6$H$_2$Me$_3$ (**5b**)

Entry	Compound	ROH (2.0 equiv)	Time	Product[a] (% yield)		
				2b–d	**3b–d**	**4b–d**
1	**1a**		3 h	76 (**2b**)	13 (**3b**)	4 (**4b**)
2	**1a**		15 h	70 (**2b**)	22 (**3b**)	8 (**4b**)
3	**1a**		24 h	67 (**2b**)	23 (**3b**)	9 (**4b**)
4	**5a**		10 min	0 (**2b**)	96 (**3b**)	trace (**4b**)
5	**5b**		10 min	0 (**2b**)	95 (**3b**)	trace (**4b**)
6	**1a**		3 h	73 (**2c**)	12 (**3c**)	2 (**4c**)
7	**1a**		15 h	69 (**2c**)	19 (**3c**)	4 (**4c**)
8	**1a**		24 h	63 (**2c**)	23 (**3c**)	5 (**4c**)
9	**5a**		10 min	0 (**2c**)	95 (**3c**)	trace (**4c**)
10	**5b**		10 min	0 (**2c**)	93 (**3c**)	trace (**4c**)
11	**1a**	PhOH	3 h	78 (**2d**)	4 (**3d**)	**2**(**4d**)
12	**1a**		15 h	76 (**2d**)	6 (**3d**)	**3**(**4d**)
13	**1a**		24 h	75 (**2d**)	7 (**3d**)	**4**(**4d**)
14	**5a**		10 min	0 (**2d**)	95 (**3d**)	trace (**4d**)
15	**5b**		10 min	0 (**2d**)	93 (**3d**)	trace (**4d**)

[a] Yields were not optimized.

As shown in Table 3, the yield of the rearranged products, i.e. 2-benzyloxycarbonylamino benzoic acid 1-methylbenzyl ester (**3b**), 2-benzyloxycarbonylamino benzoic acid diphenylmethyl ester (**3c**), and 2-benzyloxycarbonylamino benzoic acid phenyl ester (**3d**)[13] was greatly increased toward all the hydroxyl compounds, i.e. Bn(Me)OH, Bn(Ph)OH, and PhOH (entries, 1–3, 6–8, 11–13). In addition, the products, 2-benzyloxycarbonylamino benzoic acid 1-methylbenzyl ester (**4b**),[14] 2-aminobenzoic acid diphenylmethyl ester (**4c**),[15] and 2-aminobenzoic acid phenyl ester (**4d**)[16] were also generated. We then examined the reaction of corresponding tosyl ester (**5a**,**b**) was also carried out under similar conditions and the best results were obtained in shorter time (entries, 4,5, 9,10, 14,15). The results clearly indicate that in the cases of the stronger base and better leaving group the Lossen-type rearrangement products **3a–d** are favored and increased. The mechanisms were considered for the formation of **3a–d** as shown in Scheme 1. However, the mechanisms for the formation of **4a–d** were unclear yet.



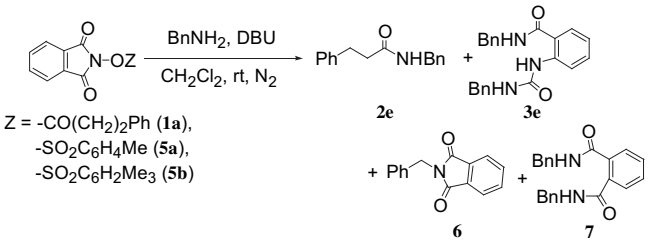
Scheme 1. Plausible mechanism for the formation of **3a–d**.

2.3. Reaction of 1a and *N*-tosyloxy derivatives (5a,b) with benzylamine in the presence of DBU

We studied the reaction of **1a** and **5a**,**b** with $BnNH_2$ having strong nucleophilicity, compared to BnOH, tend to attack the carbonyl carbon of ester group under similar conditions.

The results are summarized in Table 4. In this case the side products, *N*-benzyl-2-(3-benzylureido)benzamide (**3e**),[17] *N*-benzylphthalimide (**6**),[18] and *N*,*N*-dibenzylphthalimide (**7**)[19] were obtained when the reaction time was very short but yield was not high. The products **3e** and **7** were increased and to give relatively reduced yield of **6** after passing the reaction time. The results are shown in Table 4.

Table 4
Reaction of **1a**, **5a** or **5b** with $BnNH_2$ in the presence of DBU

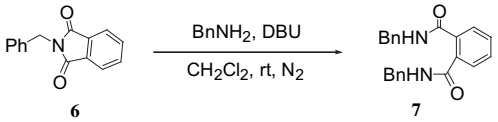


Entry	Compound	$BnNH_2$ (equiv)	DBU (equiv)	Time	Product[a] (% yield)			
					2e	**3e**	**6**	**7**
1	**1a**	2.0	2.0	3 h	58	Trace	36	6
2	**1a**	2.0	2.0	12 h	55	2	32	9
3	**1a**	2.0	2.0	24 h	54	3	19	13
4	**5a**	1.3	1.3	30 min	0	64	0	trace
5	**5a**	2.0	2.0	10 min	0	98	0	trace
6	**5b**	1.3	1.3	30 min	0	62	0	trace
7	**5b**	2.0	2.0	10 min	0	94	0	trace

[a] Yields were not optimized.

As shown in Table 4 in the reaction of **1a** we found unexpectedly the formation of **6** and **7** in low yields and **7** was obtained more than that of **6** after prolonged reaction time. In order to elucidate the possible mechanism, we carried out the reaction of **6** with $BnNH_2$ in the presence of DBU in CH_2Cl_2 at room temperature under N_2. The results are summarized in Table 5.

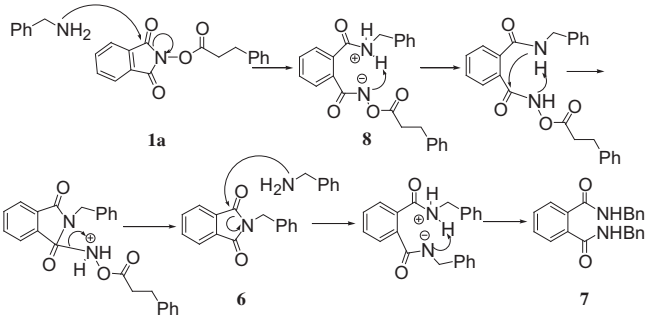
Table 5
Reaction of **6** with $BnNH_2$ in the presence of DBU



Entry	$BnNH_2$ (equiv)	DBU (equiv)	Time (h)	**7**[a] (% yield)	**6**[b] (% recover)
1	1.2	1.2	30	12	58
2	2.0	2.0	1	19	80
3	2.0	2.0	3	53	46
4	2.0	2.0	41	79	20

[a] Yields were not optimized.
[b] Compound **6** was recovered.

As shown in Table 5 the reactant **6** was decreased and the corresponding **7** was increased after passing the reaction time. Therefore, the most probable mechanism for the formation of **7** is illustrated in Scheme 2.



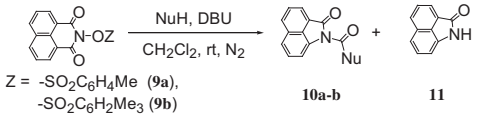
Scheme 2. Possible routes for the formation of **7** from the reaction of **1a** with $BnNH_2$.

For the mechanism of these side products, the formation of **7** was proceeded by the attack of $BnNH_2$ to the carbonyl carbon of phthalimidoyl group to generate nitrene **8** followed by Lossen-type rearrangement, which is quickly undergoes a concerted rearrangement to the **6** and finally, **7** was formed by the reaction of $BnNH_2$.

2.4. Reaction of 1,8-naphthalene derivatives (9a,b) with several nucleophiles in the presence of DBU

We prepared 1,8-naphthalene derivatives[20] i.e. 1,8-naphthalimidoyloxy tosylate (**9a**) by the reaction of *N*-hydroxy1,8-naphtha limide with tosyl chloride and *N*-mesitylenesulfonyl-1,8-naphthalimide (**9b**) by the reaction of 2-mesitylenesulfonyl chloride with *N*-hydroxy-1,8-napthalimide and examined their reaction with BnOH or BnSH in the presence of DBU in CH_2Cl_2 at room temperature under N_2. In this case, the corresponding product 1-(benzyloxycarbonyl)benzo[*c*,*d*]indol-2-one (**10a**) or 1-(benzylthiocarbonyl)benzo[*c*,*d*]indol-2-one (**10b**) was obtained via Lossen-type rearrangement together with benzo[*c*,*d*]indol-2-one (**11**).[21] The results are summarized in Table 6.

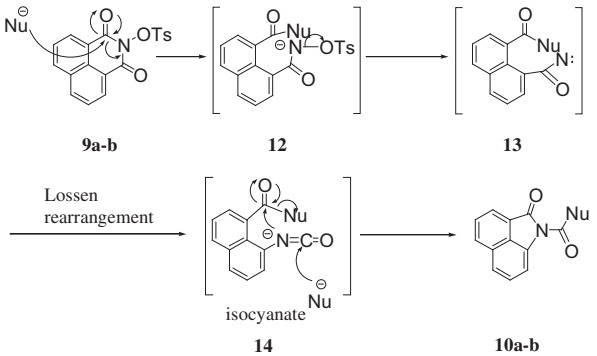
Table 6
Reaction of 1,8-naphthalimide derivative **9a** or **9b** with various nucleophiles



Entry	Compound	NuH	NuH (equiv)	DBU (equiv)	Time (h)	Product[a] (% yield)	
						10a,**b**	**11**
1	**9a**	BnOH	1.5	1.5	3	49 (**10a**)	trace
2	**9a**		2.1	2.1	2	60 (**10a**)	15
3	**9b**		1.5	1.5	3	40 (**10a**)	trace
4	**9b**		2.1	2.1	2	54 (**10a**)	9
5	**9a**	BnSH	1.5	1.5	3	45 (**10b**)	0
6	**9a**		2.1	2.1	2	58 (**10b**)	0
7	**9b**		1.5	1.5	3	41 (**10b**)	0
8	**9b**		2.1	2.1	2	51 (**10b**)	0

[a] Yields were not optimized.

Therefore, the most probable mechanism for this reaction is illustrated in Scheme 3.



Scheme 3. Possible routes for **10a**,**b** from the reactions of **9a**,**b** with BnOH and BnSH.

2.5. X-ray crystallographic analysis of 10a and 10b

Since X-ray crystal structures of **10a**, and **10b** are not available, hence, the structure of **10a**, and **10b** were also confirmed by single crystal X-ray crystallographic analysis. An ORTEP drawing and some selected bond lengths and angles are listed in Figures 1 and 2.

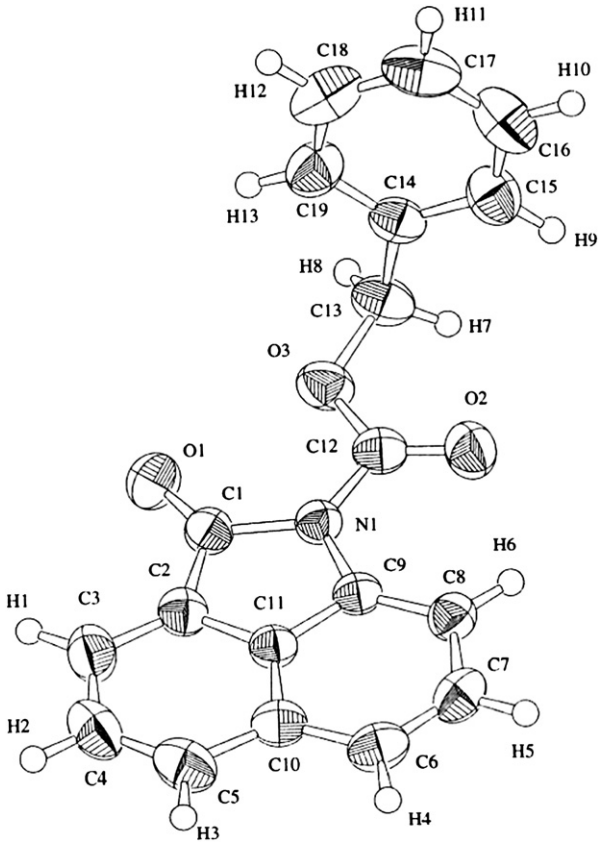


Figure 1. Crystal structure of compound **10a**. Selected bond lengths (Å) and bond angles (°): N(1)–C(1), 1.453(3); N(1)–C(9), 1.428(3); N(1)–C(12), 1.393(3); C(12)–O(2), 1.199(3); C(12)–O(3), 1.326(3); C(1)–N(1)–C(9), 109.6(2); C(1)–N(1)–C(12), 127.6(2); C(9)–N(1)–C(12), 122.6(2); N(1)–C(12)–O(2), 122.3(2); N(1)–C(12)–O(3), 11.6(2); O(2)–C(12)–O(3), 126.0(3).

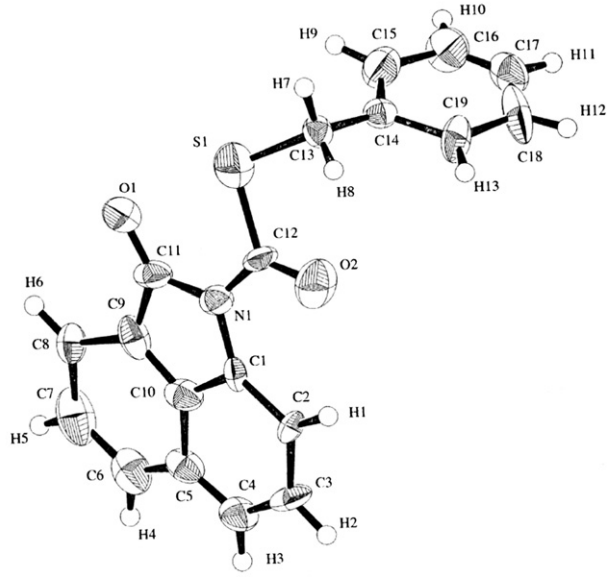
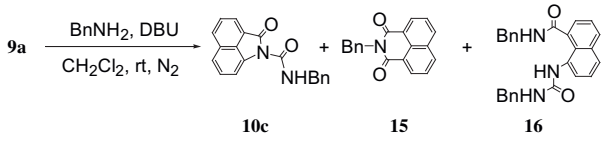


Figure 2. Crystal structure of compound **10b**. Selected bond lengths (Å) and bond angles (°): N(1)–C(1), 1.4089(9); N(1)–C(11), 1.415(10); N(1)–C(12), 1.33(1); C(12)–O(2), 1.227(10); C(12)–S(1), 1.763(6); C(1)–N(1)–C(11), 109.5(6); C(1)–N(1)–C(12), 122.9(6); C(11)–N(1)–C(12), 126.9(6); N(1)–C(12)–O(2), 124.2(6); N(1)–C(12)–S(1), 116.8(6); O(2)–C(12)–S(1), 119.0(7).

We then investigated the reaction of **9a** with $BnNH_2$ under similar conditions. The results are summarized in Table 7.

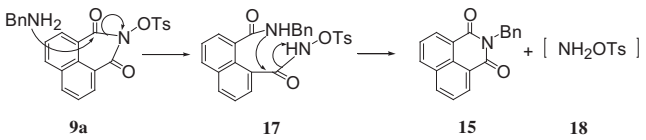
Table 7
Reaction of 1,8-naphthalimide derivative **9a** with $BnNH_2$



Entry	$BnNH_2$ (equiv)	DBU (equiv)	Time (h)	Product (% yield)[a]		
				10c	**15**	**16**
1	1.5	1.5	3	0	45	5
2	2.1	2.1	2	0	65	9

[a] Yields were not optimized.

The side products *N*-benzyl-1,8-phthalimide (**15**),[22] and 1-benzylaminocarbonylamino naphthalic acid benzylamide (**16**) were obtained when the reaction time was very short. The probable mechanism for these side products, the nucleophile will attack the carbonyl carbon of phthalimidoyl group instead of the ester group to produce the unexpected products Scheme 4.

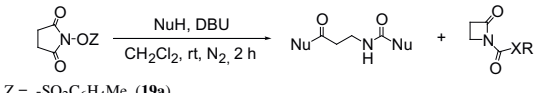


Scheme 4. Possible routes for the formation of **15** from the reaction of **9a** with $BnNH_2$.

2.6. Reaction of aliphatic dicarboxylic acid derivatives (19a,b) with several nucleophiles in the presence of DBU

Interesting sequence involving in the reaction of the aliphatic dicarboxylic acid imide derivatives.[23] Therefore, we prepared *N*-succinimidoyloxytosylate (**19a**), and *N*-mesitylenesulfonyloxysuccinimide (**19b**), and examined their reaction with several nucleophiles under similar conditions. Expectedly, the corresponding amino acid derivatives, benzyl 3-(bezyloxycarbonylamino)propionate (**20a**),[24] and *N*-{2 (benzylaminocarbonyl)ethyl}-*N*′-benzyl urea (**20b**)[25] were obtained in moderate to high yields. Experimental results of **19a** differ little from that of **19b** due to their different leaving ability of leaving group. The results are summarized in Table 8.

Table 8
Reaction of succinimide derivatives **19a** or **19b** with various nucleophiles



Z = $-SO_2C_6H_4Me$ (**19a**), $-SO_2C_6H_2Me_3$ (**19b**)

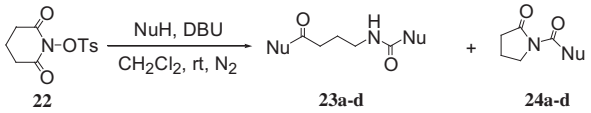
20a-b **21a-b**

Entry	Compound	NuH	NuH (equiv)	DBU (equiv)	Product[a] (% yield)	
					20a,b	**21a,b**
1	BnOH	**19a**	1.5	1.5	61 (**20a**)	0 (**21a**)
2		**19a**	2.1	2.1	75 (**20a**)	0 (**21a**)
3		**19b**	1.5	1.5	57 (**20a**)	0 (**21a**)
4		**19b**	2.1	2.1	68 (**20a**)	0 (**21a**)
5	$BnNH_2$	**19a**	1.5	1.5	44 (**20b**)	0 (**21b**)
6		**19a**	2.1	2.1	59 (**20b**)	0 (**21b**)
7		**19b**	1.5	1.5	41 (**20b**)	0 (**21b**)
8		**19b**	2.1	2.1	52 (**20b**)	0 (**21b**)

[a] Yields were not optimized.

Compounds **20a**, and **20b** are β-amino acid derivatives and will be possible to employ this method for preparing β-amino acid derivatives. Also we prepared the six membered cyclic compound, *N*-(*p*-toluenesulfoxy)glutamide (**22**) by the reaction of *N*-hydroxysuccinimide with tosyl chloride and studied their reaction with several nucleophiles under similar conditions. The results are summarized in Table 9. As shown in Table in the case of BnOH and $BnNH_2$ the corresponding amino acid derivatives, benzyl 3-(benzyloxycarbonylamino)butanoate (**23a**),[26] and *N*-{2 (benzylaminocarbonyl)propyl}-*N*′-benzyl urea (**23b**) (entries 1–4) were obtained in moderate to high yields. In contrast, when the reaction was carried out with phenol or *p*-cresol, the corresponding products, *N*-(phenyloxycarbonyl)pyrrolidine-2-one (**24c**)[27] or *N*-(methylphenyloxycarbonyl)pyrrolidine-2-one (**24d**) [28] (entries 5,6) was obtained in good yields.

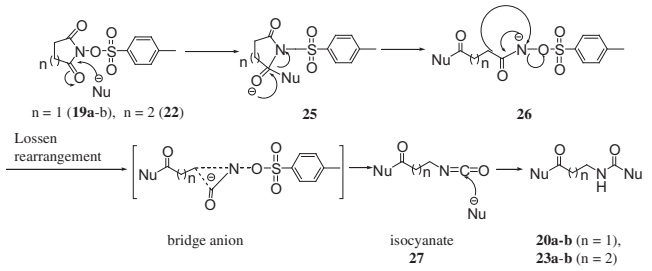
Table 9
Reaction of glutamide derivative **22** with various nucleophiles



Entry	NuH	NuH (equiv)	DBU (equiv)	Time (h)	Product[a] (% yield)	
					23a–d	**24a–d**
1	BnOH	1.5	1.5	2	68 (**23a**)	0 (**24a**)
2		2.1	2.1	2	100 (**23a**)	0 (**24a**)
3	$BnNH_2$	1.5	1.5	2	52 (**23b**)	0 (**24b**)
4		2.1	2.1	2	81 (**23b**)	0 (**24b**)
5	PhOH	2.1	2.1	2.5	0 (**23c**)	59 (**24c**)
6	*p*-Me-C_6H_4OH	2.1	2.1	2.5	0 (**23d**)	56 (**24d**)

[a] Yields were not optimized.

Therefore, it is expected that many kinds of amino acid derivatives easily attained by using the new methods described here and we have considered the reaction mechanism in Scheme 5.



Scheme 5. Probable mechanism for the formation of amino acid derivatives (**20a**,**b** and **23a**,**b**).

The unexpected formation of **20a**,**b** (n=1) or **23a**,**b** (n=2) proceeded by the attack of the nucleophile to the carbonyl carbon of imidoyl group **19a**,**b** or **22** to generate nitrene **26**, which is quite unstable and quickly undergoes a concerted rearrangement to the isocyanate **27** via bridged anion, and finally, **20a**,**b** or **23a**,**b** were formed by the reaction of BnOH or $BnNH_2$.

3. Conclusion

In conclusion, we have described the reaction of **1a** and *N*-tosyloxy derivatives **5a**,**b** with several nucleophiles in the presence of DBU under similar reaction conditions. In view of the results of the intensive mechanistic studies, it indicates clearly that the products **3a**–**e** and **4a**–**d** were formed via the Lossen-type rearrangement. In order to probe the scope further, we prepared 1,8-naphthalene derivatives **9a**,**b**, and also aliphatic dicarboxylic acid derivatives **19a**,**b** and **22**, and examined their reactions with nucleophiles under the similar conditions and expectedly obtained the Lossen-type rearranged product, i.e. **10a**,**b**, **20a**,**b**, **23a**,**b**, and **24c**–**d** in excellent yields, respectively. These new finding could be applied to the synthetic application of amino acid derivatives under mild reaction conditions with good to excellent yields. Regarding operational simplicity, mild reaction conditions, and cost, this method offers significant advantages over previously reported methods.[29]

4. Experimental section

4.1. General

All the melting points were uncorrected using micro melting point apparatus. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ using TMS as an internal standard. All the reactions were monitored with TLC and the products were separated by column chromatography using silica gel 60 and by preparative layer chromatography using silica gel 60 PF_{254} with UV or PMA and DNP detection. Mass spectra were obtained on a JEOL-JMS-D300 mass spectrometer. The elemental analyses were performed at Micro Analytical Laboratory of the Department of Material Systems Engineering and Life Science, University of Toyama.

4.2. Preparation of *N*-(3-phenylpropionyloxy)phthalimide 1a

DCC (1786.8 mg, 8.66 mmol) was added to a stirred solution of hydrocinnamic acid (500.0 mg, 6.66 mmol) and *N*-hydroxyphthalimide (1412.2 mg, 8.66 mmol) in CH_2Cl_2 at 0 °C and stirred for 3 h. The precipitate was filtered and washed with CH_2Cl_2. Purification by preparative TLC yielded *N*-(3-phenylpropionyl-oxy)phthalimide **1a** (902.2 mg, 92%) as a colorless solid; mp 84.2–84.5 °C (from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.96–3.00 (m, 2H), 3.11 (t, J=7.2 Hz, 2H), 7.23–7.27 (m, 3H), 7.31–7.35 (m, 2H), 7.77–7.81 (m, 2H), 7.86–7.91 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.6, 32.7, 123.9, 126.7, 128.3, 128.7, 128.9, 134.8, 139.2, 161.9, 168.9; IR (KBr) 1789, 1740 cm^{-1}. Anal. Calcd for $C_{17}H_{13}NO_4$: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.14; H, 4.52; N, 4.69.

4.3. General procedure for the preparation of 5a,b (5a as an example)

Pyridine (2 mL) was added to a stirred solution of *N*-hydroxyphthalimide (1000.0 mg, 6.13 mmol) and tosyl chloride (1284.9 mg, 6.74 mmol) in CH_2Cl_2 (20 mL) at room temperature under N_2 and stirred for 1 h. The crude product was washed with pure water followed by purification by silica gel chromatography (CH_2Cl_2) to afford *N*-tosyloxyphthalimide **5a** (1792.0 mg, 92%) as a colorless solid; mp 161.0–161.5 °C (from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.50 (s, 3H), 7.40–7.42 (m, 2H), 7.78–7.83 (m, 2H), 7.84–7.89 (m, 2H), 7.95–7.97 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.9, 124.3, 128.6, 129.6, 130.1, 130.6, 135.1, 147.0, 161.3; IR (KBr) 1796, 1746 cm^{-1}. Anal. Calcd for $C_{15}H_{11}NO_5S$: C, 56.78; H, 3.49; N, 4.41. Found: C, 56.81; H, 3.59; N, 4.30.

4.3.1. N-(2-Mesitylenesulfonyloxy)phthalimide ***5b***. Yield 93%; mp 174.4–175.0 °C (colorless solid from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.35 (s, 3H), 2.69 (s, 6H), 7.03 (s, 2H), 7.77–7.81 (m, 2H), 7.83–7.86 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 23.0, 124.2, 128.5, 129.4, 131.9, 135.0, 141.6, 145.2, 161.5; IR (KBr) 1798, 1752 cm^{-1}. Anal. Calcd for $C_{17}H_{15}NO_5S$: C, 59.12; H, 4.38; N, 4.06. Found: C, 59.15; H, 4.40; N, 4.09.

4.4. General procedure for the preparation of 2a–e from 1a and 5a,b (2a as an example)

DBU (50.5 μL, 0.34 mmol) was added to a stirred solution of **1a** (50.0 mg, 0.17 mmol) and benzyl alcohol (35.0 μL, 0.34 mmol) in CH_2Cl_2 (2 mL) at room temperature under N_2 and stirred for 3 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of solvent in vacuum gave a colorless oil crude product, which was purified by preparative TLC (CH_2Cl_2–hexane) to give 3-phenylpropionic acid benzyl ester **2a** (27.6 mg, 68%) as a colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.68 (t, J=7.8 Hz, 2H), 2.97 (t, J=8.0 Hz, 2H), 5.11 (s, 2H), 7.17–7.35 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.9, 35.9, 66.2, 126.2, 128.2, 128.3, 128.5, 128.5, 135.9, 140.4, 172.7; IR (NaCl disc) 1734 cm^{-1}. HRMS (EI) calcd for $C_{16}H_{16}O_2$: 240.1150; found: m/z 240.1123.

4.4.1. 3-Phenylpropionic acid 1-methylbenzyl ester ***2b***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.55 (d, J=6.8 Hz, 3H), 2.71 (dt, J=7.8, 8.2 Hz, 2H), 3.0 (t, J=8.2 Hz, 2H), 5.94 (q, J=6.4 Hz, 1H), 7.22–7.29 (m, 3H), 7.30–7.41 (m, 7H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.1, 30.9, 36.1, 72.3, 126.0, 126.2, 127.8, 128.3, 128.4, 140.4, 141.9, 172.1; IR (NaCl disc) 1733 cm^{-1}. HRMS (EI) calcd for $C_{17}H_{18}O_2$: 254.1307; found: m/z 254.1303.

4.4.2. 3-Phenylpropionic acid diphenyl-methyl ester ***2c***. Mp 50–51 °C (colorless solid from AcOEt–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.71–2.75 (m, 2H), 2.96 (t, J=7.8 Hz, 2H), 6.89 (s, 1H), 7.10–7.20 (m, 3H), 7.22–7.31 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.9, 36.0, 76.9, 126.2, 127.1, 127.8, 128.3, 128.4, 128.5, 140.1, 140.3, 171.8; IR (KBr) 1734 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{20}O_2$: 316.1463; found: m/z 316.1461.

4.4.3. 3-Phenylpropionic acid phenyl ester ***2d***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.87 (t, J=7.6 Hz, 2H), 3.06 (t, J=7.6 Hz, 2H), 6.98–7.01 (m, 2H), 7.17–7.36 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.9, 35.9, 121.5, 125.8, 126.4, 128.4, 128.6, 129.4, 140.1, 150.6, 171.4; IR (NaCl disc) 1759 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{20}O_2$: 226.0994; found: m/z 226.0990.

4.4.4. N-Benzyl-3-phenylpropionamide ***2e***. Mp 76.5–77.0 °C (colorless solid from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.51 (t, J=7.6 Hz, 2H), 2.99 (t, J=6.8 Hz, 2H), 4.39 (d, J=6.0 Hz, 2H), 5.62 (s, 1H), 7.13–7.31 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 31.7, 38.5, 43.6, 126.2, 127.4, 127.7, 128.4, 128.5, 128.6, 138.1, 140.7, 171.8; IR (KBr) 1639 cm^{-1}. Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.34; H, 7.16; N, 5.90.

4.5. General procedure for the preparation of 3a–e from 1a and 5a,b (3a as an example)

A solution of DBU (76.3 μL, 0.51 mmol) was added to a stirred solution of **1a** (50.0 mg, 0.17 mmol) and benzyl alcohol (52.8 μL, 0.51 mmol) in CH_2Cl_2 (2 mL) at room temperature under N_2 and stirred for 24 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of solvent in vacuum gave a colorless oil crude product, which was purified by preparative TLC (3:1 CH_2Cl_2–hexane) to give 2-benzyloxycarbo-nyl-*N*-(benzyloxycarbonyl)aniline **3a** (15.2 mg, 24%) as a colorless solid; mp 74.0–74.5 °C (from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.21 (s, 2H), 5.33 (s, 2H), 6.98–7.02 (m, 1H), 7.29–7.43 (m, 10H), 7.49–7.54 (m, 1H), 8.04 (dd, J=2.0, 1.6 Hz, 1H), 8.46 (d, J=8.4 Hz, 1H), 10.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 66.9, 66.9, 114.5, 118.8, 121.6, 128.2, 128.2, 128.2, 128.4, 128.5, 128.6, 130.9, 134.7, 135.4, 136.1, 141.8, 153.4, 167.7; IR (KBr) 1738, 1685 cm^{-1}. Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.37; H, 5.30; N, 3.97.

4.5.1. 2-Benzyloxycarbonylamino benzoic acid 1-methylbenzyl ester ***3b***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.46 (dd, J=5.0, 6.6 Hz, 3H), 1.54 (dd, J=3.4, 6.6 Hz, 3H), 5.76 (q, J=6.6 Hz, 1H), 5.96–6.02 (m, 1H), 6.85–6.89 (m, 1H), 7.04–7.37 (m, 11H), 7.98 (dd, J=3.9, 7.8 Hz, 1H), 8.33 (d, J=8.4 Hz, 1H), 10.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.3, 22.4, 73.1, 73.3, 114.6, 114.6, 118.6, 118.7, 121.3, 125.8, 125.9, 127.7, 127.9, 128.4, 128.6, 130.8, 134.5, 141.7, 141.9, 152.7, 152.8, 167.1; IR (KBr) 1736, 1685 cm^{-1}. HRMS (EI) calcd for $C_{24}H_{23}NO_4$: 389.1627; found: m/z 389.1627.

4.5.2. 2-Benzyloxycarbonylamino benzoic acid diphenylmethyl ester ***3c***. Mp 148.2–149 °C (colorless solid from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.87 (s, 1H), 7.03–7.05 (m, 1H), 7.11 (s, 1H), 7.23–7.43 (m, 20H), 7.49–7.54 (m, 1H), 8.21 (dd, J=2.0, 8.2 Hz, 1H), 8.46 (d, J=8.4 Hz, 1H), 10.66 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 77.7, 77.8, 114.5, 118.9, 121.7, 127.0, 127.1, 127.9, 128.2, 128.5, 128.7, 130.9, 134.8, 139.7, 140.2, 141.9, 152.7, 166.9; IR (KBr) 1729, 1695 cm^{-1}. HRMS (EI) calcd for $C_{34}H_{27}NO_4$: 513.1940; found: m/z 513.1938.

4.5.3. 2-Benzyloxycarbonylamino benzoic acid phenyl ester ***3d***. Mp 84.5–87 °C (colorless solid from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.05–7.34 (m, 7H), 7.35–7.40 (m, 2H), 7.52–7.57 (m, 1H), 8.22 (dd, J=1.6, 8.0 Hz, 1H), 8.44 (dd, J=0.4, 8.4 Hz, 1H), 10.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 114.1, 119.1, 120.6, 121.6, 121.7, 122.2, 125.6, 126.2, 126.3, 129.3, 129.5, 131.4, 135.5, 142.0, 150.3, 150.5, 151.7, 167.0; IR (KBr) 1759, 1699 cm^{-1}. HRMS (EI) calcd for $C_{20}H_{15}NO_4$: 333.1001; found: m/z 333.0999.

4.5.4. N-Benzyl-2-(3-benzylureido)benzamide ***3e***. Mp 139–140 °C (colorless solid from CH_2Cl_2–hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.44 (s, 2H), 4.54 (d, J=5.6 Hz, 2H), 5.14 (s, 2H), 6.66 (s, 1H), 6.88–6.93 (m, 1H), 7.23–7.41 (m, 12H), 8.39–8.42 (m, 1H), 10.39 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 43.9, 44.4, 118.9, 120.8, 121.0, 126.4, 127.4, 127.7, 128.6, 128.8, 132.6, 137.5, 141.1, 155.0, 169.3; IR (KBr) 1665, 1629 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{21}N_3O_2$: 359.1634; found: m/z 359.1633.

4.6. General procedure for the preparation of 4a–e from 1a and 5a,b (4a as an example)

DBU (50.5 μL, 0.34 mmol) was added to a stirred solution of **1a** (50.0 mg, 0.17 mmol) and benzyl alcohol (35.0 μL, 0.34 mmol) in CH_2Cl_2 (2 mL) at room temperature under N_2 and stirred for 40 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of solvent in vacuum gave a colorless oil crude product, which was purified by preparative TLC (CH_2Cl_2–hexane) to give 2-aminobenzoic acid benzyl ester **4a** (4.6 mg, 11%) as a colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.32 (s, 2H), 5.73 (s, 2H), 6.61–6.66 (m, 2H), 7.23–7.44 (m, 6H), 7.91 (dd, J=2.0, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 65.9, 110.6, 116.3, 116.6, 127.9, 128.1, 128.5, 131.3, 134.2, 136.3, 150.6, 167.9; IR (KBr) 1689 cm^{-1}. HRMS (EI) calcd for $C_{14}H_{13}NO_2$: 277.0946; found: m/z 277.0918.

4.6.1. 2-Aminobenzoic acid 1-methylbenzyl ester ***4b***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.58 (d, J=6.8, 3H), 5.63 (s, 2H), 6.01 (q, J=6.5 Hz, 1H), 6.56–6.61 (m, 2H), 7.17–7.24 (m, 2H), 7.27–7.31 (m, 2H), 7.35–7.37 (m, 2H), 7.89 (dd, J=2.0, 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.6, 72.2, 111.0, 116.2, 116.6, 125.9, 127.7,

128.5, 131.2, 134.1, 142.1; IR (KBr) 1685 cm^{-1}. HRMS (EI) calcd for $C_{15}H_{15}NO_2$: 241.1103; found: *m*/*z* 241.1081.

4.6.2. 2-Aminobenzoic acid phenyl ester ***4d***. Mp 57–59 °C (light yellow solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.70 (s, 2H), 6.63–6.67 (m, 2H), 7.09–7.13 (m, 2H), 7.18–7.29 (m, 2H), 7.33–7.39 (m, 2H), 8.02 (dd, *J*=1.2, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 116.4, 116.8, 121.9, 125.8, 129.5, 131.6, 134.8, 150.8, 151.0, 166.8, 166.8, 188.8; IR (KBr) 1689 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{11}NO_2$: 213.0790; found: *m*/*z* 213.0762.

4.7. *N*-Benzylphthalimide 6

Mp 113.3–113.6 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.85 (s, 2H), 7.24–7.34 (m, 3H), 7.43 (d, *J*=7.6 Hz, 2H), 7.68–7.71 (m, 2H), 7.81–7.85 (m 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 41.6, 123.3, 127.8, 128.6, 128.6, 132.1, 133.9, 136.3, 168.0; IR (KBr) 1702 cm^{-1}. Anal. Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 76.13; H, 4.77; N, 5.94.

4.8. *N,N*-Dibenzylphthalimide 7

Mp 175.5–177 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.52 (d, *J*=6.0 Hz, 4H), 6.92 (s, 2H), 7.27–7.36 (m, 8H), 7.45–7.48 (m, 2H), 7.59–7.63 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.1, 127.6, 127.9, 128.4, 128.8, 130.4, 134.5, 137.7, 168.9; IR (KBr) 1630 cm^{-1}. HRMS (EI) calcd for $C_{22}H_{20}N_2O_2$: 344.1525; found: *m*/*z* 344.1524.

4.9. General procedure for the preparation of 9a,b (9a as an example)

Hydroxylamine hydrochloride (525.9 mg, 7.56 mmol), and $NaHCO_3$ (635.1 mg, 7.56 mmol) were added to a stirred solution of 1,8-naphthalic anhydride (1000.0 mg, 5.05 mmol) in EtOH at refluxed and stirred for 30 min. The solvent was removed, and some H_2O and HCl (1 N) were added to the yellow resulting residue. The colorless solid was filtered by suction filtration and washed with ether. The solvent was removed to give *N*-hydroxy-1,8-naphthalimide (895.5 g, 90%) as a colorless solid. Then, tosyl chloride (196.7 mg, 1.03 mmol) and pyridine (82.9 μL, 1.03 mmol) were added to the solution of *N*-hydroxy-1,8-naphthalimide (200.0 mg, 0.94 mmol) in CH_2Cl_2 (10 mL) and stirred at room temperature under N_2 for 30 min. The solvent was removed, and resulting residue was separated by flash chromatography on silica gel using CH_2Cl_2 to give *N*-tosyloxy-1,8-naphthalimide **9a** (286.0 mg, 83%) as a colorless solid; mp 206–207 °C (from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.51 (s, 3H), 7.43 (d, *J*=8.0 Hz, 1H), 7.77–7.85 (m, 3H), 8.04 (d, *J*=8.4 Hz, 1H), 8.29 (dd, *J*=8.8, 8.0 Hz, 3H), 8.61–8.64 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.9, 122.2, 127.2, 127.4, 129.4, 129.8, 131.8, 132.1, 132.3, 133.4, 135.2, 135.3, 146.4, 159.8; IR (KBr) 1772, 1739, 1728, 1705 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{13}NO_5S$: 367.0514; found: *m*/*z* 367.0511.

4.9.1. N-Mesitylenesulfonyloxy-1,8-naphthalimide ***9b***. Mp 257–259 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.37 (s, 3H), 2.71 (s, 6H), 7.75–7.85 (m, 3H), 8.27 (dd, *J*=0.4, 3.8 Hz, 1H), 8.33 (dd, *J*=0.8, 3.6 Hz, 2H), 8.59–8.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 22.9, 122.3, 127.2, 127.5, 131.8, 131.9, 132.3, 133.4, 135.1, 135.3, 140.4, 144.3, 160.0; IR (KBr) 1773, 1733, 1705 cm^{-1}. HRMS (EI) calcd for $C_{21}H_{17}NO_5S$: 395.0827; found: *m*/*z* 395.0824.

4.10. General procedure for the preparation of 10a,b (10a as an example)

Benzyl alcohol (42.2 μL, 0.41 mmol) and DBU (61.0 μL, 0.41 mmol) solution was added to a stirred solution of *N*-tosyloxy-1,8-naphthalimide **9a** (100.0 mg, 0.27 mmol) in CH_2Cl_2 (3 mL) and stirred at room temperature under N_2 for 3 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2 and H_2O, dried over anhydrous $MgSO_4$, and concentrated under vacuum and the resulting residue was purified by flash chromatography on silica gel using hexane–AcOEt to give 1-(benzyloxycarbonyl)benzo[*c*,*d*]indol-2-one **10a** (40.4 mg, 49%) as a colorless solid; mp 120–121 °C (from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 5.52 (s, 2H), 7.33–7.44 (m, 3H), 7.50–7.58 (m, 3H), 7.66 (d, *J*=8.8 Hz, 1H), 7.71–7.76 (m, 1H), 7.80 (d, *J*=7.6 Hz, 1H), 8.10 (t, *J*=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 68.4, 112.4, 122.1, 124.5, 124.9, 126.1, 128.1, 128.5, 128.6, 128.7, 128.9, 129.3, 132.0, 135.1, 151.2, 165.0; IR (KBr) 1761, 1733 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{13}NO_3$: 303.0895; found: *m*/*z* 303.0897.

X-ray crystal data; Empirical formula: $C_{19}H_{13}NO_3$; Formula weight 303.32; Crystal system=triclinic; Space group $P\bar{1}$ (#2); Lattice parameters: *a*=9.655(2) Å; *b*=11.379(1) Å, *c*=7.141(1) Å; α=97.14(2)°, β=107.11(2)°,γ=100.68(1)°; *V*=724.8(2) $Å^3$; *T*=23.0 °C; Z=2; μ ($M_o K\alpha$)=0.95 cm^{-1}; 4446 reflections measured, 1763 unique (R_{int}=0.045); final *R* value 0.059. Crystallographic data has been deposited with the Cambridge Crystallographic Data Center, CCDC No. 751601.

4.10.1. 1-(Benzylthiocarbonyl)benzo[c,d]indol-2-one ***10b***. Mp 156.0–156.5 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 4.33 (s, 2H), 7.24–7.28 (m, 1H), 7.31–7.36 (m, 2H), 7.44–7.47 (m, 2H), 7.57 (dd, *J*=7.2, 8.4 Hz, 1H), 7.70 (d, *J*=8.4 Hz, 1H), 7.75 (dd, *J*=7.2, 8.0 Hz, 1H), 8.10–8.13 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 34.0, 113.4, 122.7, 123.9, 125.3, 126.2, 127.3, 128.6, 128.7, 129.1, 129.2, 129.3, 132.5, 135.3, 136.9, 166.7, 167.9; IR (KBr) 1728, 1670 cm^{-1}. Anal. Calcd for $C_{19}H_{13}NO_2S$: C, 71.45; H, 4.10; N, 4.39. Found: C, 71.45; H, 4.36; N, 4.37.

X-ray crystal data; Empirical formula: $C_{19}H_{13}NO_2S$; Formula weight 319.38; Crystal system=triclinic; Space group $P\bar{1}$ (#2); Lattice parameters: *a*=7.210(2) Å; *b*=11.405(3) Å, *c*=19.057(4) Å; α=75.84(2)°, β=81.93(2)°, γ=84.97(2)°; *V*=1502.1(7) $Å^3$; *T*=23.0 °C; *Z*=4; μ ($M_o K\alpha$)=2.24 cm^{-1}; 9151 reflections measured, 2839 unique (R_{int}=0.040); final *R* value 0.066. Crystallographic data has been deposited with the Cambridge Crystallographic Data Center, CCDC No. 751599.

4.11. Benzo[*c*,*d*]indol-2-one 11

Mp 179.5–180 °C (yellow solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.01 (d, *J*=6.8 Hz 1H), 7.46 (dd, *J*=7.2, 8.4 Hz, 1H), 7.56 (d, *J*=8.0 Hz, 1H), 7.74 (dd, *J*=7.2, 8.0 Hz, 1H), 8.06 (d, *J*=8.0 Hz, 1H), 8.10 (d, *J*=7.2 Hz, 1H), 8.69 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 106.5, 120.3, 124.4, 128.6, 128.7, 129.4, 131.2, 137.0, 170.1; IR (KBr) 1715 cm^{-1}. HRMS (EI) calcd for $C_{11}H_7NO$: 169.0528; found: *m*/*z* 169.0523.

4.12. General procedure for the preparation of 19a,b (19a as an example)

Pyridine (1 mL) was added to a stirred solution of *N*-hydroxysuccinimide (400.0 mg, 3.47 mmol) and tosyl chloride (728.8 mg, 3.82 mmol) in CH_2Cl_2 (5 mL) at room temperature under N_2 and stirred for 1 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of solvent in vacuum gave a solid

product, which was purified by preparative TLC (AcOEt) to give *N*-tosyloxysuccinimide **19a** (927.2 mg, 99%) as a colorless solid; mp 135–136 °C (from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.49 (s, 3H), 2.82 (s, 4H), 7.40 (d, J=8.0 Hz, 2H), 7.94 (dd, J=2.0, 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.9, 25.4, 129.4, 130.0, 130.9, 147.1, 168.5; IR (KBr) 1752, 1729 cm^{-1}. HRMS (EI) calcd for $C_{11}H_{11}NO_5S$: 269.0358; found: m/z 269.0352.

4.12.1. N-Mesitylenesulfonyloxysuccinimide ***19b***. Yield 96%; mp 145.5–147 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.34 (s, 3H), 2.67 (s, 6H), 2.78 (s, 4H), 7.01 (d, J=0.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.2, 22.9, 25.3, 129.9, 131.9, 141.1, 145.2, 168.6; IR (KBr) 1758, 1739 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{15}NO_5S$: 297.0671; found: m/z 297.0669.

4.13. General procedure for the preparation of 20a,b (20a as an example)

Benzyl alcohol (57.7 μL, 0.56 mmol) and DBU (83.3 μL, 0.56 mmol) solution was added to a stirred solution of **19a** (100.0 mg, 0.37 mmol) in CH_2Cl_2 (2 mL) at room temperature under N_2 and stirred for 2 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of solvent in vacuum gave a crude product, which was purified by preparative TLC (AcOEt) to give benzyl 3-(benzyloxycarbonylamino)propionate **20a** (70.2 mg, 61%) as a colorless liquid; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.58 (t, J=6.0 Hz, 2H), 3.46 (q, J=6.0 Hz, 2H), 5.08 (s, 2H), 5.11 (s, 2H), 5.33 (s, 1H), 7.23–7.36 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 34.4, 36.5, 66.4, 66.6, 128.0, 128.0, 128.1, 128.3, 128.4, 128.5, 135.5, 136.4, 156.2, 172.1; IR (KBr) 1728, 1719 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{19}NO_4$: 313.1314; found: m/z 313.1311.

4.13.1. N-{2 (Benzylaminocarbonyl)ethyl}-N′-benzyl urea ***20b***. Mp 183.5–185 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR (DMSO, 400 MHz) δ 2.23 (t, J=7.6 Hz, 2H), 3.18 (t, J=6.2 Hz, 2H), 4.10 (d, J=5.6 Hz, 2H), 4.18 (d, J=5.6 Hz, 2H), 5.92 (s, 1H), 6.39 (s, 2H), 7.02–7.38 (m, 10H), 8.32 (s, 1H); ^{13}C NMR (DMSO, 100 MHz) δ 31.6, 31.8, 37.7, 38.5, 122.2, 122.4, 122.7, 122.9, 123.9, 135.2, 136.6, 153.7, 166.5; IR (KBr) 1684, 1635 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{21}N_3O_2$: 311.1634; found: m/z 311.1632.

4.14. Preparation of *N*-tosyloxyglutarimide 22

Hydroxylamine hydrochloride (913.0 mg, 13.5 mmol), and $NaHCO_3$ (1104.7 mg, 13.15 mmol) were added to a solution of glutaric anhydride (1000.0 mg, 8.76 mmol) in ethanol at refluxed and stirred for 12 h. The solvent was removed, in vacuum, and dried at 80 °C to give crude solid. Then, tosyl chloride (1837.9 mg, 9.64 mmol) and pyridine (1219.0 μL, 13.15 mmol) were added to the crude solid in CH_2Cl_2 and stirred at room temperature under N_2 for 30 min. The solvent was removed, and resulting residue was separated by flash chromatography on silica gel using CH_2Cl_2 to give **22** (1315.0 mg, 53%) as a colorless solid; mp 145.5–146 °C (from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.99–2.05 (m, 2H), 2.47 (s, 3H), 2.81 (t, J=6.6 Hz, 4H), 7.37 (dd, J=0.8, 8.4 Hz, 2H), 7.89–7.92 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 16.5, 21.8, 33.3, 129.3, 129.8, 131.8, 146.4, 166.7; IR (KBr) 1757, 1728 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_5S$: C, 50.87; H, 4.63; N, 4.94. Found: C, 50.84; H, 4.62; N, 4.87.

4.15. General procedure for the preparation of 23a–d and 24a–d (23a as an example)

Benzyl alcohol (38.3 μL, 0.37 mmol) and DBU (55.2 μL, 0.37 mmol) solution was added to a stirred solution of **22** (50.0 mg, 0.18 mmol) in CH_2Cl_2 (1.5 mL) at room temperature under N_2 and stirred for 2 h. Then, the reaction mixture was neutralized by dil AcOH solution and extracted with CH_2Cl_2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous $MgSO_4$. Removal of solvent in vacuum gave a crude product, which was purified by preparative TLC (hexane–AcOEt–CH_2Cl_2; 1:1:1) to give benzyl 3-(benzyloxycarbonylamino)butanoate **23a** (57.5 mg, 100%) as a colorless oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.81–1.88 (m, 2H), 2.40 (t, J=7.2 Hz, 2H), 3.22 (q, J=6.4 Hz, 2H), 4.92 (s, 1H), 5.08 (s, 1H), 5.08 (s, 2H), 5.10 (s, 2H), 7.24–7.38 (m 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.1, 31.4, 40.3, 66.3, 66.6, 128.1, 128.2, 128.2, 128.5, 128.5, 135.8, 136.5, 156.4, 172.9; IR (KBr) 1730, 1706 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{19}NO_4$: 327.1471; found: m/z 327.1452.

4.15.1. N-{2 (Benzylaminocarbonyl)propyl}-N′-benzyl urea ***23b***. Mp 188–189 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 1.71–1.78 (m, 2H), 2.22 (t, J=7.2 Hz, 2H), 3.14 (t, J=6.4 Hz, 2H), 4.27 (s, 2H), 4.33 (d, J=5.6 Hz, 2H), 5.87 (s, 1H), 6.21 (s, 1H), 7.20–7.29 (m, 10H), 8.21 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.2, 31.7, 37.7, 41.1, 41.9, 125.1, 125.3, 125.7, 125.8, 126.7, 126.7, 137.9, 139.1, 157.4, 170.2; IR (KBr) 1672, 1631 cm^{-1}. HRMS (EI) calcd for $C_{19}H_{23}N_3O_2$: 325.1790; found: m/z 325.1785.

4.15.2. N-(Phenyloxycarbonyl)pyrrolidine-2-one ***24c***. Mp 114.5–115.5 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.02–2.10 (m, 2H), 2.56 (t, J=8.2 Hz, 2H), 3.89 (t, J=7.0 Hz, 2H), 7.09–7.20 (m, 3H), 7.29–7.34 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 32.8, 46.7, 121.5, 126.1, 129.4, 150.2, 173.8; IR (KBr) 1795, 1781 cm^{-1}. HRMS (EI) calcd for $C_{11}H_{11}NO_3$: 205.0739; found: m/z 205.0725.

4.15.3. N-(Methylphenyloxycarbonyl)pyrrolidine-2-one ***24d***. Mp 98.0–99.0 °C (colorless solid from CH_2Cl_2–hexane); ^1H NMR ($CDCl_3$, 400 MHz) δ 2.00–2.08 (m, 2H), 2.27 (s, 3H), 2.54 (t, J=8.0 Hz, 2H), 3.87 (t, J=7.2 Hz, 2H), 6.96–6.99 (m, 2H), 7.10 (d, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.6, 20.8, 32.8, 46.7, 121.1, 129.9, 135.8, 148.0, 173.9; IR (KBr) 1786, 1697 cm^{-1}. HRMS (EI) calcd for $C_{12}H_{13}NO_3$: 219.0895; found: m/z 219.0901.

Supplementary data

Supplementary data that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office. Supplementary data associated with this article can be found in the online version at, doi:10.1016/j.tet.2010.01.074.

References and notes

1. For reviews and recent examples, see: (a) Dubowchick, G. M.; Walker, M. A. *Pharmacol. Ther.* **1999**, *83*, 67; (b) Rusiecki, V. K.; Warne, S. A. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 707; (c) Janda, K. D.; Ashley, J. A.; Jones, T. M.; McLeod, D. A.; Schloeder, D. M.; Weinhouse, M. I. *J. Am. Chem. Soc.* **1990**, *112*, 8886; (d) Pietersz, G. A. *Bioconjugate Chem.* **1990**, *1*, 89.
2. Dalton, K. H.; Dubowchik, G. M.; Michael, A. W. *Tetrahedron Lett.* **2002**, *43*, 1987.
3. (a) Morita, H.; Byung, J. K. *Chem. Lett.* **2000**, 42; (b) Morita, H.; Byung, J. K.; Yamada, S.; Funada, T.; Kadoma, Y. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 357.
4. Morita, H; Sheikh, M.C.; Byung, J.K.; Takagi, S.; Sakai, M.; unpublished work.
5. Sheikh, M. C.; Takagi, S.; Sakai, M.; Abe, H.; Morita, H. *Org. Biomol. Chem.* **2008**, *6*, 4505.
6. Katrizky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409.
7. Takagi, S.; Sheikh, M. C.; Ogasawara, A.; Ohira, M.; Abe, H.; Morita, H. *Heterocycles* **2009**, *78*, 1433.
8. (a) Fahmy, A. F. M.; Ali, N. F.; Nada, A.; Ali, N. Y. *Bull. Chem. Jpn.* **1977**, *50*, 2678; (b) Lossen, W. *Liebigs Ann. Chem.* **1872**, *175*, 271; (c) Ulrich, H.; Tucer, B.; Richter, R. *J. Org. Chem.* **1978**, *43*, 1544; (d) Maillard, T. L.; Benohoud, M.; Durand, P.; Badet, B. *J. Org. Chem.* **2005**, *70*, 6303; (e) Stolberg, M. A.; Tweit, R. C.; Steinberg, G. M.; Wagner-Jauregg, T. *J. Am. Chem. Soc.* **1955**, *77*, 765; (f) Hurd, C. D.; Bauer, L. *J. Am. Chem. Soc.* **1954**, *76*, 2791; (g) Castro, E. A.; Pavez, P.; Santos, J. G. *J. Org.*

Chem. **2002**, *67*, 4494; (h) Tundo, P.; Selve, M. *Acc. Chem. Res.* **2002**, *35*, 706; (i) Castro, E. A. *Chem. Rev.* **1999**, *99*, 3505.
9. (a) Hoare, D. G.; Olson, A.; Koshland, D. E. *J. Am. Chem. Soc.* **1968**, *90*, 1638; (b) Linke, S.; Tisue, G. T.; Lwowski, W. *J. Am. Chem. Soc.* **1967**, *89*, 6308; (c) Joensson, N. A.; Moses, P. *Acta Chem. Scand.* **1974**, *28*, 441; (d) Groutas, W. C.; Stanga, M. A.; Brubaker, M. J. *J. Am. Chem. Soc.* **1989**, *111*, 1931; (e) Adams, G. W.; Bowie, J. H.; Hayes, R. N. *J. Chem. Soc., Perkin Trans. 2* **1991**, 689.
10. (a) Jin, W.; Trzupec, J. D.; Rayl, T. J.; Broward, M. A.; Weir, S. J.; Hwang, I.; Boger, D. L. *J. Am. Chem. Soc.* **2007**, *129*, 15391; (b) Stefanowiez, P.; Jaremko, L.; Jaremko, M.; Lis, T. *New J. Chem. Soc.* **2006**, *30*, 258.
11. (a) Aoai, T.; Kodama, K.; Yamanaka, T.; Yagihara, M. *J. Photopolym. Sci. Technol.* **1998**, *11*, 409; (b) Abramovitch, R.; Beckert, J. M.; Chinnasamy, P. X. H.; Pennington, W.; Sanjivamurthy, A. R. V. *Heterocycles* **1989**, *28*, 623.
12. (a) Roos, G. H. P.; Dastlik, K. A. *Heterocycles* **2003**, *60*, 2023; (b) Barker, D.; McLeod, M. D.; Brimble, M. A.; Savage, G. P. *Tetrahedron Lett.* **2001**, *42*, 1785.
13. (a) Chapman, T. M.; Freedman, E. A. *J. Org. Chem.* **1973**, *38*, 3908; (b) Grochowski, E.; Jurezak, J. *J. Org. Chem.* **1978**, *43*, 2541.
14. (a) Barker, D.; Brimble, M. A.; McLeod, M. D. *Tetrahedron* **2004**, *60*, 5953; (b) Kiely, J. S.; Huang, S. *J. Heterocycl. Chem.* **1987**, *24*, 1137.
15. (a) Venuti, M. C. *Synthesis* **1982**, *4*, 266; (b) Ongania, K. H.; Egerbacher, H. *Monatshefte fur chemie* **1985**, *116*, 979.
16. (a) Nammert, V.; Travnikova, O.; Vahur, S.; Leito, I.; Piiralu, M.; Maemets, V.; Koppel, I.; Ilmar, A. *J. Phys. Org. Chem.* **2006**, *19*, 654; (b) Fife, T. H.; Singh, R.; Bembi, R. *J. Org. Chem.* **2002**, *67*, 3179.
17. (a) Imai, Y.; Ueda, M.; Ishimori, M. *J. Polym. Sci.* **1975**, *13*, 1969; (b) El-Soghier, A. H. *Egypt. J. Chem.* **1997**, *40*, 339.
18. Worlikar, S. A.; Larock, R. C. *J. Org. Chem.* **2008**, *73*, 7175.
19. (a) Okunrobo, L. O.; Usifoh, C. O. *Pak. J. Pharm.. Sci.* **2006**, *19*, 309; (b) Sheehan, J. C.; Holland, G. I. *J. Am. Chem. Soc.* **1956**, *78*, 5631.
20. (a) Molval, J. P.; Suzuki, S.; Mortel-Saary, F.; Takahara, S.; Yamaoka, T. *J. Phys. Chem. A* **2008**, *112*, 3879; (b) Neumann, U.; Guetschow, M. *J. Biol. Chem.* **1994**, *269*, 21561.
21. Stradin, J.; Baumane, L.; Gavars, R.; Magda, V.; Samusenko, Y. *Khimiya Geterotsiklieheskikh Soedinnenii* **1993**, *8*, 1068.
22. (a) Takas, A.; Acs, P.; Kollar, L. *Tetrahedron* **2007**, *64*, 983; (b) Barooah, N.; Tamuly, C.; Baruah, J. B. *J. Chem. Sci. (Banglalore, India)* **2005**, *117*, 117.
23. (a) Tokita, S.; Watanabe, F.; Hashimoto, K.; Tachikawa, T. *J. Photopolym. Sci. Technol.* **2001**, *14*, 221; (b) Adegawa, Y. *Jpn. kokai Tokkyo koho* **2002**, 44.
24. Khumtaveeporn, K.; Ullmann, A.; Matsumoto, K.; Davis, B. G.; Jones, J. B. *Tetrahedron: Asymmetry* **2001**, *12*, 249.
25. (a) Imi, Y.; Ueda, M.; Ishimori, M. *J. Polymer Sci. Polymer Chemistry Edition* **1976**, *14*, 299; (b) Gross, H.; Bilk, L. *Tetrahedron* **1968**, *24*, 6935.
26. Barbayianni, E.; Fotakopoulou, I.; Schmidt, M.; Constantinou-kokotou, V.; Bornscheuer, U. *J. Org. Chem.* **2005**, *70*, 8730.
27. (a) Yano, T.; Shinohara, S.; Takeyama, C. *PCT Int. Appl.* **2003**, 33; (b) Onomura, O.; Moriyama, A.; Fukae, K.; Yamamoto, Y.; Maki, T.; Matsumura, Y.; Demizu, Y. *Tetrahedron Lett.* **2008**, *49*, 6728.
28. Hamaguchi, F.; Nagasaka, T.; Sakurai, E. *Eur. Pat. Appl.* **1991**, 16.
29. (a) Kobayashi, S.; Matsubara, R.; Kitagawa, H. *Org. Lett.* **2002**, *4*, 143; (b) Ueno, M.; Ishitani, H.; Kobayashi, S. *Org. Lett.* **2002**, *4*, 3395; (c) Badorrey, R.; Cativiela, C.; Daiz-de-Villegas, M. D.; Galvez, J. A. *Tetrahedron Lett.* **2003**, *44*, 9189; (d) Periasamy, M.; Suresh, S.; Ganesan, S. S. *Tetrahedron Lett.* **2005**, *46*, 5521; (e) Jacobsen, M. F.; Ionita, L.; Skrydstrup, T. *J. Org. Chem.* **2004**, *69*, 4792; (f) Komoto, I.; Kobayashi, S. *J. Org. Chem.* **2004**, *69*, 680; (g) Chung, W. J.; Omote, M.; Welch, J. T. *J. Org. Chem.* **2005**, *70*, 7784; (h) Pandey, G.; Singh, R. P.; Garg, A.; Singh, V. K. *Tetrahedron Lett.* **2005**, *46*, 2137.