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Efficient one-pot synthesis of cyclic β-enaminoamides by thermal Wolff rearrangement of cyclic 2-diazo-1,3-dicarbonyls and conversion to uracil derivatives

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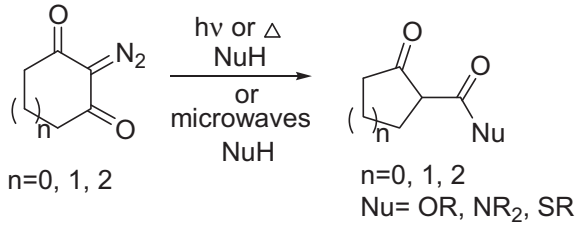
ABSTRACT

This paper describes simple and efficient approaches for the preparation of β-enaminoamides through thermal Wolff rearrangement of cyclic diazodicarbonyls followed by trapping with various amines. The synthesized β-enaminoamides were readily converted into uracil derivatives.

1. Introduction

Decomposition of diazocarbonyl compounds has been a widely applied method in organic synthesis.[1] Among these, transition metal-catalyzed cycloaddition of diazocarbonyl compounds to substrates has become an important method for the synthesis of a wide variety of heterocyclic compounds.[2] Also, the thermal, photochemical, and transition metal-catalyzed Wolff rearrangement is a well-known and useful reaction for the homologation of carboxylic acids and for ring contraction.[3] Application of such a phenomenon in terms of biochemical interest includes DNA cleavage, β-peptides, and photo-affinity labeling.[3] The Wolff rearrangement has also achieved commercial importance in the photolithography industry.[3]

In particular, the ring contraction of cyclic 2-diazo-1,3-dicarbonyls by thermal or photo Wolff rearrangement followed by trapping of the transient α-oxoketene with nucleophiles is a well-known method for the preparation of β-keto carbonyl compounds (Scheme 1).[4] Recently, the microwave-assisted Wolff rearrangement of cyclic 2-diazo-1,3-dicarbonyls in the presence of amines to form β-keto amides has been reported.[5] Also, microwave-assisted domino multi-component reactions of 2-diazo-1,3-dicarbonyls in the presence of amines and aldehydes or α,β-unsaturated aldehydes for the formation of oxazinones or α-spiro-γ-lactams and pyrazolidinones have also been described.[6]



Scheme 1.

Recently, we have been interested in rhodium(II)-catalyzed reactions of cyclic diazodicarbonyl compounds with several substrates, such as nitriles, isocyanates, ketones, vinyl ethers, and halides for the formation of a number of heterocycles[7] and β-substituted α-haloenones.[8] We have also developed a new methodology for the synthesis of oxindoles by rhodium(II)-catalyzed Wolff rearrangement of diazoquinolinediones.[9] In continuation with our previous studies on the development of a new methodology starting from cyclic diazodicarbonyls, in the present work, we have investigated thermal Wolff rearrangement of cyclic diazodicarbonyls with amines to form a variety of β-enaminoamides. We

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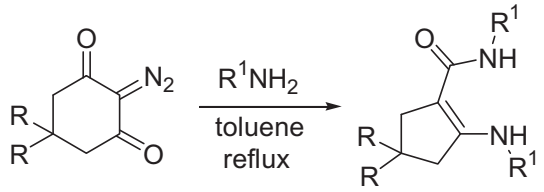
report herein a facile and efficient one-pot preparation of cyclic β-enaminoamides starting from cyclic diazodicarbonyl compounds (Scheme 2). As an application of this methodology, we also report an efficient conversion of synthesized β-enaminoamides to biologically interesting uracil derivatives.



Scheme 2.

2. Results and discussion

Although a few synthetic approaches for the preparation of β-enaminoamides have been reported, those synthetic routes have many reaction steps, harsh reaction conditions, and low yields.[10,15] Therefore, there is still a demand for efficient methods that can efficiently provide five-membered ring β-enaminoamides through a one-pot reaction.

The starting cyclic diazodiarbonyls **1**–**3** were prepared by the diazotransfer reaction of the corresponding cyclic 1,3-dicarbonyls with tosyl azide or mesyl azide according to the known procedure (Fig. 1).[11] In order to check the reactivity of 2-diazocyclohexane-1,3-dione (**1**) to form cyclic β-enaminoamide **4**, thermal reactions of **1** with 2.2 equiv of 1-propylamine under several solvents were first examined (Table 1). When THF, acetonitrile, or benzene was used in refluxing condition at 66 °C, 82 °C, and 80 °C for 12 h, respectively, only starting material **1** was recovered. With toluene at 110 °C for 6 h, the desired β-enaminoamide **4** was obtained in 67% yield after column chromatography. However, when the reaction mixture was heated at 140 °C in *p*-xylene for 6 h, compound **4** was produced in 60% yield. Support for the structural assignment of **4** came from its spectroscopic analysis. In the ^{1}H NMR spectrum of **4**, three methylene peaks due to cyclopentene ring were apparent at δ 2.51 (t, J=7.8 Hz), 2.38 (t, J=7.2 Hz), and 1.88–1.78 (m), whereas two methylene peaks next to an amide and an amine showed at 3.24–3.17 and 3.09–3.03 as multiplets. In the IR spectrum, a carbonyl absorption of amide group was observed at 1630 cm^{-1}.

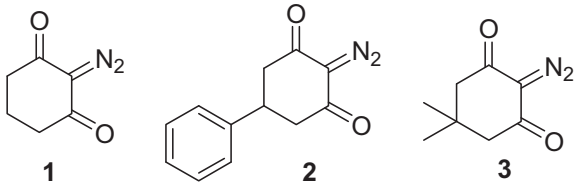
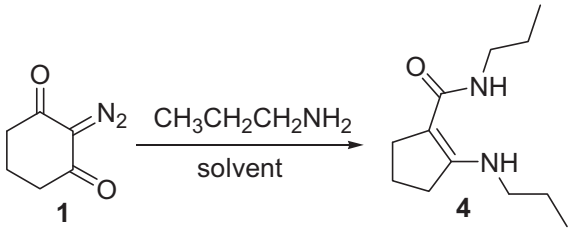


Fig. 1. Synthesized cyclic diazodicarbonyls.

To explore the generality and scope of this methodology, additional reactions of cyclic diazodicarbonyls **1**–**3** with several amines were performed in refluxing toluene. The outcomes of the reaction are summarized in Table 2. Reaction of 2-diazocyclohexane-1,3-dione (**1**) with 1-butylamine for 5 h produced **5** in 53% yield (entry 1, Table 2), whereas that with cyclohexanemethylamine formed **6** in 59% yield (entry 2). The 2-phenylethylamine and benzylamine resulted in the formation of **7**–**8** in 57 and 83% yield, respectively (entries 3–4). Reaction of tryptamine with indole moiety was also successful. Treatment of **1** with tryptamine for 7 h formed the

Table 1
Thermal reaction of **1** with 1-propylamine under several solvents



Solvent	Temp (°C)	Time (h)	Yield (%)
THF	66	12	0
Acetonitrile	82	12	0
Benzene	80	12	0
Toluene	110	6	67
p-Xylene	140	6	60

desired product **9** in 61% yield (entry 5). Reaction with aniline for 5 h produced **10** in 64% yield (entry 6). Similarly, reactions of other diazodicarbonyls **2**–**3** with a number of amines formed the desired products **11**–**24** in 52–81% yield (entries 7–20). Importantly, these reactions provided rapid synthetic approaches for the preparation of a variety of β-enaminoamides with several substituents on the five-membered ring.

Interestingly, reaction of **3** with 1 equiv of benzylamine in refluxing toluene for 4 h provided β-keto amide **25** in 80% yield (Scheme 3), without any isolation of the desired cyclic β-enaminoamide **22** in Table 2. In the ^{1}H NMR spectrum of **25**, the methine proton appeared at δ 3.14 ppm as a triplet. However, reactions of acyclic 2-diazo-1,3-dicarbonyls of 3-diazopentane-2,4-dione and 2-diazo-1,3-diphenylpropane-1,3-dione with 2 equiv of benzylamine in refluxing toluene for 5 h did not afford the desired acyclic β-enaminoamides. In these cases, a mixture of unidentifiable and decomposed products was obtained.

The formation of **4** can be explained by the mechanism as shown in Scheme 4. The diazodicarbonyl compound **1** first gives a carbene intermediate **26** by the loss of nitrogen under thermal reaction condition.[3,4] A 1,2-shift of **26** leads to α-oxoketene **27**, which reacts with 1-propylamine to give **28**. Further reaction of carbonyl group of **28** with 1-propylamine gives final product **4**. Importantly, when we used 1 equiv of amine as shown in Scheme 3, the desired β-enaminoamide product was not produced. In view of this result, the formation of **4** is likely to proceed via the proposed mechanism excluding other possible pathway through imine formation before the carbene intermediate formation.

Moreover, to verify this stepwise mechanism, a cross reaction with two different primary amines was next performed (Scheme 5). A reaction of **3** with 1 equiv of 1-propylamine and benzylamine in refluxing toluene for 6 h afforded β-enaminoamides **29** and **30** (32%) as an 84:16 ratio of isomers and keto amides **25** (9%) and **31** (7%) together with a trace amount of β-enaminoamides **18** and **22**, described in Table 2. The β-enaminoamides **29** and **30** were easily separated from β-keto amides **25** and **31** by column chromatography, but each individual component was not separable. The ratio of **29** and **30** to **25** and **31** was calculated by integration of the respective protons in the ^{1}H NMR spectra.

In order to increase the usefulness of this methodology, conversion of synthesized β-enaminoamide **22** to uracil derivative **32** was next attempted (Scheme 6). Uracil derivatives bearing substituents at positions 5 and 6 display a wide range of biological activities.[12] Reaction of **22** with 1.1 equiv of triphosgene and 5 equiv of K_2CO_3 in refluxing toluene for 10 h formed uracil derivative **32** in 52% yield. The structure of **32** was assigned by ^{1}H NMR analysis and by comparison with previously reported data.[13] The methylene

Table 2
Additional reaction of cyclic diazodicarbonyls **1**–**3** with several amines

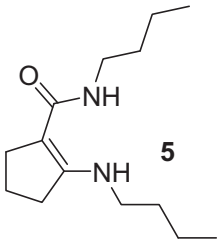
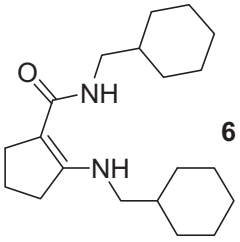
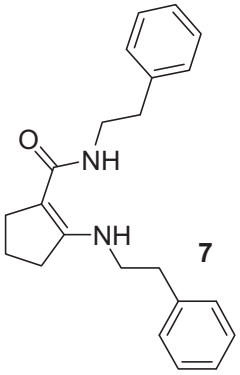
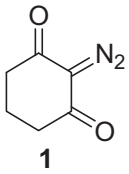
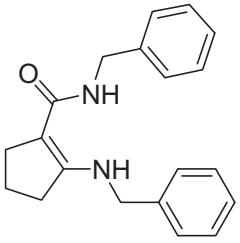
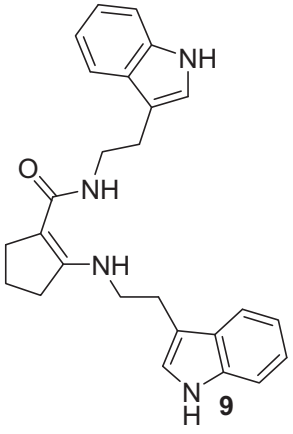
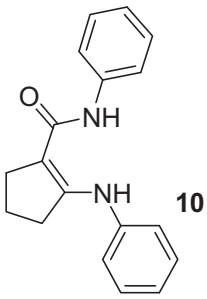
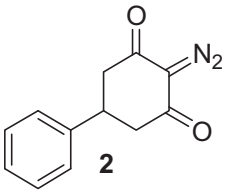
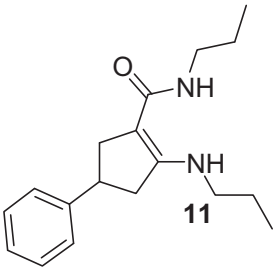
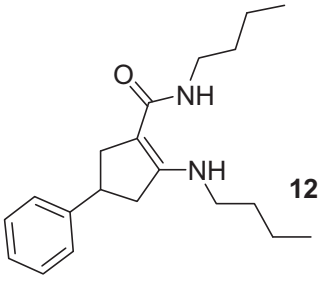
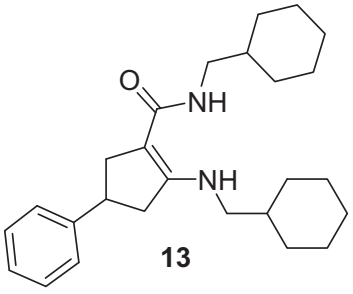
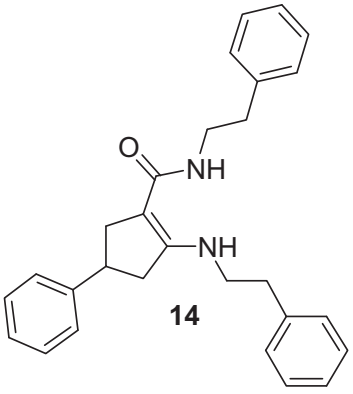
Entry	Diazodicarbonyl	Amine	Time (h)	Product	Yield (%)
1		1-Butylamine	5	 **5**	53
2		Cyclohexanemethylamine	7	 **6**	59
3		2-Phenylethylamine	6	 **7**	57
4	 **1**	Benzylamine	5	 **8**	83
5		Tryptamine	7	 **9**	61

Table 2 (*continued*)

Entry	Diazodicarbonyl	Amine	Time (h)	Product	Yield (%)
6		Aniline	5	 **10**	64
7	 **2**	1-Propylamine	8	 **11**	55
8		1-Butylamine	7	 **12**	62
9		Cyclohexanemethylamine	7	 **13**	52
10		2-Phenylethylamine	8	 **14**	54

(*continued on next page*)

Table 2 (*continued*)

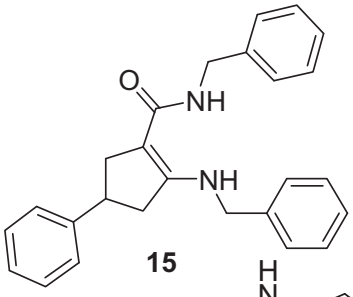
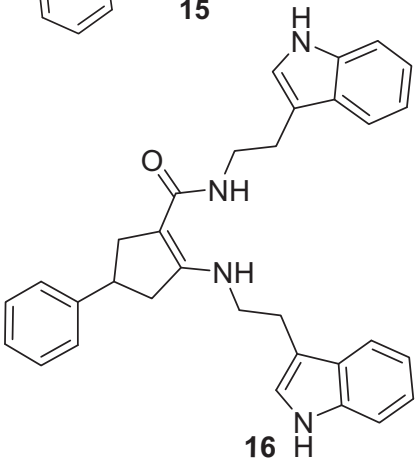
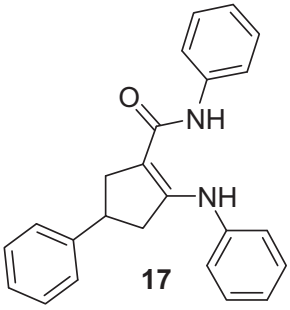
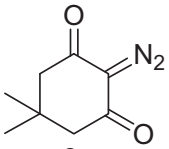
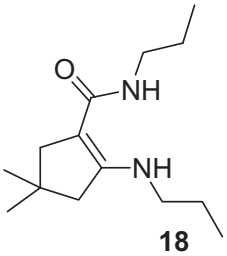
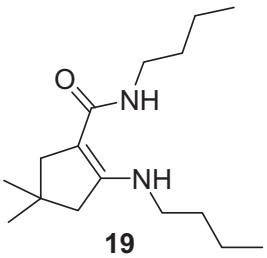
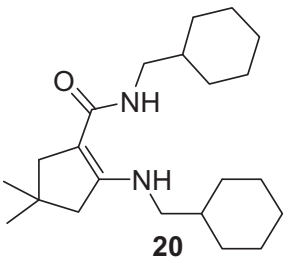
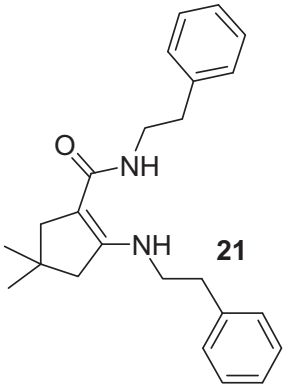
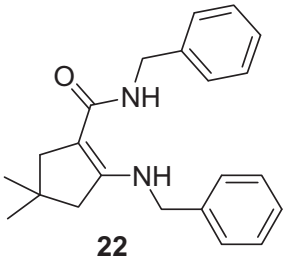
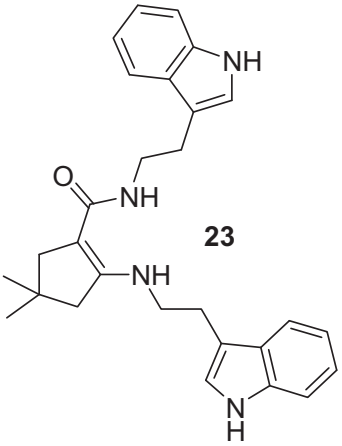
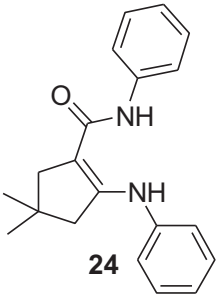
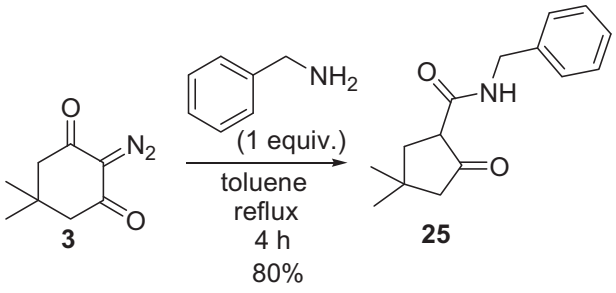
Entry	Diazodicarbonyl	Amine	Time (h)	Product	Yield (%)
11		Benzylamine	7	 **15**	63
12		Tryptamine	7	 **16**	60
13		Aniline	6	 **17**	55
14	 **3**	1-Propylamine	8	 **18**	65
15		1-Butylamine	6	 **19**	63

Table 2 (*continued*)

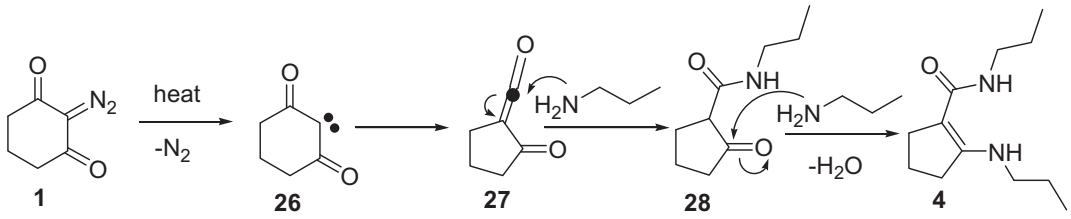
Entry	Diazodicarbonyl	Amine	Time (h)	Product	Yield (%)
16		Cyclohexanemethylamine	7	 **20**	59
17		2-Phenylethylamine	5	 **21**	54
18		Benzylamine	5	 **22**	81
19		Tryptamine	7	 **23**	61
20		Aniline	5	 **24**	63



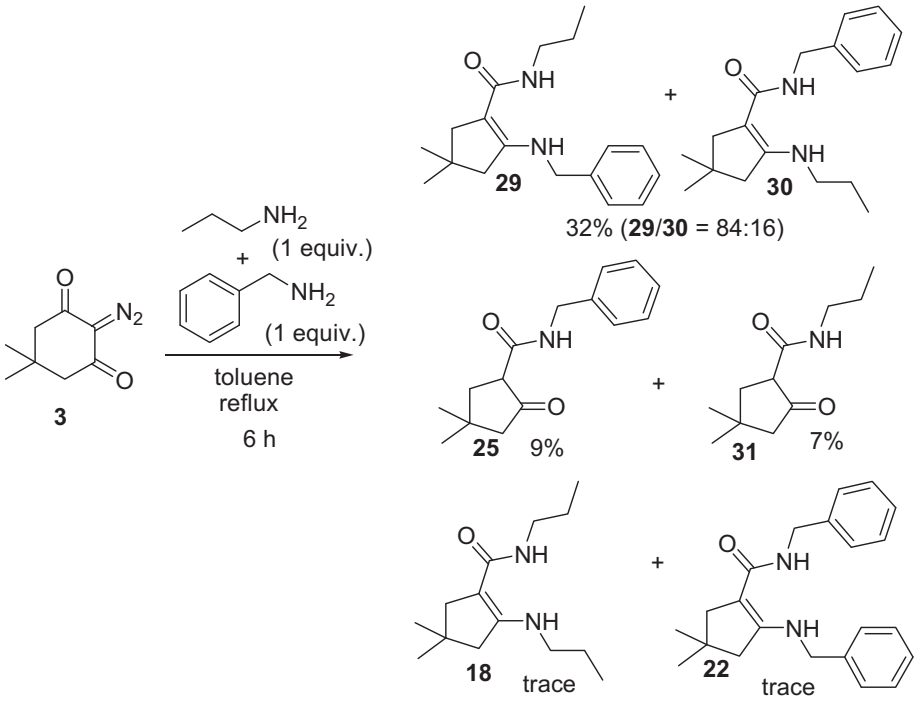
Scheme 3.

wet ethanol at reflux for 12 h gave β-keto amide **25** in 84% yield. As a stoichiometric reaction, manganese(III) acetate and copper(II) acetate mediated oxidations of β-enaminoamides to form the corresponding β-keto amides have already been reported by the Cossy group.[15]

For the further formation of uracil derivatives bearing substituents at positions 5 and 6, additional reactions of synthesized β-enaminoamides with triphosgene were carried out in the presence of K_2CO_3. The results are summarized in Table 3. Treatment of compound **8** with 1.1 equiv of triphosgene in refluxing toluene for 10 h formed uracil derivative **34** in 42% yield (entry 1, Table 3), whereas reactions of compounds **12**, **13**, **15**, **18**–**20** formed uracil



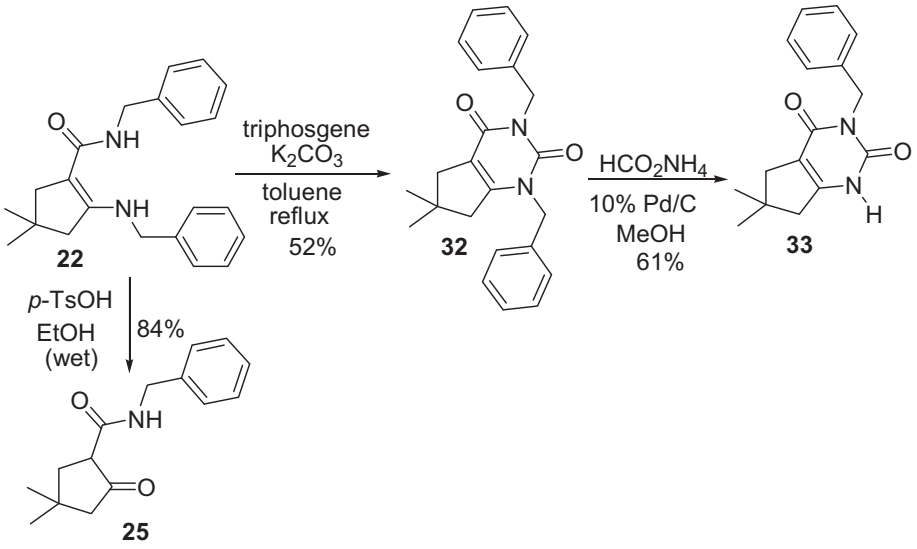
Scheme 4.



Scheme 5.

protons of a benzyl group at N-1 appeared at δ 4.94 ppm, whereas those at N-3 showed peak at δ 5.14 ppm. Selective deprotection of **32** was successfully performed using catalytic transfer hydrogenation with ammonium formate over 10% Pd/C to give **33** in 61% yield.[14] The structure of **33** was also confirmed by ^{1}H NMR analysis and by comparison with the previously reported data.[13] In the ^{1}H NMR spectrum of **33**, the methylene protons of a benzyl group at N-1 were not seen, but those at N-3 were apparent at δ 5.02 ppm. Importantly, treatment of **22** with *p*-TsOH as a metal-free catalyst in derivatives **35**–**40** with 40–54% yield (entries 2–7). These reactions provided a rapid synthetic entry to biologically interesting uracil derivatives from the corresponding β-enaminoamides.

In conclusion, a simple and efficient method for the preparation of a variety of cyclic β-enaminoamides starting from readily available cyclic diazodicarbonyls and amines has been developed. The key strategy is thermal Wolff rearrangement. Conversion of synthesized β-enaminoamides into uracil derivatives was also performed by reaction with triphosgene in the presence of K_2CO_3.



Scheme 6.

3. Experimental section

3.1. General

All the experiments were carried out in a nitrogen atmosphere. Merck precoated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical TLC. Flash column chromatography was performed using silica gel 9385 (Merck). The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Model ARX (300 and 75 MHz, respectively) spectrometer in $CDCl_3$ as the solvent. The IR spectra were recorded on a Jasco FTIR 5300 spectrophotometer. The HRMS were carried out at the Korea Basic Science Institute.

3.2. General procedure for the preparation of substituted β-enaminoamides (4–24)

To a solution of cyclic diazodicarbonyls (1.0 mmol) in toluene (5 mL) was added amines (2.2 mmol). The resulting mixture was heated at 110 °C until completion of the reaction as indicated by TLC. The solvent was removed under reduced pressure to give an oily residue, which was purified by silica gel column chromatography using *n*-hexane/ethyl acetate (10:1) as eluent to give desired products.

3.3. General procedure for the preparation of uracil derivatives (32, 34–40)

To a solution of β-enaminoamides (0.13–0.40 mmol) in toluene (5 mL) was added potassium carbonate (5 equiv) and triphosgene (1.1 equiv). The resulting mixture was heated at 110 °C in sealed tube until completion of the reaction as indicated by TLC. The solvent was removed under reduced pressure and water (25 mL) was added to the residue, and then extracted with EtOAc (3×25 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate (10:1) as eluent to give desired products.

*3.3.1. N-Propyl-2-(propylamino)cyclopent-1-enecarboxamide (**4**).* A reaction of **1** (138 mg, 1.0 mmol) with 1-propylamine (130 mg, 2.2 mmol) in refluxing toluene for 6 h afforded compound **4** (141 mg, 67%) as a solid; mp 56–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (1H, br s), 4.83 (1H, br s), 3.24–3.17 (2H, m), 3.09–3.03 (2H, m), 2.51 (2H, t, *J*=7.8 Hz), 2.38 (2H, t, *J*=7.2 Hz), 1.88–1.78 (2H, m), 1.56–1.44 (4H, m), 0.93–0.87 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 161.6, 93.2, 46.3, 40.6, 31.8, 29.3, 24.3, 23.5, 20.7, 11.5, 11.4; IR (KBr): 3352, 2960, 1630, 1525, 1447, 1289, 1144 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{12}H_{22}N_2O$: 210.1732, found: 210.1734.

*3.3.2. N-Butyl-2-(butylamino)cyclopent-1-enecarboxamide (**5**).* A reaction **1** (138 mg, 1.0 mmol) with 1-butylamine (161 mg, 2.2 mmol) in refluxing toluene for 5 h afforded compound **5** (126 mg, 53%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (1H, br s), 4.79 (1H, br s), 3.23–3.16 (2H, m), 3.09–3.02 (2H, m), 2.47 (2H, t, *J*=7.5 Hz), 2.34 (2H, t, *J*=7.2 Hz), 1.83–1.74 (2H, m), 1.48–1.38 (4H, m), 1.34–1.24 (4H, m), 0.87–0.81 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 161.7, 93.2, 44.3, 38.7, 33.3, 32.5, 31.9, 29.3, 20.8, 20.3, 20.1, 14.0, 13.9; IR (neat): 3322, 2955, 1632, 1530, 1453, 1280, 1146 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{14}H_{26}N_2O$: 238.2045, found: 238.2044.

*3.3.3. N-(Cyclohexylmethyl)-2-(cyclohexylmethylamino)cyclopent-1-enecarboxamide (**6**).* A reaction of **1** (138 mg, 1.0 mmol) with cyclohexanemethylamine (249 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **6** (188 mg, 59%) as a solid; mp 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98 (1H, br s), 4.87 (1H, br s), 3.07 (2H, t, *J*=6.6 Hz), 2.91 (2H, t, *J*=6.6 Hz), 2.48 (2H, t, *J*=7.5 Hz), 2.38 (2H, t, *J*=7.2 Hz), 1.86–1.76 (2H, m), 1.74–1.59 (10H, m), 1.47–1.32 (2H, m), 1.24–1.04 (6H, m), 0.92–0.82 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 161.7, 93.0, 51.3, 45.2, 39.4, 38.4, 31.9, 31.0, 30.9, 29.4, 26.6, 26.5, 26.0, 25.9 20.7; IR (KBr): 3318, 2917, 2851, 2664, 2345, 1741, 1631, 1523, 1447, 1268 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{20}H_{34}N_2O$: 318.2671, found: 318.2669.

*3.3.4. N-Phenethyl-2-(phenethylamino)cyclopent-1-enecarboxamide (**7**).* A reaction of **1** (138 mg, 1.0 mmol) with 2-phenylethylamine (267 mg, 2.2 mmol) in refluxing toluene for 6 h afforded compound **7** (191 mg, 57%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.03 (1H, br s), 7.31–7.16 (10H, m), 4.87 (1H, br s), 3.55–3.49 (2H, m), 3.39–3.32 (2H, m), 2.84–2.78 (4H, m), 2.41 (2H, t, *J*=7.5 Hz), 2.28 (2H, t, *J*=7.2 Hz), 1.81–1.72 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 161.3, 139.4, 139.0, 128.8, 128.7, 128.5, 128.4, 126.3, 126.2, 93.7, 46.3, 39.9, 38.0, 36.3, 31.5, 28.9, 20.5; IR (neat): 3315, 3026,

Table 3
Synthesis of uracil derivatives from the corresponding β-enaminoamides

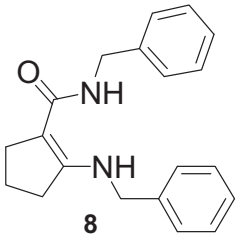
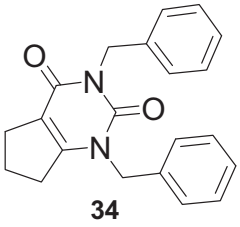
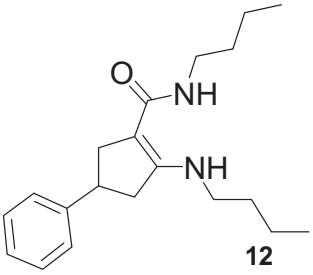
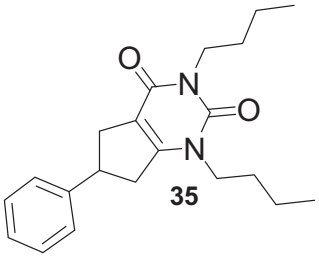
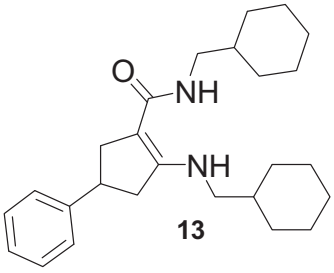
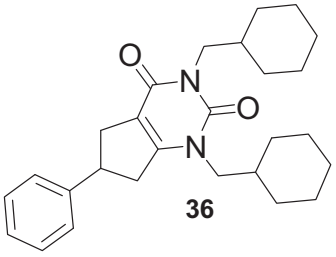
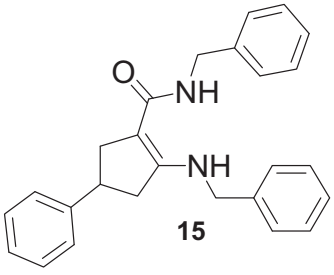
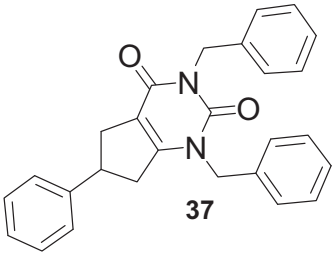
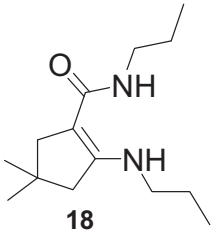
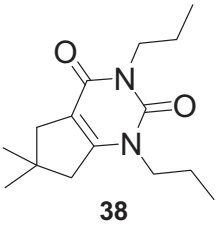
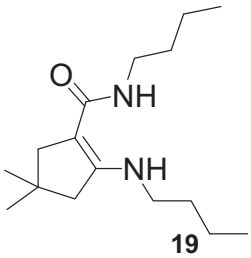
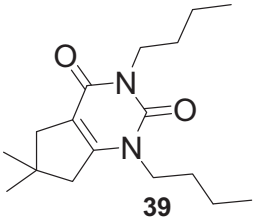
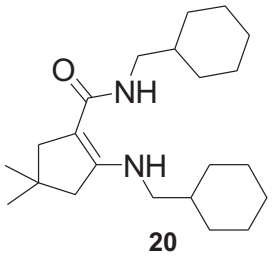
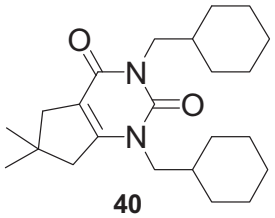
Entry	β-Enaminoamide	Time (h)	Product	Yield (%)
1	 **8**	10	 **34**	42
2	 **12**	8	 **35**	40
3	 **13**	4	 **36**	43
4	 **15**	5	 **37**	52
5	 **18**	10	 **38**	45
6	 **19**	10	 **39**	43

Table 3 (*continued*)

Entry	β-Enaminoamide	Time (h)	Product	Yield (%)
7	 **20**	4	 **40**	54

2934, 1630, 1518, 1448, 1276, 748 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{22}H_{26}N_2O$: 334.2045, found: 334.2042.

*3.3.5. N-Benzyl-2-(benzylamino)cyclopent-1-enecarboxamide (**8**).* A reaction of **1** (138 mg, 1.0 mmol) with benzylamine (236 mg, 2.2 mmol) in refluxing toluene for 5 h afforded compound **8** (254 mg, 83%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.29 (1H, br s), 7.23–7.12 (10H, m), 5.18 (1H, br s), 4.39 (2H, d, *J*=6.0 Hz), 4.25 (2H, d, *J*=6.6 Hz), 2.43 (2H, t, *J*=7.5 Hz), 2.33 (2H, t, *J*=7.2 Hz), 1.78–1.68 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 161.8, 139.8, 139.7, 128.7, 128.6, 127.6, 127.2, 127.1, 126.9, 94.3, 48.3, 42.8, 31.8, 29.3, 20.6; IR (neat): 3319, 3028, 2925, 1631, 1515, 1448, 1281, 735 cm^{-1}; HRMS *m*/*z* (M^+) $C_{20}H_{22}N_2O$: 306.1732, found: 306.1731.

*3.3.6. N-(2-(1H-Indol-3-yl)ethyl)-2-(2-(1H-indol-3-yl)ethylamino) cyclopent-1-enecarboxamide (**9**).* A reaction of **1** (138 mg, 1.0 mmol) with tryptamine (352 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **9** (251 mg, 61%) as a solid; mp 80–82 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.89 (1H, br s), 8.57 (1H, br s), 8.24 (1H, t, *J*=6.0 Hz), 7.77–7.71 (2H, m), 7.48–7.24 (6H, m), 7.02 (2H, s), 5.25 (1H, t, *J*=5.7 Hz), 3.82–3.76 (2H, m), 3.62–3.55 (2H, m), 3.14–3.06 (4H, m), 2.65–2.59 (2H, m), 2.44–2.39 (2H, m), 1.96–1.86 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 161.9, 136.5, 136.4, 127.5, 127.2, 122.7, 122.4, 121.9, 121.8, 119.2, 119.1, 118.7, 118.5, 113.0, 112.4, 111.5, 111.4, 93.6, 45.0, 39.6, 31.9, 29.2, 27.1, 25.9, 20.6; IR (KBr): 3413, 3297, 3058, 2931, 1730, 1626, 1521, 1445, 1276, 1100 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{26}H_{28}N_4O$: 412.2263, found: 412.2261.

*3.3.7. N-Phenyl-2-(phenylamino)cyclopent-1-enecarboxamide (**10**).* A reaction of **1** (138 mg, 1.0 mmol) with aniline (205 mg, 2.2 mmol) in refluxing toluene for 5 h afforded compound **10** (178 mg, 64%) as a solid; mp 128–130 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 10.37 (1H, br s), 7.47–6.97 (10H, m), 6.71 (1H, br s), 2.83–2.78 (2H, m), 2.59–2.55 (2H, m), 1.94–1.89 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.6, 159.4, 141.1, 138.6, 129.3, 129.0, 123.7, 122.9, 120.8, 120.2, 98.5, 33.7, 29.1, 21.7; IR (KBr): 3242, 3044, 2956, 2360, 1596, 1431, 1237, 1144, 754 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{18}H_{18}N_2O$: 278.1419, found: 278.1421.

*3.3.8. 4-Phenyl-N-propyl-2-(propylamino)cyclopent-1-enecarboxamide (**11**).* A reaction of **2** (214 mg, 1.0 mmol) with 1-propylamine (130 mg, 2.2 mmol) in refluxing toluene for 8 h afforded compound **11** (157 mg, 55%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.92 (1H, br s), 7.28–7.10 (5H, m), 4.78 (1H, br s), 3.45–3.34 (1H, m), 3.21–3.14 (2H, m), 3.07–3.00 (2H, m), 2.99–2.91 (1H, m), 2.85–2.78 (1H, m), 2.65–2.57 (1H, m), 2.51–2.45 (1H, m), 1.51–1.42 (4H, m), 0.89–0.83 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 160.2, 146.1, 128.6, 126.9, 126.4, 92.4, 46.5, 40.8, 40.7, 40.0, 38.2, 24.5, 23.6, 11.6, 11.5; IR (neat): 3337, 2961, 1632, 1527, 1267, 1148 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{18}H_{26}N_2O$: 286.2045, found: 286.2047.

*3.3.9. N-Butyl-2-(butylamino)-4-phenylcyclopent-1-enecarboxamide (**12**).* A reaction of **2** (214 mg, 1.0 mmol) with 1-butylamine (161 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **12** (195 mg, 62%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.94 (1H, br s), 7.32–7.12 (5H, m), 4.78 (1H, br s), 3.48–3.36 (1H, m), 3.32–3.18 (2H, m), 3.16–3.04 (2H, m), 3.02–2.93 (1H, m), 2.86–2.79 (1H, m), 2.67–2.59 (1H, m), 2.53–2.47 (1H, m), 1.51–1.41 (4H, m), 1.37–1.28 (4H, m), 0.92–0.82 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8, 160.0, 146.1, 128.6, 126.9, 126.4, 92.4, 44.3, 40.7, 39.9, 38.6, 38.2, 33.3, 32.4, 20.3, 20.0, 14.0, 13.9; IR (neat): 3325, 2954, 1632, 1522, 1445, 1282, 1147 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{20}H_{30}N_2O$: 314.2358, found: 314.2356.

*3.3.10. N-(Cyclohexylmethyl)-2-(cyclohexylmethylamino)-4-phenylcyclopent-1-enecarboxamide (**13**).* A reaction of **2** (214 mg, 1.0 mmol) with cyclohexanemethylamine (249 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **13** (205 mg, 52%) as a solid; mp 112–114 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.99 (1H, br s), 7.25–7.10 (5H, m), 4.82 (1H, br s), 3.43–3.32 (1H, m), 3.11–2.98 (2H, m), 2.93–2.75 (4H, m), 2.61–2.44 (2H, m), 1.72–1.52 (10H, m), 1.44–1.26 (2H, m), 1.19–1.02 (6H, m), 0.90–0.76 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 160.1, 145.9, 128.5, 126.8, 126.3, 92.1, 51.2, 45.1, 40.6, 39.9, 39.3, 38.2, 38.1, 30.9, 30.8, 26.5, 26.4, 25.9, 25.8; IR (KBr): 3323, 3060, 3026, 2922, 2849, 2357, 1738, 1633, 1588, 1521, 1447, 1259, 1181, 1150, 762 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{26}H_{38}N_2O$: 394.2984, found: 394.2986.

*3.3.11. N-Phenethyl-2-(phenethylamino)-4-phenylcyclopent-1-enecarboxamide (**14**).* A reaction of **2** (214 mg, 1.0 mmol) with 2-phenylethylamine (267 mg, 2.2 mmol) in refluxing toluene for 8 h afforded compound **14** (222 mg, 54%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.05 (1H, br s), 7.28–7.12 (15H, m), 4.79 (1H, br s), 3.49–3.44 (2H, m), 3.33–3.26 (2H, m), 2.99–2.89 (1H, m), 2.78–2.74 (4H, m), 2.69–2.56 (2H, m), 2.47–2.31 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.7, 160.0, 145.9, 139.5, 139.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 126.9, 126.5, 126.4, 92.9, 46.5, 40.6, 40.2, 39.8, 38.3, 37.9, 36.4; IR (neat): 3312, 3027, 2928, 1632, 1521, 1451, 1266, 751 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{28}H_{30}N_2O$: 410.2358, found: 410.2356.

*3.3.12. N-Benzyl-2-(benzylamino)-4-phenylcyclopent-1-enecarboxamide (**15**).* A reaction of **2** (214 mg, 1.0 mmol) with benzylamine (236 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **15** (240 mg, 63%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.36 (1H, t, *J*=6.3 Hz), 7.28–7.07 (15H, m), 5.13 (1H, t, *J*=5.7 Hz), 4.44–4.40 (2H, m), 4.29 (2H, d, *J*=6.6 Hz) 3.42–3.31 (1H, m), 2.96–2.78 (2H, m), 2.64–2.45 (2H, m); ^{13}C NMR (75 MHz,

$CDCl_3$): δ 168.5, 160.4, 145.8, 139.7, 139.5, 128.8, 128.7, 128.6, 127.8, 127.4, 127.3, 127.0, 126.9, 126.5, 93.5, 48.4, 43.1, 40.7, 39.9, 38.2; IR (neat): 3325, 3060, 2926, 1632, 1520, 1449, 1263, 736 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{26}H_{26}N_2O$:382.2045, found: 382.2043.

*3.3.13. N-(2-(1H-Indol-3-yl)ethyl)-2-(2-(1H-indol-3-yl)ethylamino)-4-phenylcyclopent-1-enecarboxamide (**16**).* A reaction of **2** (214 mg, 1.0 mmol) with tryptamine (352 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **16** (293 mg, 60%) as a solid; mp 87–89 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.12 (1H, br s), 7.99 (2H, br s), 7.61–7.52 (2H, m), 7.33–6.98 (13H, m), 4.93 (1H, br s), 3.64–3.57 (2H, m), 3.45–3.40 (2H, m), 3.31–3.26 (1H, m), 2.99–2.95 (4H, m), 2.87–2.81 (1H, m), 2.69–2.62 (1H, m), 2.51–2.43 (1H, m), 2.36–2.30 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.9, 160.4, 145.8, 136.5, 128.6, 127.4, 127.1, 126.9, 126.4, 122.8, 122.3, 121.9, 121.8, 119.3, 119.2, 118.8, 118.5, 113.0, 112.4, 111.5, 111.4, 92.6, 45.1, 40.5, 39.9, 39.5, 37.5, 27.2, 25.9; IR (KBr): 3414, 3053, 2922, 2346, 1740, 1629, 1519, 1445, 1268, 1096, 910, 739 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{32}H_{32}N_4O$:488.2576, found: 488.2578.

*3.3.14. N,4-Diphenyl-2-(phenylamino)cyclopent-1-enecarboxamide (**17**).* A reaction of **2** (214 mg, 1.0 mmol) with aniline (205 mg, 2.2 mmol) in refluxing toluene for 6 h afforded compound **17** (195 mg, 55%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 10.42 (1H, br s), 7.45–7.25 (2H, m), 7.28–6.95 (11H, m), 6.71 (1H, br s), 6.61–6.58 (2H, m), 3.53–3.42 (1H, m), 3.24–3.15 (1H, m), 2.99–2.91 (2H, m), 2.73–2.67 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.4, 157.6, 146.2, 144.8, 140.5, 138.3, 129.2, 129.1, 128.8, 128.6, 126.8, 126.5, 123.5, 123.0, 120.6, 119.9, 118.4, 115.0, 97.1, 41.4, 41.3, 37.4; IR (neat): 3362, 3055, 2922, 2356, 1630, 1499, 1437, 1243, 754 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{24}H_{22}N_2O$: 354.1732, found: 354.1732.

*3.3.15. 4,4-Dimethyl-N-propyl-2-(propylamino)cyclopent-1-enecarboxamide (**18**).* A reaction of **3** (166 mg, 1.0 mmol) with 1-propylamine (130 mg, 2.2 mmol) in refluxing toluene for 8 h afforded compound **18** (155 mg, 65%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.85 (1H, br s), 4.76 (1H, br s), 3.23–3.17 (2H, m), 3.06–2.99 (2H, m), 2.33 (2H, s), 2.20 (2H, s), 1.56–1.44 (4H, m), 1.05 (6H, s), 0.93–0.87 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 160.0, 92.1, 46.3, 46.1, 44.3, 40.4, 35.5, 29.8. 24.3, 23.3, 11.4, 11.3; IR (neat): 3323, 2957, 1633, 1526, 1446, 1286, 1168 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{14}H_{26}N_2O$: 238.2045, found: 238.2044.

*3.3.16. N-Butyl-2-(butylamino)-4,4-dimethylcyclopent-1-enecarboxamide (**19**).* A reaction of **3** (166 mg, 1.0 mmol) with 1-butylamine (161 mg, 2.2 mmol) in refluxing toluene for 6 h afforded compound **19** (168 mg, 63%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.78 (1H, br s) 4.71 (1H, br s), 3.22–3.15 (2H, m), 3.02–2.98 (2H, m), 2.28 (2H, s), 2.15 (2H, s), 1.46–1.36 (4H, m), 1.33–1.24 (4H, m), 1.05 (6H, s), 0.87–0.81 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 160.0, 92.2, 46.5, 44.5, 44.1, 38.6, 35.6, 33.3, 32.4, 30.0, 20.2, 19.9, 13.9, 13.8; IR (neat): 3319, 2953, 1633, 1524, 1444, 1282, 1166 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{16}H_{30}N_2O$: 266.2358, found: 266.2354.

*3.3.17. N-(Cyclohexylmethyl)-2-(cyclohexylmethylamino)-4,4-dimethylcyclopent-1-enecarboxamide (**20**).* A reaction of **3** (166 mg, 1.0 mmol) with cyclohexanemethylamine (249 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **20** (204 mg, 59%) as a solid; mp 85–87 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.93 (1H, br s), 4.79 (1H, br s), 3.06 (2H, t, *J*=6.6 Hz), 2.88 (2H, t, *J*=6.6 Hz), 2.30 (2H, s), 2.19 (2H, s), 1.80–1.56 (10H, m), 1.44–1.36 (2H, m), 1.20–1.11 (6H, m), 1.08 (6H, s), 0.96–0.81 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 160.2, 91.9, 51.1, 46.5, 45.0, 44.4, 39.3, 38.2, 35.6, 30.9, 30.8, 29.9, 26.5, 26.4, 25.9, 25.8; IR (KBr): 3316, 2920, 2854, 2666, 2344, 1632, 1523, 1448, 1272 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{22}H_{38}N_2O$: 346.2984, found: 346.2982.

*3.3.18. 4,4-Dimethyl-N-phenethyl-2-(phenethylamino)cyclopent-1-enecarboxamide (**21**).* A reaction of **3** (166 mg, 1.0 mmol) with 2-phenylethylamine (267 mg, 2.2 mmol) in refluxing toluene for 5 h afforded compound **21** (196 mg, 54%) as an oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.91 (1H, t, *J*=6.0 Hz), 7.24–7.07 (10H, m), 4.73 (1H, t, *J*=5.4 Hz), 3.46–3.39 (2H, m), 3.22–3.20 (2H, m), 2.75–2.68 (4H, m), 2.11 (2H, s), 1.99 (2H, s), 0.95 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.0, 160.0, 139.6, 139.1, 128.9, 128.8, 128.6, 128.5, 126.4, 126.3, 92.8, 46.4, 46.3, 44.3, 40.1, 38.2, 36.4, 35.5, 29.9; IR (neat): 3325, 3062, 2950, 1633, 1516, 1448, 1282 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{24}H_{30}N_2O$: 362.2358, found: 362.2361.

*3.3.19. N-Benzyl-2-(benzylamino)-4,4-dimethylcyclopent-1-enecarboxamide (**22**).* A reaction of **3** (166 mg, 1.0 mmol) with benzylamine (236 mg, 2.2 mmol) in refluxing toluene for 5 h afforded compound **22** (271 mg, 81%) as a solid; mp 69–71 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.24 (1H, br s), 7.29–7.14 (10H, m), 5.06 (1H, br s), 4.41 (2H, d, *J*=5.7 Hz), 4.26 (2H, d, *J*=6.6 Hz), 2.28 (2H, s), 2.18 (2H, s), 1.02 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.8, 160.3, 139.7, 139.4, 128.5, 127.6, 127.0, 126.9, 126.6, 93.2, 48.1, 46.3, 44.4, 42.8, 35.8, 29.8; IR (KBr): 3351, 3060, 2945, 1628, 1518, 1430, 1259, 612 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{22}H_{26}N_2O$: 334.2043, found 334.2043.

*3.3.20. N-(2-(1H-Indol-3-yl)ethyl)-2-(2-(1H-indol-3-yl)ethylamino)-4,4-dimethylcyclopent-1-enecarboxamide (**23**).* A reaction of **3** (166 mg, 1.0 mmol) with tryptamine (352 mg, 2.2 mmol) in refluxing toluene for 7 h afforded compound **23** (268 mg, 61%) as a solid; mp 69–71 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.56 (1H, br s), 8.23 (1H, br s), 7.90 (1H, t, *J*=6.0 Hz), 7.48–7.40 (2H, m), 7.20–6.94 (6H, m), 6.74 (2H, s), 4.88 (1H, t, *J*=6 Hz), 3.52–3.46 (2H, m), 3.29–3.23 (2H, m), 2.87–2.76 (4H, m), 2.13 (2H, s), 1.94 (2H, s), 0.89 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.4, 160.6, 136.5, 127.5, 127.1, 122.7, 122.4, 121.9, 121.7, 119.2, 119.1, 118.8, 118.4, 113.0, 112.3, 111.5, 111.4, 92.5, 46.5, 44.9, 44.2, 39.6, 35.5, 29.9, 27.1, 25.9; IR (KBr): 3410, 3285, 2938, 1908, 1730, 1629, 1521, 1445, 1279, 1100 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{28}H_{32}N_4O$: 440.2576, found: 440.2579.

*3.3.21. 4,4-Dimethyl-N-phenyl-2-(phenylamino)cyclopent-1-enecarboxamide (**24**).* A reaction of **3** (166 mg, 1.0 mmol) with aniline (205 mg, 2.2 mmol) in refluxing toluene for 5 h afforded compound **24** (193 mg, 63%) as a solid; mp 140–142 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 10.41 (1H, br s), 7.51–6.97 (10H, m), 6.71 (1H, br s), 2.69 (2H, s), 2.44 (2H, s), 1.18 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.9, 157.7, 140.8, 138.4, 129.1, 128.9, 123.4, 122.7, 120.5, 119.9, 97.2, 48.1, 43.9, 36.7, 29.5; IR (KBr): 3361, 3055, 2953, 1628, 1500, 1434, 1244, 1182 cm^{-1}; HRMS *m*/*z* (M^+) $C_{20}H_{22}N_2O$: 306.1732, found: 306.1734.

*3.3.22. N-Benzyl-4,4-dimethyl-2-oxocyclopentanecarboxamide (**25**).* A reaction of **3** (166 mg, 1.0 mmol) with benzylamine (107 mg, 1.0 mmol) in refluxing toluene for 4 h afforded compound **25** (196 mg, 80%) as an oil; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26–7.16 (5H, m), 7.10 (1H, br s), 4.44–4.28 (2H, m), 3.14 (1H, t, *J*=9.6 Hz), 2.30–1.95 (4H, m), 1.08 (3H, s), 0.97 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 216.3, 167.0, 138.3, 128.8, 127.8, 127.5, 53.9, 53.7, 43.8, 39.4, 34.2, 28.9, 27.9; IR (neat): 3306, 2954, 2357, 1740, 1648, 1537, 1455, 1365, 1232, 1126 cm^{-1}; HRMS *m*/*z* (M^+) calculated for $C_{15}H_{19}NO_2$: 245.1416, found: 245.1414.

*3.3.23. 2-(Benzylamino)-4,4-dimethyl-N-propylcyclopent-1-enecarboxamide (**29**), N-benzyl-4,4-dimethyl-2-(propylamino)cyclopent-1-enecarboxamide (**30**), N-benzyl-4,4-dimethyl-2-*

*oxocyclopentane carboxamide (**25**), and 4,4-dimethyl-2-oxo-N-propylcyclopentanecarboxamide (**31**).* A reaction of **3** (166 mg, 1.0 mmol) with 1-propylamine (59 mg, 1.0 mmol) and benzylamine (107 mg, 1.0 mmol) in refluxing toluene for 6 h afforded compounds **29** and **30** (92 mg, 32%) as a 84:16 ratio of isomers and β-keto amides **25** (22 mg, 9%) and **31** (14 mg, 7%) as a 60:40 ratio of inseparable mixtures together with a trace amount of β-enaminoamides **18** and **22**.

Compound **29**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (1H, br s) 7.23–7.18 (5H, m), 5.01 (1H, br s), 4.40 (2H, d, J=5.7 Hz), 3.03–2.96 (2H, m), 2.29 (2H, s), 2.16 (2H, s), 1.49–1.42 (2H, m), 1.05 (6H, s), 0.86 (3H, t, J=7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 160.9, 139.9, 128.7, 127.8, 126.9, 92.1, 46.7, 46.4, 44.5, 43.0, 35.9, 30.1, 24.6, 11.5; HRMS (FAB) m/z ($M+H^+$) calculated for $C_{18}H_{27}N_2O$: 287.2123, found: 287.2126.

Compound **30**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (1H, br s), 7.23–7.18 (5H, m), 5.10 (1H, br s), 4.25 (2H, d, J=6.6 Hz), 3.03–2.96 (2H, m), 2.27 (2H, s), 2.18 (2H, s), 1.49–1.42 (2H, m), 1.01 (6H, s), 0.86 (3H, t, J=7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 160.9, 139.9, 128.8, 127.9, 127.2, 94.0, 48.3, 46.6, 44.6, 43.1, 35.9, 30.0, 24.3, 11.5; IR (neat): 3315, 3061, 3029, 2953, 2869, 1633, 1588, 1517, 1448, 1282, 1168, 734 cm^{-1}; HRMS m/z (FAB) ($M+H^+$) calculated for $C_{18}H_{27}N_2O$: 287.2123, found: 287.2126.

Compound **25**: These spectral data of ^{1}H NMR, ^{13}C NMR, and IR are the same as described above. HRMS m/z (FAB) ($M+H^+$) calculated for $C_{15}H_{20}NO_2$: 246.1494, found: 246.1492.

Compound **31**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (1H, br s), 4.44–4.28 (2H, m), 3.19–3.07 (1H, m), 2.35–1.95 (4H, m), 1.48–1.41 (2H, m), 1.08 (3H, s), 0.98 (3H, s), 0.84 (3H, t, J=7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 216.1, 167.8, 53.6, 43.4, 41.2, 39.1, 33.9, 28.6, 27.6, 22.6, 11.3; HRMS m/z (M^+) calculated for $C_{15}H_{19}NO_2$: 245.1416, found: 245.1414 and HRMS (FAB) m/z ($M+H^+$) calculated for $C_{11}H_{20}NO_2$: 198.1494, found: 198.1497.

*3.3.24. 1,3-Dibenzyl-6,6-dimethyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**32**).* A reaction of **22** (100 mg, 0.30 mmol) with triphosgene (98 mg, 0.33 mmol) in refluxing toluene in the presence of K_2CO_3 (207 mg, 1.5 mmol) for 10 h afforded compound **32** (56 mg, 52%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.14 (10H, m), 5.14 (2H, s), 4.94 (2H, s), 2.53 (4H, s), 1.10 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.3, 153.4, 153.0, 137.3, 136.1, 129.1, 128.9, 128.3, 127.8, 126.6, 110.9, 49.1, 46.8, 44.6, 42.4, 37.5, 29.4; IR (neat): 3332, 3031, 2954, 2358, 1697, 1656, 1481, 1389, 1261, 1074, 1028 cm^{-1}; HRMS m/z (M^+) calculated for $C_{23}H_{24}N_2O_2$: 360.1838, found: 360.1840.

*3.3.25. 3-Benzyl-6,6-dimethyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**33**).* A reaction of **32** (100 mg, 0.28 mmol) with ammonium formate (10 mL of a 0.4 N solution in dry MeOH) and 10% palladium on charcoal (319 mg) was refluxed for 15 h. The mixture was filtered through filter paper, and the solid residue was extensively washed with MeOH (50 mL) and $CHCl_3$ (50 mL). Removal of solvents under reduced pressure and following column chromatography on silica gel using chloroform/methanol (99:1) as eluent gave products **33** (46 mg, 61%) as a solid; mp 213–215 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.10 (1H, br s), 7.40–7.37 (2H, m), 7.24–7.18 (3H, m), 5.02 (2H, s), 2.44 (4H, s), 1.11 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.7, 154.1, 151.8, 137.3, 129.2, 128.5, 127.8, 110.8, 46.2, 43.9, 42.4, 38.2, 29.8. IR (KBr): 3247, 3030, 2953, 2861, 1708, 1641, 1531, 1435, 1330, 1261, 1071 cm^{-1}; HRMS m/z (M^+) calculated for $C_{16}H_{18}N_2O_2$: 270.1368, found: 270.1369.

*3.3.26. N-Benzyl-4,4-dimethyl-2-oxocyclopentanecarboxamide (**25**).* To a solution of **22** (100 mg, 0.30 mmol) in wet ethanol (5 mL) was added *p*-toluenesulfonic acid monohydrate (6 mg). The reaction mixture was refluxed for 12 h. After cooling to room temperature, water (25 mL) was added and the mixture was extracted with EtOAc (3×25 mL). The organic layer was washed saturated $NaHCO_3$ solution (30 mL), dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate (10:1) as eluent to give **25** (62 mg, 84%) as an oil. The spectral data of **25** are the same as described above.

*3.3.27. 1,3-Dibenzyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**34**).* A reaction of **8** (100 mg, 0.33 mmol) with triphosgene (107 mg, 0.36 mmol) in refluxing toluene in the presence of K_2CO_3 (228 mg, 1.65 mmol) for 10 h afforded compound **34** (46 mg, 42%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.46 (10H, m), 5.15 (2H, s), 4.97 (2H, s), 2.77–3.69 (4H, m), 2.04–1.94 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.7, 154.8, 153.0, 137.2, 136.1, 128.9, 128.8, 128.3, 127.8, 127.4, 126.7, 112.2, 49.3, 44.6, 32.3, 27.7, 21.0; IR (neat): 3328, 3031, 2953, 2359, 1695, 1656, 1482, 1389, 1354, 1075, 1029, 912, 818, 734, 701 cm^{-1}; HRMS m/z (M^+) calculated for $C_{21}H_{20}N_2O_2$: 332.1525, found: 332.1525.

*3.3.28. 1,3-Dibenzyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**35**).* A reaction of **12** (70 mg, 0.22 mmol) with triphosgene (72 mg, 0.24 mmol) in refluxing toluene in the presence of K_2CO_3 (152 mg, 1.09 mmol) for 8 h afforded compound **35** (30 mg, 40%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.20 (5H, m), 3.96–3.91 (2H, m), 3.79–3.62 (3H, m), 3.32–3.16 (2H, m), 2.98–2.80 (2H, m), 1.68–1.56 (4H, m), 1.40–1.30 (4H, m), 0.96–0.88 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.7, 152.8, 152.5, 144.2, 128.8, 126.8, 126.7, 110.7, 46.5, 41.3, 40.4, 35.9, 31.1, 29.8, 20.3, 20.0, 13.8, 13.7; IR (neat): 2956, 2868, 2358, 1696, 1656, 1484, 1364, 1323, 1253, 1188, 1079, 763 cm^{-1}; HRMS m/z (M^+) calculated for $C_{21}H_{28}N_2O_2$: 340.2151, found: 340.2154.

*3.3.29. 1,3-Bis(cyclohexylmethyl)-6-phenyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**36**).* A reaction of **13** (158 mg, 0.40 mmol) with triphosgene (131 mg, 0.44 mmol) in refluxing toluene in the presence of K_2CO_3 (276 mg, 2 mmol) for 4 h afforded compound **36** (72 mg, 43%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.15 (5H, m), 3.81–3.69 (2H, m), 3.67–3.55 (1H, m), 3.54–3.43 (2H, m), 3.26–3.11 (2H, m), 2.92–2.76 (2H, m), 1.77–1.50 (12H, m), 1.22–1.03 (6H, m), 0.99–0.76 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.1, 153.2, 152.9, 150.2, 144.1, 128.7, 126.7, 110.5, 52.8, 47.1, 41.3, 10.9, 37.3, 36.3, 35.9, 30.8, 30.7, 26.3, 26.1, 25.8, 25.7; IR (neat): 2924, 2851, 2356, 1697, 1657, 1482, 1395, 1355, 1268, 1144, 1108, 1078, 762 cm^{-1}; HRMS m/z (M^+) calculated for $C_{27}H_{36}N_2O_2$: 420.2777, found: 420.2780.

*3.3.30. 1,3-Dibenzyl-6-phenyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**37**).* A reaction of **15** (50 mg, 0.13 mmol) with triphosgene (43 mg, 0.14 mmol) in refluxing toluene in the presence of K_2CO_3 (90 mg, 0.65 mmol) for 5 h afforded compound **37** (28 mg, 52%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80–7.41 (15H, m), 5.46 (2H, s), 5.36–5.17 (2H, m), 3.94–3.83 (1H, m), 3.52–3.44 (2H, m), 3.19–3.07 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.5, 153.3, 153.0, 143.9, 137.2, 135.9, 129.1, 128.9, 128.7, 128.4, 127.9, 127.5, 126.8, 126.7, 126.6, 111.2, 49.3, 44.7, 41.2, 40.4, 36.0; IR (neat): 3038, 2944, 2344, 2252, 1656, 1482, 1345, 1189, 1080, 912, 733 cm^{-1}; HRMS m/z (M^+) calculated for $C_{37}H_{24}N_2O_2$: 408.1838, found: 408.1836.

*3.3.31. 6,6-Dimethyl-1,3-dipropyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**38**).* A reaction of **18** (50 mg, 0.21 mmol) with triphosgene (69 mg, 0.23 mmol) in refluxing toluene in the presence of K_2CO_3 (145 mg, 1.05 mmol) for 10 h afforded compound **38** (25 mg, 45%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.86 (2H, t, J=7.5 Hz), 3.62 (2H, t, J=7.5 Hz), 2.61 (2H, s),

2.51 (2H, s), 1.68–1.55 (4H, m), 1.17 (6H, s), 0.94–0.88 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.3, 153.0, 152.5, 110.4, 48.0, 46.7, 42.8, 42.4, 37.4, 29.6, 22.2, 21.0, 11.4, 11.1; IR (neat): 3356, 2959, 2871, 1697, 1657, 1482, 1366, 1263, 1074, 765 cm^{-1}; HRMS m/z (M^+) calculated for $C_{15}H_{24}N_2O_2$: 264.1838, found: 264.1836.

*3.3.32. 1,3-Dibutyl-6,6-dimethyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**39**).* A reaction of **19** (60 mg, 0.23 mmol) with triphosgene (75 mg, 0.25 mmol) in refluxing toluene in the presence of K_2CO_3 (159 mg, 1.15 mmol) for 10 h afforded compound **39** (29 mg, 43%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.90 (2H, t, J=7.5 Hz), 3.65 (2H, t, J=7.5 Hz), 2.60 (2H, s), 2.51 (2H, s), 1.64–1.53 (4H, m), 1.38–1.30 (4H, m), 1.17 (6H, s), 0.96–0.89 (6H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.2, 152.8, 152.5, 110.5, 46.7, 46.3, 42.5, 41.2, 37.4, 31.1, 29.8, 29.6, 20.2, 20.0, 13.7, 13.6; IR (neat): 3335, 2955, 1695, 1658, 1482, 1366, 1317, 1255, 1135, 1079, 766 cm^{-1}; HRMS m/z (M^+) calculated for $C_{17}H_{28}N_2O_2$: 292.2151, found: 292.2148.

*3.3.33. 1,3-Bis(cyclohexylmethyl)-6,6-dimethyl-6,7-dihydro-1H-cyclopenta[d]pyrimidine-2,4(3H,5H)-dione (**40**).* A reaction of **20** (100 mg, 0.29 mmol) with triphosgene (95 mg, 0.32 mmol) in refluxing toluene in the presence of K_2CO_3 (200 mg, 1.45 mmol) for 4 h afforded compound **40** (58 mg, 54%) as an oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.75 (2H, d, J=3.6 Hz), 3.47 (2H, d, J=3.6 Hz), 2.59 (2H, s), 2.50 (2H, s), 1.80–1.59 (12H, m), 1.21–1.08 (12H, m), 1.04–0.89 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.7, 153.5, 153.2, 110.4, 53.6, 52.9, 47.5, 47.3, 42.6, 37.6, 37.4, 36.5, 31.0, 30.9, 29.7, 26.6, 26.4, 26.0, 25.9; IR (neat): 3053, 2924, 2851, 2358, 1697, 1657, 1480, 1394, 1357, 1314, 1267, 1171, 1142, 1105, 734 cm^{-1}; HRMS m/z (M^+) calculated for $C_{23}H_{36}N_2O_2$: 372.2777, found: 372.2779.

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References and notes

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