# Some reactions of 2-(4-substitutedphenyl)-2-(N-methyl-N-4-substitutedbenzamido) acetic acids

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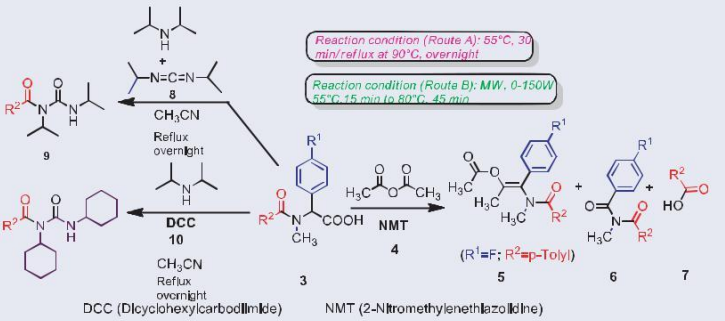
ABSTRACT

In situ generated 2,4-diaryl substituted munchnones€ from 2-(4-substi-tutedphenyl)-2-(N-methyl-N-4-substitutedbenzamido)acetic acids react with acetic anhydride in the presence of 2-nitromethylene thia-zolidine, which is most likely acting as a base, and unexpectedly undergo a Dakin–West type reaction and a concurrent autoxidation reaction leading to the formation of (E)-1-(N,4-dimethylbenzamido)-1-(4-fluorophenyl)prop-1-en-2-yl acetate, 4-substitutedphenyl-N-methyl-N-(4-substitutedbenzoyl) benzamides and p-substituted benzoic acids. In addition, a novel and efficient access to N-acyl urea deriva-tives is described by the reaction between 2-(4-substitutedphenyl)-2-(N-methyl-N-4-substitutedbenzamido)acetic acids and cyclohexyl, iso-propyl carbodiimides in the presence of a base. The structures of all new products were identified on the basis of NMR and IR spectra, along with X-ray diffraction data and HRMS measurements.

GRAPHICAL ABSTRACT

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Acyl urea; Dakin–West reaction; M€unchnone precursor; nitromethylene thiazolidine

## Introduction

Munchnones,€ so-called, 1,3-oxazolium-5-olates, are among the five-membered mesoionic compounds which can be easily prepared by cyclodehydration of N-substi-tuted-N-acyl-a-amino acids with acetic anhydride, N,N$^{0}$-dicyclohexylcarbodiimide,

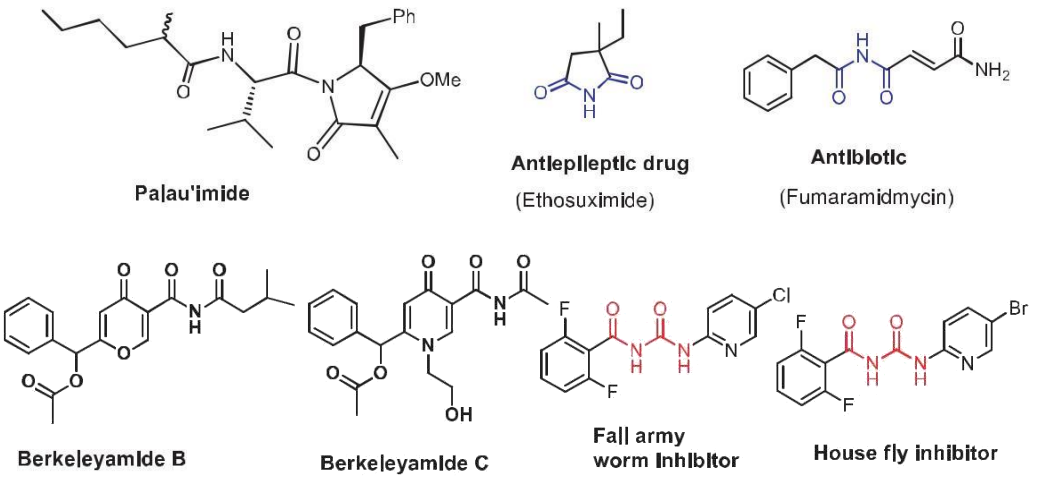



Figure 1. Some biologically important imides and N-acylureas.

N,N′-diisopropylcarbodiimide and they are utilized in the synthesis of many valuable heterocycles such as substituted pyrroles through 1,3-dipolar cycloaddition with a wide range of doubly or triply bonded electron-deficient dipolarophilic reagents.[1–8] There are many examples regarding the munchnones€ as 1,3-dipoles in cycloaddition reactions, but other reactions of these ring systems have not been fully explored.

[10,11]

The Dakin–West reaction[9] is a well-known procedure for the preparation of espe-cially a-acetamido methyl and b-aryl ketones, which are important skeletons of biologic-ally or pharmacologically important compounds, by treatment of N-acylated a-amino acids or aryl acetic acids with acetic anhydride or trifluoroacetic anhydride in the pres-ence of a base.

Imides in general are one of the most important structural motif for natural and pharmaceutical compounds such as palau'imide,[12] coniothyriomycin,[13] ethosuximide,[14] fumaramidmycin,[15] and berkeleyamide B and C.[16] The N-acyl urea derivatives are an important sub-class of such substrates especially for medicinal and agrochemical applications. In addition, N-acylurea derivatives are used as inhibitors of the reproduction and growth for the house fly and fall army worm (Figure 1).[17]

There are various methods to synthesize N-acylurea derivatives from the reactions of carboxylic acids with carbodiimides.[18–20] Soeta and Ukaji have reported oxidative coupling reaction of various kind of aldehydes with N,N′-disubstituted carbodiimides catalyzed by N-heterocyclic carbene under aerobic conditions to furnish N-acyl derivatives.[21]

Taking account of the above considerations and literature-based knowledge of munchnones,€ Dakin–West reaction which can be realized as a reaction pathway for our work, we have focused on some reactions of the munchnone€ precursors which have turned out to be a practical one-pot protocol for the synthesis of N-acyl urea derivatives.

## Results and discussion

Recently, we have reported some chemistry incorporating mesoionic 1,3-dipoles; namely sydnones, nitrile oxides, nitrile imines and electron-deficient alkenes, alkynes,[22]

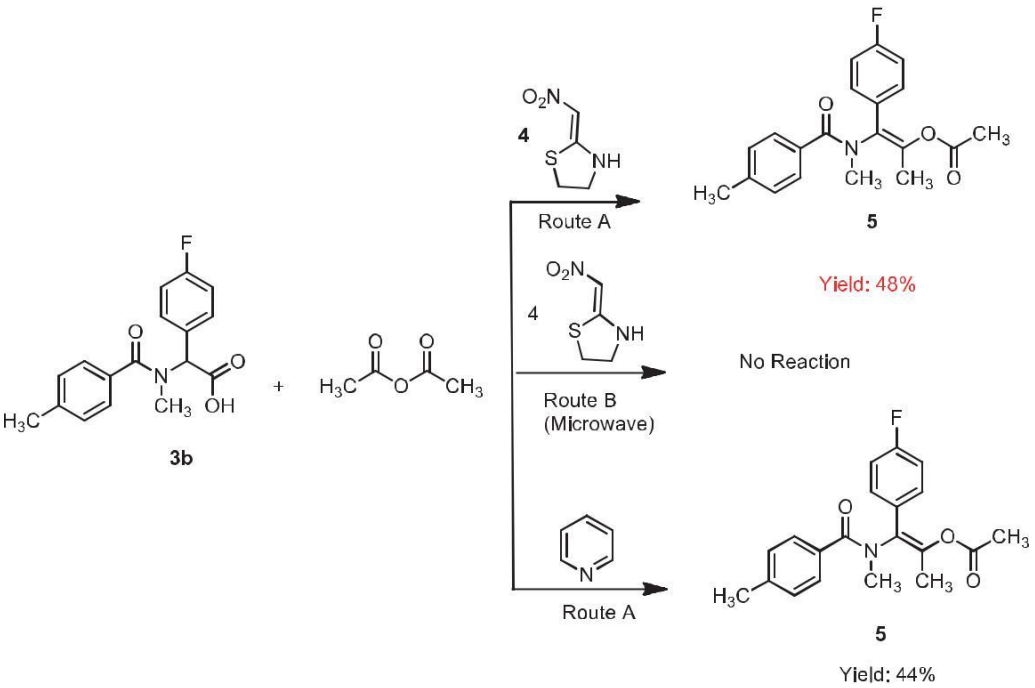
2-nitromethylenethiazolidine and benzothiophene 1,1-dioxide.[23–28] Herein, we report a study of munchnones€ generated from 2-(4-substitutedphenyl)-2-(N-methyl-N-4-substitutedbenzamido)acetic acids 3 and acetic anhydride, DCC and DIPC in the presence of 2-nitromethylenethiazolidine 4 and diisopropylamine. In this regard, the products were one enol ester, five imides and seven benzoic acid derivatives obtained by the autoxidation reaction between munchnone€ precursors (amino acids) and acetic anhydride in the presence of 2-nitromethylenethiazolidine. To the best of our knowledge, 2-nitromethylenethiazolidine has not been reported so far as a base in such reactions, but in our case, it might have behaved as a base through its imine tautomeric form. On the other hand, N-acylureas derivatives have also been generated through a substitution reaction in which 2-(4-substitutedphenyl)-2-(N-methyl-N-4-substitutedbenzamido)acetic acids 3 were interacted with dehydrating agents, DCC and DIPC in the presence of diisopropyl-amine under reflux conditions in acetonitrile. There is no reported example for the synthesis of N-acylureas from munchnone€ precursors by means of N,N$^0$-disubstituted carbodiimides in the presence of a base.

4-Substituted N-methylgylcine hydrochloride 1a and 1 b play a key role in the synthesis of unsymmetrical munchnone€ derivatives which were generated in situ from C-(4-substitutedphenyl)-N-(benzoyl)-N-methylglycines 3a-k which were synthesized according to the literature procedures[1–3] and used in the subsequent steps without further purification.

2-(N,4-Dimethylbenzamido)-2-(4-fluorophenyl)acetic acid 3 b underwent a reaction affording an enol ester 5 through a Dakin–West type transformation both in the pres-ence of pyridine and 2-nitromethylene thiazolidine 4, but no reaction occurred under microwave heating (Scheme 1). IR spectrum showed two carbonyl absorptions and pro-ton NMR gave four singlet peaks between 3.31-1.98 ppm, one of them was of p-tolyl methyl protons. After obtaining a fine crystal of the compound 5, we were able to establish full structural characterization by means of X-ray diffraction data.

Other substituted amino acids 3 were tried under the same conditions for obtaining derivatives of enol ester 5, but, amino acids 3a, 3ck have been found to be transformed into imides 6d, 6f, 6i-k and 4-substituted benzoic acids 7a-g through sequential Dakin–West and autoxidation reactions (Scheme 2). Huisgen and co-workers were first to report the autooxidation of munchnone€ generated from N-benzoyl-N-methyl phenylglycine.[29] Also, Kawase investigated the autoxidation reaction of munchnones€ derived from cyclic a-amino acids.[30] Although, in some cases, both structures (6 and 7) were obtained, some of the reactions gave only one product (i.e. imides 6 or carboxylic acids 7) and also no 2-nitromethylenethiazolidine residue was detected along with the products.

We began the reaction using amino acid 3 b (1 mmol): after addition of acetic anhydride (3 mmol) and heated the mixture at 55 C for 15 min 2-nitromethylenethia-zolidine 4 was added and the resulting mixture heated at 90 C overnight. Only enol ester 5 was obtained, possibly through a Dakin–West type reaction pathway at which a tautomeric form of 2-nitromethylenethiazolidine might behaved as a base (Scheme 3). A similar product obtained through a rearrangement process with N-acyl prolines in the presence of inorganic bases such as $K_2CO_3$, $Na_2CO_3$ was reported by the Kawase group.[31]




Scheme 1. Reactions between 3b and acetic anhydride in the presence of 2-nitromethylenethiazoli-dine 4 and pyridine to afford enol ester 5.

We have utilized the same reaction conditions for other amino acids (3a-k) to obtain a variety of enol esters 5, but all the attempts failed, that is, no ester products were formed.

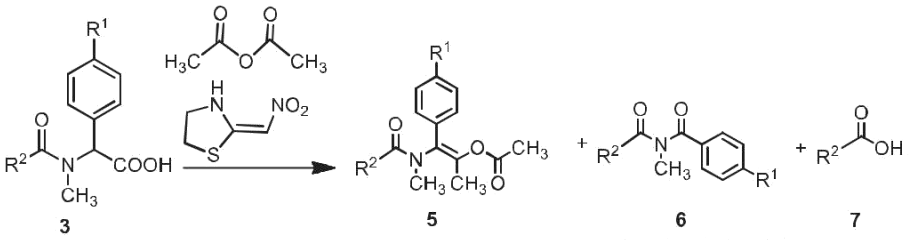
In order to provide a full characterization of the structure, an X-ray ORTEP view for enol ester 5 was obtained (Figure 2).

However, when the compounds 3d, 3f, 3i-k were used as starting aminoacids, some new benzoyl, methyl substituted benzamides 6d, 6f, 6i-k were obtained as the only products. IR spectra of the products showed two carbonyl absorption bands. Since pro-ton NMR spectra did not give four singlet peaks as in compound 5 and only one singlet peak appeared at approximately 3.50 ppm (N-$CH_3$), we concluded that these products were the imides 6. A possible reaction mechanism can be proposed in which, after munchnone€ formation, the ketene is likely attacked by a water molecule and a subsequent release of carbon dioxide may be considered (Scheme 4).

Formation of similar imides, but not exactly the same, through peroxidation of C-H bonds in amides, via the reaction of nitrones with aroyl chlorides; imidoyl chlorides with phenols and by thermal transformations of oxazole endoperoxides has been reported.[32–37] We used the amino acids (3d, 3f, 3i-k) and obtained similar proton and carbon NMR resonances for the products.

We were able to establish exact structure of 6d by X-ray diffraction data (Figure 3). In some cases, the carboxylic acids 7 were obtained possibly via a mechanism depicted below (Scheme 5).

In order to identify the carboxylic acid formed above reaction exactly, X-Ray diffraction data of 4-trifluoromethylbenzoic acid 7f was obtained using a fine crystal of it



3 5 6 7

Isolated Yields (%)

| Entry | Substrate | $R^1$ | $R^2$ | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| 1 | 3a | F | $C_6H_5$ | — | — | **7a** (39)[a] |
| 2 | 3b | F | 4-$CH_3$-$C_6H_4$ | **5** (48)[a] | — | — |
| 3 | 3c | F | 4-$CH_3O$-$C_6H_4$ | — | — | **7c** (83)[a] (54)[b] |
| 4 | 3d | F | 4-$NO_2$-$C_6H_4$ | — | **6d** (34)[a] | **7d** (66)[b] |
| 5 | 3e | F | 4-Cl-$C_6H_4$ | — | — | **7e** (83)[a] (36)[b] |
| 6 | 3f | F | 4-$CF_3$-$C_6H_4$ | — | **6f** (16)[a] | **7f** (70)[a] (19)[b] |
| 7 | 3g | F | $C_6H_5$-$CH_2CH_2$ | — | — | **7g** (75)[a] |
| 8 | 3h | F | $CH_3$ | — | — | — |
| 9 | 3i | $CH_3O$ | p-$CH_3$-$C_6H_4$ | — | **6i** (16%)[b] | **7b** (66%)[a] (70%)[b] |
| 10 | 3j | $CH_3O$ | p-$NO_2$-$C_6H_4$ | — | **6j** (21%)[b] | — |
| 11 | 3k | $CH_3O$ | p-$CF_3$-$C_6H_4$ | — | **6k** (20%)[b] | — |

*Only Route A was applied in entry 1 and 7*
*Only Route B was applied in entry 10 and 11.*

***Route A**: Münchnone precursors **3**, $Ac_2O$, 55°C, 30 min, then 2-(nitromethylene)thiazolidine **4**, 90°C, overnight*

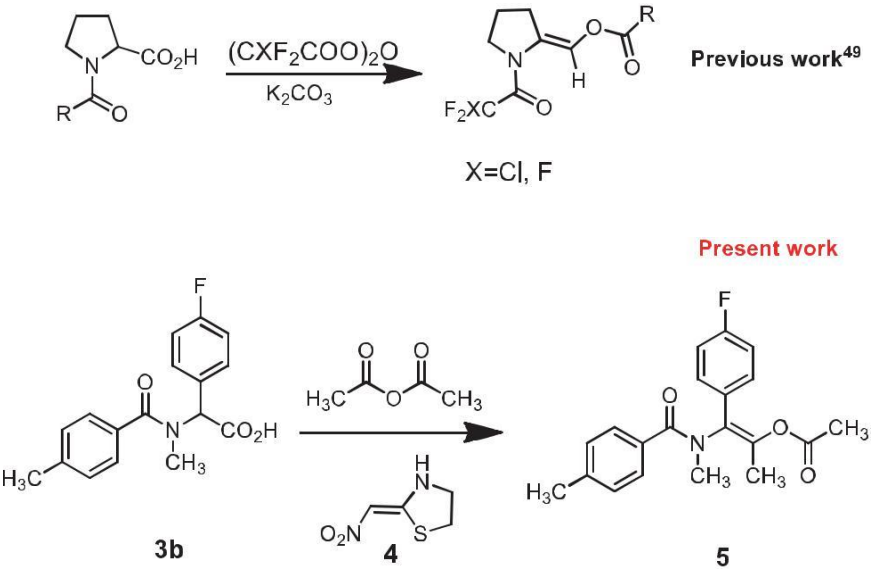
***Route B**: Münchnone precursors **3**, $Ac_2O$, 55°C, 30 min, then 2-(nitromethylene)thiazolidine **4**, MW, 0-150 W, 45 min*

Scheme 2. The reaction between munchnone€ precursors 3 and acetic anhydride in the presence of 2-nitromethylenethiazolidine 4.

(Figure 4). Finger print region in the IR spectrum of 7f is exactly same with the one of euthentic sample.

In order to rationalize whether aromatic substituent on nitrogen affects the product formation, we used N-acetyl substituted amino acid 3 h both under classical and microwave heating conditions and observed no reaction at all, confirming that aromatic group has the major impact on this reaction.

Then, munchnone€ precursors 3 were reacted both with cyclohexyl and isopropyl carbodiimides in the presence of diisopropyl amine and a series of urea derivatives 9, 11 have been obtained. Their IR spectra showed two carbonyl absorptions between 1720




Scheme 3. Formation of enol ester 5.

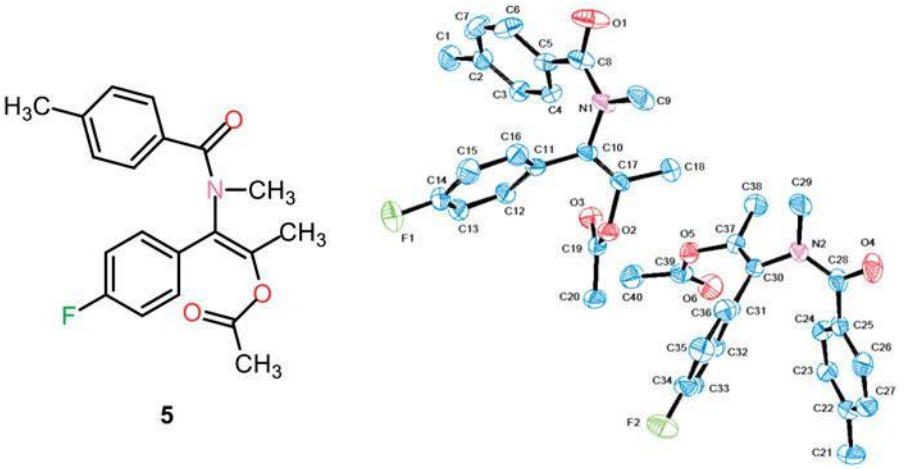
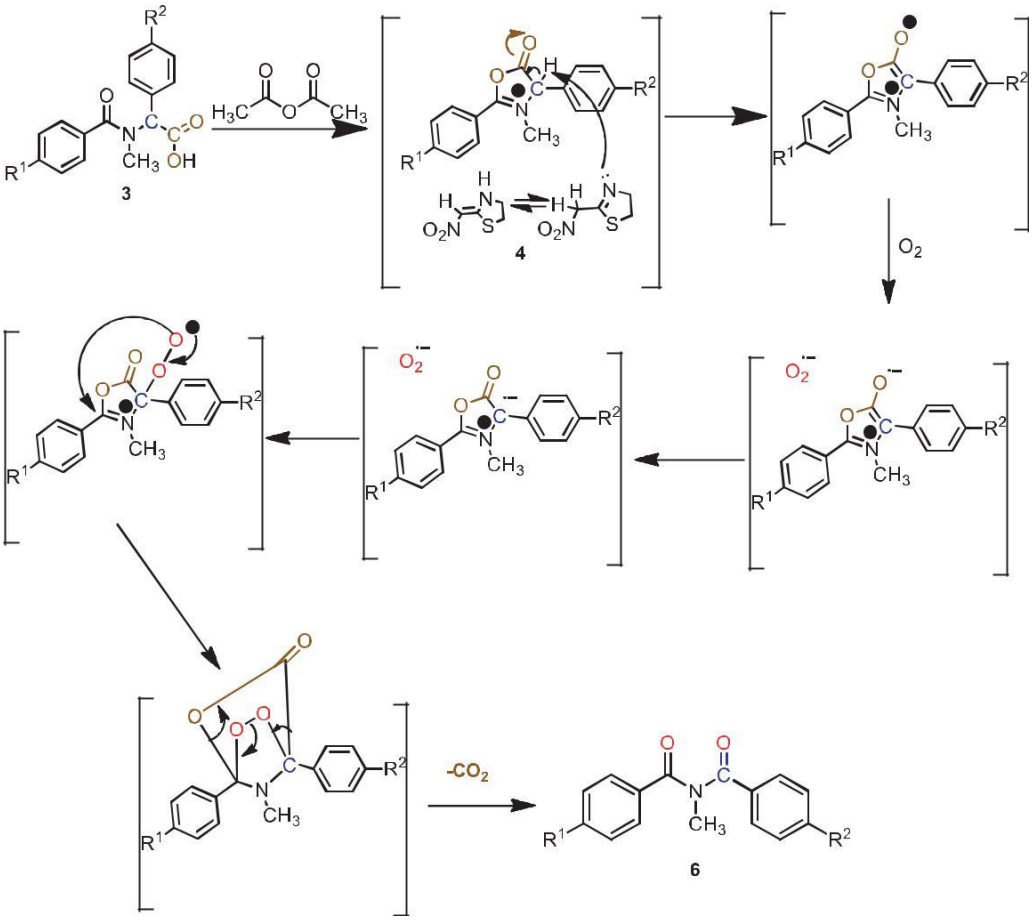



Figure 2. X-Ray ORTEP view of enol ester 5.

and 1690 cm $^{1}$. Also, proton NMR spectra showed one singlet signal between 6.70 and 6.00 ppm, two multiplet peaks between 4.50 and 3.75 ppm (Figure 5). These spectral data were not enough for full structural characterization of these compounds. But, how-ever, we were able to obtain fine crystals of the compound 11e. X-ray diffraction ORTEP view which confirmed the structures is shown (Scheme 6, Figure 6

On the basis of these results, we were able to write a Dakin–West type reaction mechanism for the formation of N-acylurea products. Thus, initially, N-acylamino acids 3 reacted with carbodiimides to give a mesoionic 1,3-oxazolium-5-olate form which may be in equilibrium with ketene whose formation could be facilitated by the elevated temperature of refluxing acetonitrile.




Scheme 4. Possible reaction mechanism involving an autoxidation pathway leading to N-acyl amides 6d, 6f, 6i-k.

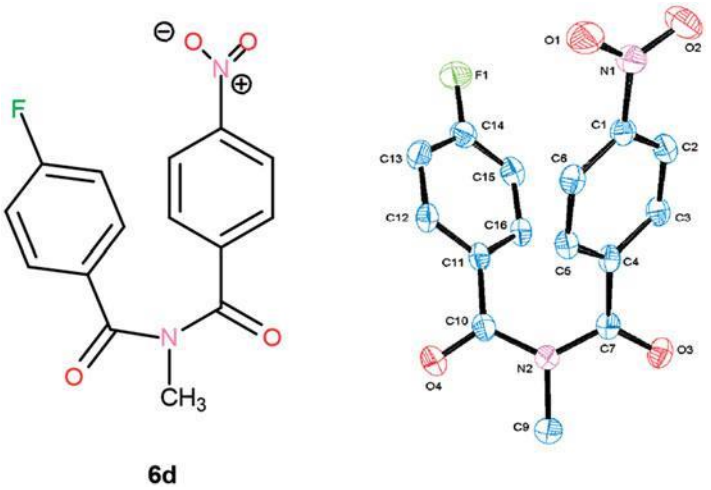
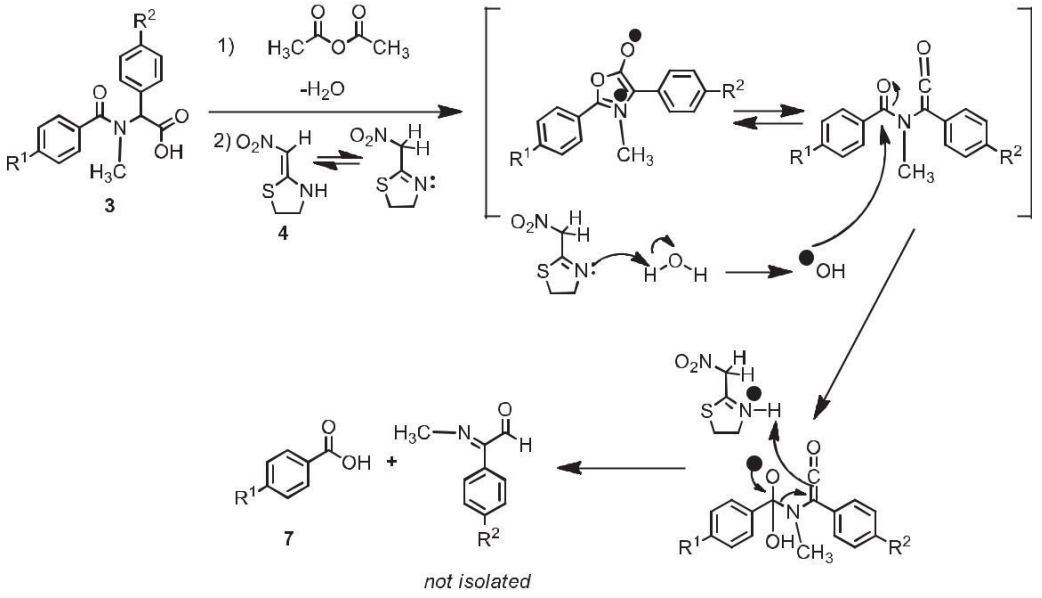



Figure 3. X-Ray ORTEP view of 6d.




Scheme 5. Possible reaction mechanism leading to 4-substituted benzoic acids 7a-g.

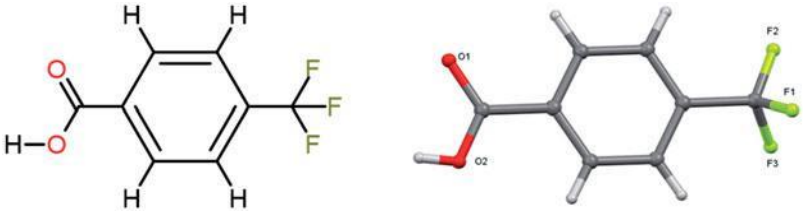



Figure 4. X-Ray ORTEP view of 7f.

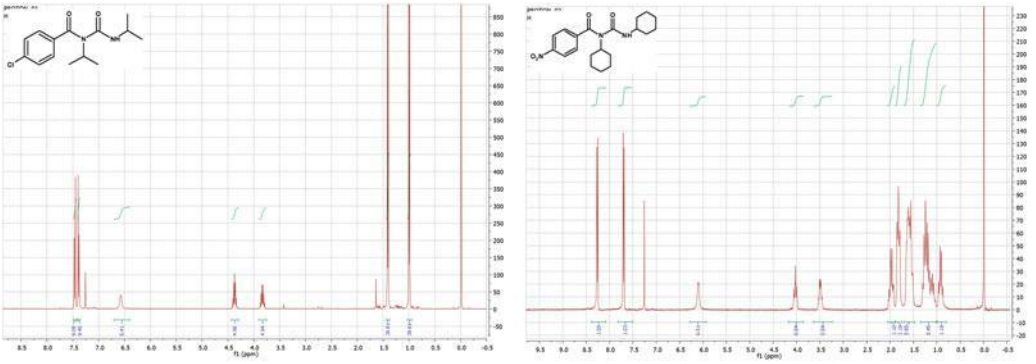
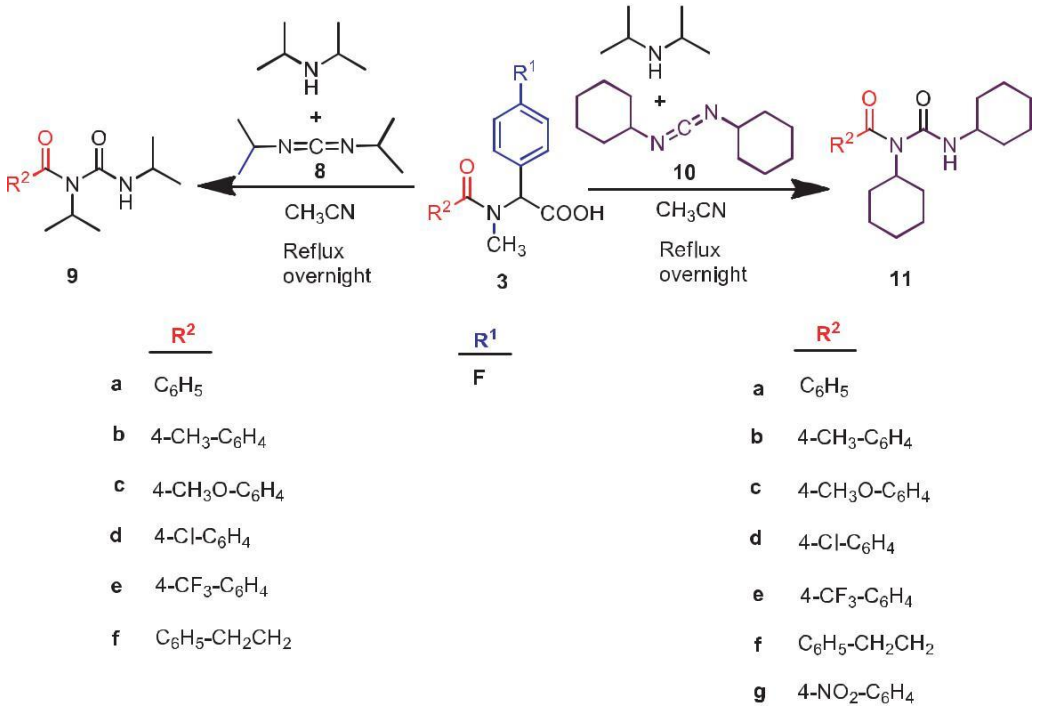


Figure 5. $^{1}$H NMR spectra of 9d and 11g.




Scheme 6. Reactions of munchnone€ precursors 3 with diisopropyl carbodiimide (DIPC) 8 and dicy-clohexyl carbodiimide (DCC) 10 in the presence of diisopropyl amine (DIPA) to afford 9a-f and 11a-g. Reagents and solvent: 3 (0.47 mmol), 8 (3.0 mL), 10 (1.91 mmol), DIPA (0.2 mL), $CH_3CN$ (10.0 mL).

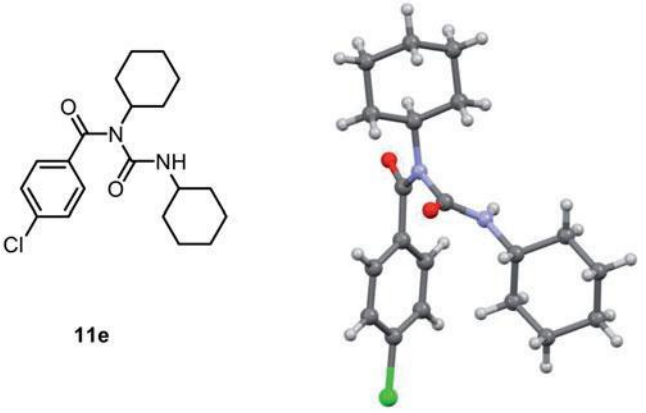
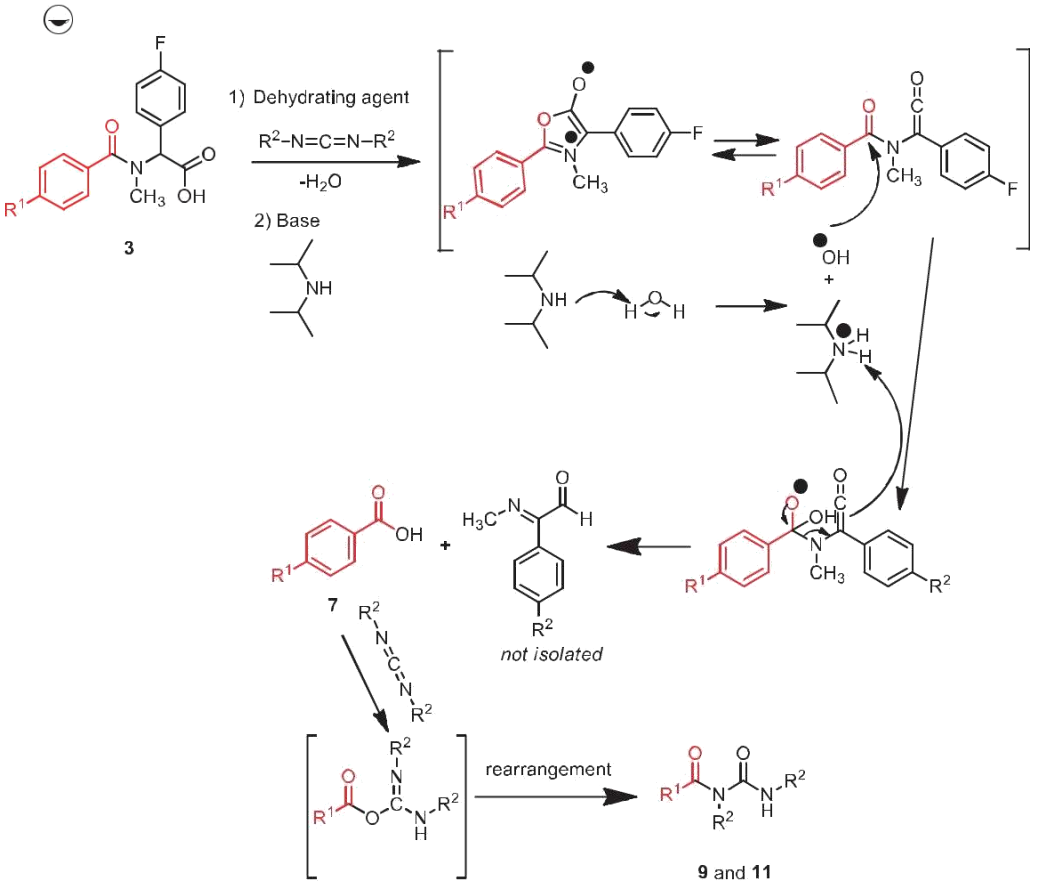



Figure 6. X-Ray ORTEP view of 11e.

Then, amide carbonyl was attacked by $OH^-$ later converted to carboxylic acid 7 and formyl imine which could not be detected or isolated. Finally, excess carbodiimide underwent a reaction with carboxylic acid 7, namely, acyl transfer leads to the corresponding N-acylureas 9 and 11 (Scheme 7).




Scheme 7. A plausible reaction mechanism leading to N-acylureas 9 and 11.

## Conclusion

In summary, we demonstrated that a Dakin–West type transformation and autoxidation reaction occur in the interactions between munchnone€ precursors (amino acids) and acetic anhydride in the presence of 2-nitromethylenethiazolidine which likely acts as a base through its enamine tautomer to afford an enol ester; (E)-1-(N,4-dimethylbenza-mido)-1-(4-fluorophenyl)prop-1-en-2-yl acetate 5, 4-substituted-N-methyl-N-(4-substitutedbenzoyl)benzamides 6 and substituted benzoic acids 7. A plausible mechanism where munchnones€ are being converted into imides through an autoxidation process was proposed. In addition, we introduced a novel, efficient and one-pot protocol to give N-acylurea derivatives 9 and 11 through the reaction between munchnone€ precursors with carbodiimides in the presence of a base. This reaction sequence demonstrates the influence of the carbodiimides both as a dehydrating agent and a reactant.

## Experimental: Reactions between munchnone€ precursors 3a-k and acetic anhydride in the presence of 2-nitromethylenethiazolidine 4

### General procedure

### Route A

Synthesis of E-1-(N,4-dimethylbenzamido)-1-(4-fluorophenyl)prop-1-en-2-yl acetate 5: 2-(N,4-Dimethylbenzamido)-2-(4-fluorophenyl)acetic acid 3 b (2.80 mmol, 806 mg) was

heated in acetic anhydride (8 mL) at 55 C for 30 min. Then, 2-(nitromethylene) thiazolidine 4 (1.00 mmol, 146 mg) was added to the reaction mixture and refluxed overnight at 90 C. After cooling the reaction mixture to room temperature, the solvent was removed under the reduced pressure and the crude residue was purified by flash col-umn chromatography (silica gel, EtOAc/n-hexane; 1:7) to give 5 as yellow solid. Yield: 1 48%; mp 98–100 ¼

H NMR (400 MHz, $CDCl_3$): d 7.27 (d, J ¼ 8.1 Hz, 2H), 7.13–7.10 (m, 2H), 7.01 (d, J ¼ 7.9 Hz, 2H), 6.90 (t, J ¼ 8.7 Hz, 2H), 3.31 (s, 3H), 2.30 (s, 3H), 1.98 (d, J ¼ 4.8 Hz, 6H). 13 C NMR (100 MHz, $CDCl_3$): d 171.6, 168.6, 162.0 (d, C-F carbon, J ¼ 247.0 Hz), 144.7, 140.4, 132.6 (d, b-C to C-F, $J_{meta}$= 18.0 Hz), 131.2, 129.4, 129.3, 128.4, 127.5, 115.2 (d, a-C to C-F, $J_{ortho}$= 22.0 Hz), 37.2, 21.4, 20.9, 17.3. LC-MS (ESþ) m/z (%): 342.2 $[M þ H]^þ$. HRMS: m/z (ESI-TOF, $[M þ H]^þ$) calcd for $C_{20}H_{20}FNO_3$: 342.1505. Found: 342.1500.

## Route B

4-Chlorobenzoic acid 7e: 2-(4-Chloro-N-methylbenzamido)-2-(4-fluorophenyl)acetic acid 3e (0.715 mmol, 230 mg) in acetic anhydride (2.23 mL) was irradiated at 0–150 W for 15 min in closed glass vial in a CEM Discover microwave reactor at 55 C. Then, 2-(nitromethylene)thiazolidine 4 (0.255 mmol, 38 mg) was added the reaction mixture and irradiated at 0-150 W for further 45 min at 80 C. After cooling the reaction mixture to room temperature, the solvent was removed under the reduced pressure and the residue was purified by flash column chromatography (silica gel, EtOAc/n-hexane;1:18) to give 7e.

4-Fluoro-N-methyl-N-(4-nitrobenzoyl)benzamide 6d (route a): Yellow solid. Yield: 34%; mp 131-133 C. IR (KBr): ¼ 3117, 1701, 1651, 1600, 1519, 1342, 1288, 1041, 852 cm $^{1}$. $^{1}$ H NMR (400 MHz, $CDCl_3$): d 8.10 (d, J ¼ 8.0 Hz, 2H), 7.62-7.56 (m, 4H), 7.00 (t, J ¼ 8.0 Hz, 2H), 3.50 (s, 3H). 13 C NMR (100 MHz, $CDCl_3$): d 172.9, 171.9, 165.3 (d, C-F carbon, J ¼ 154.0 Hz), 149.2, 141.6, 131.7 (d, b-C to C-F, $J_{meta}$= 9.0 Hz), 131.1, 129.3, 123.7, 116.2 (d, a-C to C-F, $J_{ortho}$= 22.0 Hz), 34.6. LC-MS (ESþ) m/z (%): 297 $[M-4H]^þ$. Calculated for $C_{15}H_{11}FN_2O_4$; 302.0703; C, 59.61; H, 3.67; N, 9.27. Found: C, 59.84; H, 3.84; N, 9.22.

4-Chlorobenzoic acid 7e (route a and route B): White solid. Yield: 83%; mp 235-237C (lit.[38,39] mp 236-237 C). IR (KBr): ¼ 3093, 1685, 1593, 1423, 1280, 1176, 1091, 759 cm $^{1}$. $^{1}$ H NMR (400 MHz, DMSO-$d_6$): d 13.1 (s, 1H), 7.90 (dd, J ¼ 8.0, 4.0 Hz, 2H), 7.53 (d, J ¼ 8.0, 4.0 Hz, 2H). 13 C NMR (100- MHz, DMSO-$d_6$): d 169.9, 138.3, 131.7, 130.2, 129.3. LC-MS (ES-) m/z (%): 155 $[M-H]^-$.

## General procedure

### Synthesis of 4-substituted-N-isopropyl-N-(isopropylcarbamoyl)benzamides 9a-f and 4-substituted-N-cyclohexyl-N-(cyclohexylcarbamoyl)benzamides 11a-g

2-(4-Chloro-N-methylbenzamido)-2-(4-fluorophenyl) acetic acid 3e (0.47 mmol, 151 mg) was dissolved in acetonitrile (10 mL) and DIPC (diisopropyl carbodiimide) 8 (0.3 mL) was added. Then, the reaction mixture was heated at 55 C for 30 min. Then, DIPA

(diisopropyl amine) (0.2 mL) was added and refluxed overnight at 90 C. After cooling the reaction to room temperature, the solvent was removed under vacuum and the resi-due was purified by flash column chromatography (silica gel, EtOAc/n-hexane;1:8) to give 9a-f and when DCC (dicyclohexylcarbodiimide) was used at the same reaction con-ditions and molar amounts of reagents, the compounds 11a-g were obtained (Scheme 6).

### N-isopropyl-N-(isopropylcarbamoyl)-4-chlorobenzamide 9d

White solid. Yield: 50%; mp 154–156 C. IR (KBr): ¼ 3321, 2974, 1705, 1631, 1546, 1373, 1257, 1091, 833 cm $^{1}$. $^{1}$ H NMR (400 MHz, $CDCl_3$): d 7.46 (d, J ¼ 8.4 Hz, 2H), 7.39 (d, J ¼ 8.5 Hz, 2H), 6.57 (s, 1 H, NH), 4.42–4.32 (m, 1H), 3.88–3.78 (m, 1H), 1.41 (d, J ¼ 6.8 Hz, 6H), 1.00 (d, J ¼ 6.6 Hz, 6H). 13 C NMR (100 MHz, $CDCl_3$): d 171.0, 153.9, 136.9, 135.4, 128.9, 127.9, 50.3, 42.8, 22.3, 20.9. LC-MS (ES-) m/z (%): 281.3 [M-H]$^{-}$, 326.9 [M þ Na þ $CH_3CN$]. HRMS: m/z (ESI-TOF, [M þ H]$^{þ}$) calcd for $C_{20}H_{20}FNO_3$: 342.1505. Found: 342.1500.

### N-cyclohexyl-N-(cyclohexylcarbamoyl)-4-chlorobenzamide 11d

White solid. Yield: 75%; mp 181–183 C. (lit.[21] mp 183.1–183.3 C). IR (KBr): ¼ 3306, 2931, 1701, 1647, 1543, 1342, 1234, 1087, 833 cm $^{1}$. $^{1}$ H NMR (400 MHz, $CDCl_3$): d 7.49 (d, J ¼ 8.4 Hz, 2H), 7.37 (d, J ¼ 8.4 Hz, 2H), 6.08 (s, 1H), 4.10–4.02 (m, 1H), 3.54–3.46 (m, 1H), 2.08–1.95 (m, 2H), 1.81–1.77 (m, 4H), 1.65–1.51 (m, 5H), 1.32–1.04 (m, 7H), 0.91 (dd, J ¼ 24.1, 13.0 Hz, 2H). 13 C NMR (100 MHz, $CDCl_3$): d 170.1, 154.0, 135.3, 130.0, 128.8, 128.2, 57.5, 49.7, 32.3, 30.8, 26.2, 25.3, 25.2, 24.5. LC-MS (ES-) m/z (%): 363.6 [M þ H]$^{þ}$.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## References


[1] Ollis, W. D.; Ramsden, C. A. Adv. Heterocycl. Chem. 1976, 19, 1–122. DOI: 10.1016/S0065-2725(08)60230-5.

[2] Ollis, W. D.; Stanforth, S. P.; Ramsden, C. A. Heterocyclic Mesomeric Betaines. Tetrahedron. 1985, 41, 2239–2329. DOI: 10.1016/S0040-4020(01)96625-6.

[3] Gribble, G. W. Mesoinoic Oxazoles. In: Palmer DC Ed. The Chemistry of Heterocyclic Compounds: Oxazoles, Part A Wiley: Hoboken (N. J.), 2003; Vol. 60, pp. 473–576.

[4] Gribble, G. W. Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products. In The Chemistry of Heterocyclic Compounds, (Padwa, A.; Pearson, W.H., Eds).; Wiley: New York, 2002; Vol. 59, pp. 681–753.
[5] Dhawan, R.; Arndtsen, B. A. Palladium-Catalyzed Multicomponent Coupling of Alkynes, Imines, and Acid Chlorides: A Direct and Modular Approach to Pyrrole Synthesis. J. Am. Chem. Soc. 2004, 126, 468–469. DOI: 10.1021/ja039152v.
[6] Lopchuk, J. M.; Gribble, G. W. The Reaction of Arynes with Munchnones:€ synthesis of Isoindoles and Azaisoindoles. Tetrahedron Lett. 2014, 55, 2809–2812. DOI: 10.1016/j.tetlet.2014.03.055.
[7] Lopchuk, J. M.; Hughes, R. P.; Gribble, G. W. What Controls Regiochemistry in 1,3-Dipolar Cycloadditions of Munchnones€ with Nitrostyrenes? Org. Lett. 2013, 15, 5218–5221. DOI: 10.1021/ol402385v.
[8] Marco-Martınez, J.; Reboredo, S.; Izquierdo, M.; Marcos, V.; Lopez, J. L.; Filippone, S.; Martın, N. Enantioselective Cycloaddition of Munchnones€ onto [60]Fullerene: organocatalysis versus Metal Catalysis. J. Am. Chem. Soc. 2014, 136, 2897–2904. DOI: 10.1021/ja500071k.
[9] Dakin, H. D.; West, R. A general reaction of amino acids. J. Biol. Chem. 1928, 78, 91–105.
[10] Tran, K.-V.; Bickar, D. Dakin-West Synthesis of Beta-Aryl Ketones. J. Org. Chem. 2006, 71, 6640–6643. DOI: 10.1021/jo0607966.
[11] Khodaei, M. M.; Khosropour, A. R.; Fattahpour, P. A Modified Procedure for the Dakin–West Reaction: An Efficient and Convenient Method for a One-Pot Synthesis of b-Acetamido Ketones Using Silica Sulfuric Acid as Catalyst. Tetrahedron Lett. 2005, 46, 2105–2108. DOI: 10.1016/j.tetlet.2005.01.149.
[12] Luesch, H.; Yoshida, W. Y.; Moore, R. E.; Paul, V. J. Structurally Diverse New Alkaloids from Palauan Collections of the Apratoxin-Producing Marine Cyanobacterium Lyngbya Sp. J. Tetrahedron. 2002, 58, 7959–7966. DOI: 10.1016/S0040-4020(02)00895-5.
[13] Krohn, K.; Franke, C.; Jones, P. G.; Aust, H.-J.; Draeger, S.; Schulz, B. Wirkstoffe Aus Pilzen, I. Isolierung, Synthese Und Biologische Wirkung Von Coniothyriomycin Sowie Synthese Und Biotestung Analoger Offenkettiger Imide. Liebigs Ann. Chem. 1992, 1992, 789–798. DOI: 10.1002/jlac.1992199201130.
[14] Flatters, S. J. L.; Bennett, G. Ethosuximide Reverses Paclitaxel- and Vincristine-Induced Painful Peripheral Neuropathy. J. Pain 2004, 109, 150–161. DOI: 10.1016/j.pain.2004.01.029.
[15] Maruyama, H. B.; Suhara, Y.; Suzuki-Watanabe, J.; Maeshima, Y.; Shimizu, N.; Ogura-Hamada, M.; Fujimoto, H.; Takano, K. A New Antibiotic, Fumaramidmycin I. Production, Biological Properties and Characterization of Producer Strain. J. Antibiot. 1975, 28, 636–647. DOI: 10.7164/antibiotics.28.636.
[16] Stierle, A. A.; Stierle, D. B.; Patacini, B. The Berkeleyamides, Amides from the Acid Lake Fungus Penicillum Rubrum. J. Nat. Prod. 2008, 71, 856–860. DOI: 10.1021/np0705054.
[17] DeMilo, A. B.; Ostromecky, D. M.; Chang, S. C.; Redfern, R. E.; Fye, R. L. Heterocyclic Analogs of Diflubenzuron as Growth and Reproduction Inhibitors of the Fall Armyworm and House Fly. J. Agric. Food Chem. 1978, 26, 164–166. DOI: 10.1021/jf60215a035.
[18] DeTar, F. D. L.; Silverstein, R. Reactions of Carbodiimides. I. The Mechanisms of the Reactions of Acetic Acid with Dicyclohexylcarbodiimide 1,2. J. Am. Chem. Soc. 1966, 88, 1013–1019. DOI: 10.1021/ja00957a027.
[19] Benoiton, N. L.; Chen, F. M. F. Reaction of N-t-Butoxycarbonylamino Acid Anhydrides with Tertiary Amines and Carbodi-Imides. New Precursors for 2-t-Butoxyoxazol-5(4H)-One and N-Acylureas. J. Chem. Soc, Chem. Commun. 1981, 23, 1225–1227.
[20] Slebioda, M. Substituent Effect in Reaction of Dicyclohexylcarbodiimide with Substituted Benzoic Acids. Tetrahedron. 1995, 51, 7829–7834. DOI: 10.1016/0040-4020(95)00400-3.
[21] Soeta, T.; Tabatake, Y.; Fujinami, S.; Ukaji, Y. N-Heterocyclic Carbene Catalyzed Oxidative Coupling of Aldehydes with Carbodiimides under Aerobic

Conditions: efficient Synthesis of N-Acylureas. Org. Lett. 2013, 15, 2088–2091. DOI: 10.1021/ol400672c.
[22] Dur€ust,€ Y.; Sagırlı, A.; Kariuki, B. M.; Knight, D. W. Tetrahedron. 2014, 70, 6012–6019. DOI: 10.1016/j.tet.2014.04.083.
[23] Dur€ust,€ Y.; Sagırlı, A. Microwave-Assisted Coupling Reaction of N-Aryl Sydnones with 2-Nitromethylenethiazolidine: unexpected Formation of (Z)-2-(Nitro((E)-p-Substitutedphenyldiazenyl)Methylene)Thiazolidines. J. Org. Chem. 2014, 79, 6380–6384. DOI: 10.1021/jo5010229.
[24] Yıldırım, M.; C¸elikel, D.; Dur€ust,€ Y.; Knight, D. W.; Kariuki, B. M. A Rapid and Efficient Protocol for the Synthesis of Novel Nitrothiazolo[3,2-c]Pyrimidines via Microwave-Mediated Mannich Cyclisation. Tetrahedron. 2014, 70, 2122–2128. DOI: 10.1016/ j.tet.2014.02.003.
[25] Altug, C.; Burnett, A. K.; Caner, E.; Dur€ust,€ Y.; Elliott, M. C.; Glanville, R. P. J.; Guy, C.; Westwell, A. D. An Efficient One-Pot Multicomponent Approach to 5-Amino-7-Aryl-8-Nitrothiazolo[3,2-a]Pyridines. Tetrahedron. 2011, 67, 9522–9528. DOI: 10.1016/ j.tet.2011.10.005.
[26] Altug, C.; Dur€ust,€ Y.; Elliott, M. C. Reactions of Alkylidenepyrrolidines with a-Chlorooximes and a-Chlorohydrazones. Tetrahedron Lett. 2009, 50, 7392–7394. DOI: 10.1016/j.tetlet.2009.10.086.
[27] Altug, C.; Dur€ust,€ Y.; Elliott, M. C.; Kariuki, B. M. Tandem Nitrosation/Cycloaddition of Heterocyclic Enamines Using Nitrolic Acids. Tetrahedron Lett. 2009, 50, 4919–4921. DOI: 10.1016/j.tetlet.2009.06.065.
[28] Dur€ust,€ Y.; Sagırlı, E.; Sagırlı, A. Microwave-Assisted Regioselective [1,3]-Dipolar Cycloaddition of 3-Methyl-2-(Substitutedbenzylidene)-5-Oxopyrazolidin-2-Ium-1-Ides to Benzothiophene 1,1-Dioxide. Turk. J. Chem. 2015, 39, 789–800. DOI: 10.3906/ kim-1502-3.
[29] Bayer, H. O.; Huisgen, R.; Knorr, R.; Schaefer, F. C. Darstellung Und Eigenschaften Mesoionischer Oxazolone. Chem. Ber. 1970, 103, 2581–2597. DOI: 10.1002/ cber.19701030830.
[30] Kawase, M. Autoxidation of Intermediary Mesoionic 1,3-Oxazolium-5-Olates Generated from Cyclic N-Acyl.ALPHA.-Amino Acids. Chem. Pharm. Bull. 1997, 45, 1248–1253. DOI: 10.1248/cpb.45.1248.
[31] Saeki, M.; Hagimoto, Y.; Uno, H.; Kawase, M. The Dakin-West Reaction of N-Acylprolines in the Presence of Inorganic Bases: Unexpected Formation of Enol Esters. Heterocycles. 2009, 79, 821–830.
[32] Yu, H.; Shen, J. Peroxidation of C-H Bonds Adjacent to an Amide Nitrogen Atom under Mild Conditions. Org. Lett. 2014, 16, 3204–3207. DOI: 10.1021/ol5012168.
[33] Heine, H. W.; Zibuck, R.; Vandenheuvel, W. J. A. Mechanisms for the Reactions of Nitrones with Aroyl Chlorides. J. Am. Chem. Soc. 1982, 104, 3691–3694. DOI: 10.1021/ ja00377a025.
[34] Rowe, J. E. The Preparation of Aryl Imidates and Diaroylamides by Phase-Transfer Catalysis. Synthesis. 1980, 1980, 114–115. DOI: 10.1055/s-1980-28934.
[35] Roux, M. V.; Jimenez, P.; Martın-Luengo, M. A.; Davalos, J. Z.; Sun, Z.; Hosmane, R. S.; Liebman, J. F. The Elusive Antiaromaticity of Maleimides and Maleic Anhydride: Enthalpies of Formation of N-Methylmaleimide, N-Methylsuccinimide, N-Methylphthalimide, and N-Benzoyl-N-Methylbenzamide. J. Org. Chem. 1997, 62, 2732–2737. DOI: 10.1021/jo9621985.
[36] Iesce, M. R.; Graziano, M. L.; Cimminiello, G.; Cermola, F.; Parrilli, M.; Scarpati, R. Route of Triacylamine Formation in the Thermal Conversion of 2,3,7-Trioxa-5-Azabicyclo[2.2.1]Hept-5-Enes Investigated by Nuclear Magnetic Resonance Experiments. J. Chem. Soc, Perkin Trans. 2 1991, 7, 1085–1089.
[37] Gollnick, K.; Koegler, S. Thermal Transformations of Oxazole Endoperoxides: Rearrangements, Fragmentations and Methanol Additions. Tetrahedron Lett. 1988, 29, 1007–1010. DOI: 10.1016/0040-4039(88)85320-6.

[38] Shaikh, T. M.; Hong, F. E. Efficient Method for the Oxidation of Aldehydes and Diols with Tert-Butylhydroperoxide under Transition Metal-Free Conditions. Tetrahedron. 2013, 69, 8929–8935. DOI: 10.1016/j.tet.2013.07.101.

[39] Trincado, M.; Grutzmacher,€ H.; Vizza, F.; Bianchini, C. Domino Rhodium/Palladium-Catalyzed Dehydrogenation Reactions of Alcohols to Acids by Hydrogen Transfer to Inactivated Alkenes. Chem. Eur. J. 2010, 16, 2751–2757. DOI: 10.1002/chem.200903069.