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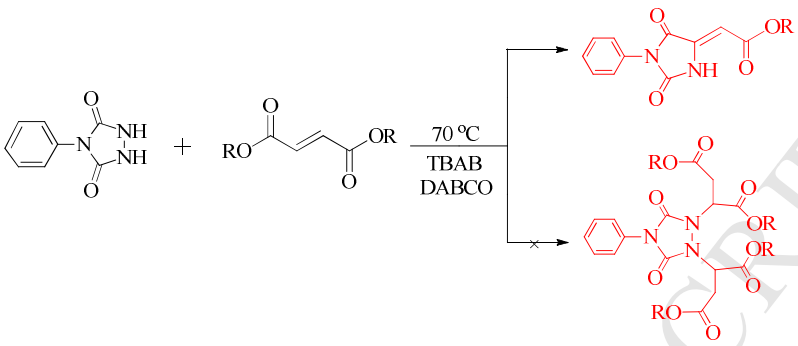

# Unexpected formation of 5-alkylidene derivatives of hydantoin from the Michael addition of 4-phenylurazole to fumaric esters

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**Abstract:** An unexpected reaction between 4-phenylurazole and fumaric esters which led to the formation of 5-alkylidene derivatives of hydantoin is described in this paper. The reaction takes place in the presence of tetrabutylammonium bromide (TBAB), and 1,4-diaza-bicyclo[2,2,2]octane (DABCO) at 70 °C under solvent-free conditions.

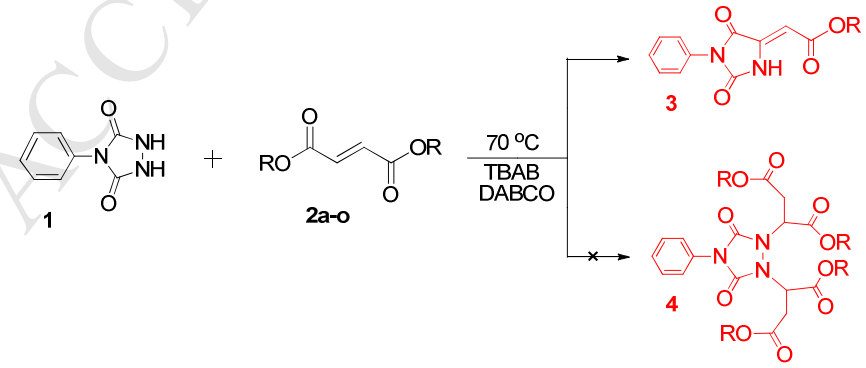
*Keywords:* Unexpected products, Hydantoin derivatives, Michael addition, 4-Phenylurazole, Fumaric ester

## 1. Introduction

The hydantoin (imidazolidine-2,4-dione) skeleton is a 5-membered heterocyclic ring system having two nitrogen atoms at positions 1 and 3 of the ring. This skeleton is found in a large number of naturally occurring and synthetic biologically active heterocyclic compounds.[1] The chemistry and the properties of hydantoin and its derivatives have been investigated for more than 140 years. The studies indicate that these compounds have a broad range of biological activities including anticonvulsants,[2,3] antiarithmics,[4] antitumor,[5] antidepressants,[6] antiviral agents,[7] treatment of epileptic seizures,[8,9] epidermolysis bullosa,[10] inflammatory conditions,[11] cardiac antiarrhythmic,[12] and for the treatment of many more diseases including HIV.[13] Additionally, hydantoin and its derivatives are also precursors for the synthesis of α-amino acids and pyruvic acid derivatives.[14-17] In this regard, 5-arylidene and 5-alkylidene derivatives of hydantoin are potentially useful starting materials for the preparation of these acids because a broad range of synthetic methodologies can be used to modify the exocyclic double bond to produce structural diversity.[18] For these reasons, among the 5-membered heterocyclic ring systems, hydantoin has a privileged position in medicinal chemistry.

## 2. Results and Discussion

In line with our interest in the aza-Michael addition of amides and imides to α,β-unsaturated esters,[19-21] in a recent project we reported that the addition of 4-phenylurazole to acrylic esters produced the corresponding N1,N2-bis-Michael adducts in good yield.[22] This pleasing result inspired us, herein, to examine this process for fumaric esters instead of acrylic esters. Therefore, we tried the Michael addition reaction of urazole **1** (1 mmol) to n-butyl fumarate **2d** (1 mmol) as a model reaction, in order to produce the corresponding bis-Michael adduct. However, when the reaction was conducted in the presence of the base DABCO (1 mmol) and organic salt TBAB (0.5 mmol) at 70 °C, surprisingly, a solid product was obtained with spectral data and an elemental analysis inconsistent with the expected structure of Michael adduct **4** (R = n-Bu). Indeed, the data were in good agreement with the structure of an unprecedented product **3d** (R = n-Bu) assembled via ring-opening of urazole, followed by the formation of a hydantoin ring (Scheme 1).




**Scheme 1.** The reaction leading to the synthesis of **3**.

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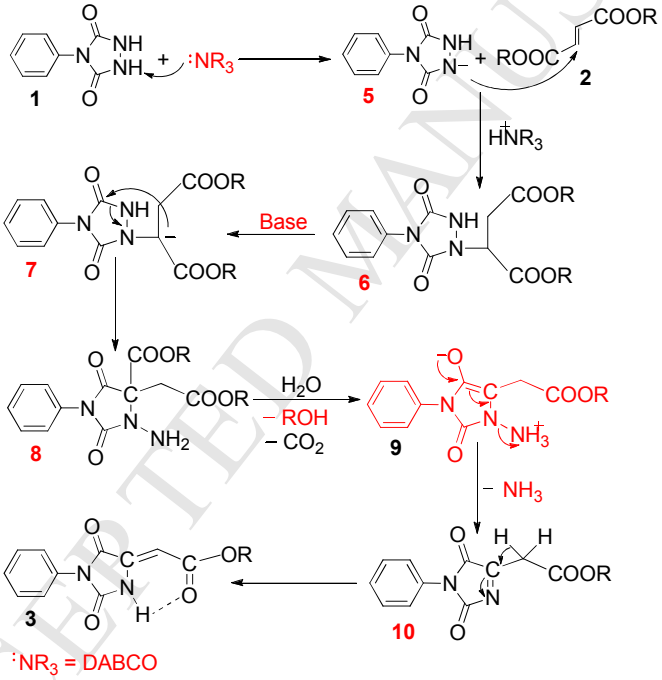
The mass spectrum of **3d** showed a molecular ion peak at *m/z*= 288 which was consistent with the mass of a 1:1 condensation product of the urazole **1** and ester **2d** releasing 1 equivalent of ammonia, n-butanol, carbon dioxide, and abstracting one molecule of water. The $^{1}$H NMR spectrum of the product exhibited a triplet at δ 0.96 (3H) corresponding to the methyl group coupled to equivalent hydrogens of methylene group and clearly indicating that only one n-butyl group has participated in the structure of the product. There were also a sextet and a quintet in the spectrum at δ 1.43 (2H) and 1.69 (2H) that were related to the resonances of the methylene protons of $CH_3$-**$CH_2$**- and $CH_3CH_2$-**$CH_2$**- groups, respectively. We observed another triplet at δ 4.24 (2H) in the $^{1}$H NMR spectrum of this product that was assigned to the $CH_2$ group attached to an oxygen and split by two equivalent hydrogens, O-**$CH_2$**-$CH_2$-. Also, there were two singlets in the spectrum at δ 6.04 (1H) and 9.18 that were related to hydrogen resonances of vinyl and amide groups respectively. The aromatic region of spectrum showed a multiplet at δ 7.39-7.52 (5H) that was in agreement with the presence of a mono-substituted benzene ring in the structure of the product **3d**. Further support for the structures of compounds **3** was obtained from the $^{13}$C NMR spectra of products where three downfield signals (152.4, 161.3, 166.9 for **3d**) corresponded to the presence of three carbonyl groups in the molecules. These features were consistent with the production of (Z)-butyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3d**).

Mechanistically, it is conceivable that the reaction initially proceeds via a proton abstraction from urazole **1** by DABCO to produce anion intermediate **5**. Michael addition reaction of this ion to fumaric ester **2** formed Michael adduct **6** that in the DABCO media this adduct can be converted to anion intermediate **7**. This intermediate produces compound **8** through urazole ring-opening (arrows on **7**). Compound **8** undergoes hydrolysis by adventitious water and is subsequently decarboxylated to compound **9**. Loss of an ammonia molecule from **9** (we confirmed the releasing of ammonia gas by keeping of wet pH paper over the reaction flask) gives compound **10** which can be tautomerized to corresponding (Z)-alkyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate **3** (Scheme 2).




**Scheme 2.** Proposed mechanism for the formation **3**.

Different solvents as well as solvent-free conditions were tested for the model reaction. The reaction failed in DMF, DMSO, dichloromethane, chloroform, methanol, ethanol, acetone, ethyl acetate and water. The reaction is successful only in the presence of organic salt TBAB, and made no significant progress without this salt under solvent-free conditions.

In another study, we investigated the effect of organic and inorganic bases on the model reaction. All of tested bases had catalytic effect on the reaction (Table 1). However, under the same experimental conditions, DABCO showed excellent catalytic activity, which gave product **3d** in a yield of 73% (Table 1, entry 9). In the presence of NaOH, KOH and none alkaline media this product was produced in a trace yield (Table 1, entries 1,6,7).

**Table 1.** The reaction of urazole **1** with n-butyl fumarate in the presence of different bases and TBAB under solvent-free conditions

| Entry | Base[a] | Time (min) | Yield (%)[b] |
|---|---|---|---|

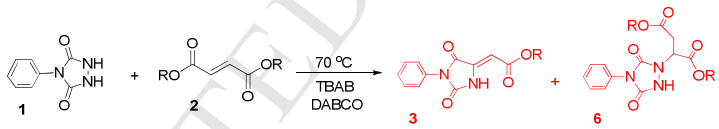
| | | | |
|---|---|---|---|
| 1 | None | 360 | Trace |
| 2 | $Na_2CO_3$ | 360 | 30 |
| 3 | $K_2CO_3$ | 360 | 40 |
| 4 | $NEt_3$ | 360 | 15 |
| 5 | Pyridine | 360 | 20 |
| 6 | NaOH | 360 | Trace |
| 7 | KOH | 360 | Trace |
| 8 | $Sr_2CO_3$ | 360 | 5 |
| 9 | DABCO | 100 | 73 |

[a]With 4-phenylurazole(1.0 mmol), base (1.0 mmol), TBAB (0.5 mmol) and n-butyl fumarate (1.2 mmol) at 70°C.

[b]Isolated yield.

With the best reaction conditions in hand (DABCO 1.0 mmol, TBAB 0.5 mmol, 4-phenylurazole 1.0 mmol and n-butyl fumarate 1.2 mmol at 70 °C), we next considered the scope of the reaction by employing different fumaric esters **2** with 4-phenyl urazole **1** (Table 2). From the Table 2, it is clear that, generally, the reactions in which alkoxy fumarate had been employed, produced the corresponding hydantoin products **3** in moderate to good yields within 100-180 minutes (Table 2, entries 1-9,11,12). However, when benzyloxy fumarates were employed as Michael acceptors, the TLC test not showed any progress to the reaction even after a long time (Table 2, entries 13-15). These results can be attributed to the increased steric hindrance of the Michael acceptors. The existence of hindered -OR groups on fumaric esters make them a weak Michael acceptors and hence addition is much more difficult to occur. Under our conditions, the addition of Michael donor **1** to n-butyl fumarate (bearing small-OR groups) afforded the desired product **3** in 73% yield within 100 min (Table 2, entry 4), while this addition to cyclohexyl fumarate (bearing large -OR groups) provided a relatively low yield of 65% (Table 2, entry 12) than butyl fumarate within 180 min. There was an exception that when decyl fumarate was used as a Michael acceptor, only the corresponding mono-Michael adduct was obtained (Table 2, entry 10).

**Table 2.** The addition of urazole **1** to *α,β*-unsaturated esters **2** under solvent-free conditions




| Entry | R | Product | Time (min) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | $CH_3CH_2$ | 3a | 100 | 60 |
| 2 | $CH_3CH_2CH_2$ | 3b | 100 | 65 |
| 3 | $CH_3CHCH_3$ | 3c | 100 | 85 |
| 4 | $CH_3(CH_2)_3$ | 3d | 100 | 73 |
| 5 | $CH_3CHCH_2CH_3$ | 3e | 150 | 80 |
| 6 | $CH_3CHCH_2CH_2CH_3$ | 3f | 150 | 70 |
| 7 | $(CH_3)_2CHCH_2CH_2$ | 3g | 150 | 70 |
| 8 | $CH_3(CH_2)_3CH(CH_2CH_3)CH_2$ | 3h | 180 | 75 |
| 9 | $CH_3(CH_2)_7$ | 3i | 150 | 65 |
| 10 | $CH_3(CH_2)_9$ | 6j | 150 | 85 |
| 11 | $CH_3OCH_2CH_2$ | 3k | 150 | 80 |
| 12 | $(CH_2)_5CH$ | 3l | 180 | 65 |
| 13 | $PhCH_2$ | - | 1000 | - |
| 14 | $PhCHCH_3$ | - | 1000 | - |
| 15 | Cl-$PhCH_2$ | - | 1000 | - |

[a]Isolated yields.

## 3. Summary

In summary, we have described an unexpected novel and interesting reaction between 4-phenylurazole and fumaric esters in which different 5-alkylidene derivatives of hydantoin are formed. The products were produced under classic reaction conditions in the presence of tetrabutylammonium bromide (TBAB) as an available organic salt. It was found that 1,4-diaza-bicyclo[2,2,2]octane (DABCO) is the most suitable base for this reaction. The crystal structure of one of the products showed both intra- and inter-molecular H-bonds. This later H-bond caused to dimeric form of this molecule including eight-membered ring with centrosymmetric $C_i$ form.

## 4. Experimental

### *4.1. General*

α,β-Unsaturated esters were synthesized according to literature procedures.[23] 4-Phenylurazole was purchased from Merck and used without further purification. Esters were transferred via syringe. Organic solvents were removed under reduced pressure by rotary evaporator. Reactions were monitored by thin-layer chromatography (TLC) carried out on silica gel plates (SILG/UV 254, Merk) using UV light as the visualizing agent. Chromatography was performed on Merk 60 silica gel (230–240 mesh) with n-hexane and ethyl acetate mixtures (80:20) as eluent. FT-IR spectra were recorded on a Perkin-Elmer RX-1 instrument. Mass spectra were recorded on a Shimadzu GC-MS-QP 1000PX. Elemental analysis for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. $^1$H NMR and $^{13}$C NMR spectra were recorded mostly on a Bruker 400 MHz instrument. The melting points were determined in open capillaries with a Stuart Melting Point Apparatus and are uncorrected. Chemical shifts were recorded in ppm downfield from tetramethylsilane. *J* values were given in Hz. Abbreviations used in $^1$H NMR are s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet).

### *4.2. General procedure for the Michael addition of 4-phenylurazole to fumaric esters*

A well ground mixture of 4-phenylurazole (1.0 mmol), DABCO (1.0 mmol), and TBAB (0.5 mmol) was placed in a flask. Fumaric ester (1.2 mmol) was added to this mixture and the flask was heated in the oil bath. When the oil bath temperature reached 70 ˚C, a brown solution was formed. After keeping the reaction flask at this temperature for stipulated time (Table 2), the reaction was completed as monitored by TLC. The flask was allowed to cool down to room temperature and chloroform (30 mL) was added. The solution was stirred to dissolve all the solids. TBAB was recovered by the addition of water (15 mL) to this solution, then collected and dried under vacuum. The chloroform layer was washed with water (3×15 mL). After dried with sodium sulfate and removal of the organic solvent, the residue was purified on short silica-gel column with n-hexane / ethyl acetate (9:1) as the eluent.

*4.2.1. (Z)-ethyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3a**).* White crystal, mp 186-187 ˚C (191 ˚C)[24]; $R_f$ (20% ethyl acetate/hexane) 0.30; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 1.34 (t, 3H, J = 7.1 Hz), 4.29 (q, 2H, J = 7.1 Hz), 6.02 (s, 1H), 7.39-7.51 (m, 5H), 9.18 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 13.1, 60.4, 96.0, 124.8, 127.6, 128.2, 129.5, 137.7, 151.3, 160.3, 165.7; IR (KBr, $cm^{-1}$): 3297, 2933, 1782, 1733, 1698, 1413, 1262, 772, 691; Anal. Calcd. for $C_{13}H_{12}N_2O_4$: C, 60.00; H, 4.65; N, 10.76. Found: C, 60.56; H, 4.16; N, 10.23.

*4.2.2. (Z)-propyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3b**).* White solid, mp 187-188 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.50; $^1$H NMR (500 MHz, $CDCl_3$): δ ppm 1.02 (t, 3H, J = 7.4 Hz), 1.77 (sextet, 2H, J = 7.3 Hz), 4.23 (t, 2H, J = 6.7 Hz), 6.07 (s, 1H), 7.43-7.55 (m, 5H), 9.20 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): 10.3, 21.9, 67.1, 97.1, 125.9, 128.7, 129.3, 130.6, 138.7, 152.3, 161.3, 166.9; IR (KBr, $cm^{-1}$): 3299, 2965, 1788, 1734, 1681, 1411, 1274, 774, 691; Ms m/z (%): 274 ($M^+$) (97), 270 (23), 251 (38), 232 (90), 224 (29), 214 (100), 188 (78), 119 (83), 68 (83); Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.23; H, 5.09; N, 10.13.

*4.2.3. (Z)-isopropyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3c**).* White crystal, mp 158-159 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.40; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 1.31 (d, 6H, J = 6.3 Hz), 5.15 (septet, 1H, J = 6.3 Hz), 5.99 (s, 1H), 7.38-7.51 (m, 5H), 9.26 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 20.6, 68.1, 96.5, 124.8, 127.5, 128.2, 129.5, 137.4, 151.3, 160.3, 165.2; IR (KBr, $cm^{-1}$): 3298, 2982, 1788, 1737, 1691, 1415, 1273, 771, 694; Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.89; H, 5.54; N, 10.16.

*4.2.4. (Z)-butyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3d**).* White solid, mp 153-155 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.52; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.96 (t, 3H, J = 7.3 Hz), 1.43 (sextet, 2H, J = 7.3 Hz), 1.69 (quintet, 2H, J = 6.6 Hz), 4.24 (t, 3H, J = 6.6 Hz), 6.04 (s, 1H),7.39-7.52 (m, 5H), 9.18 (s, 1H);$^{13}$C NMR (100 MHz, $CDCl_3$): 13.7, 19.1, 30.8, 65.3, 97.1, 125.9, 128.7, 129.3, 130.6, 138.7, 152.4, 161.3, 166.9; IR (KBr, $cm^{-1}$): 3303, 2967, 1789, 1735, 1683, 1408, 1178, 773, 692; Ms m/z (%): 288 (M+) (51), 232 (27), 214 (62), 188 (23), 142 (100), 119 (91),100 (53), 91 (41), 68 (94), 57 (100); Anal. Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.21; H, 5.46; N, 9.41.

*4.2.5. (Z)-sec-butyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3e**).* White crystal, mp 134-135 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.40; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.86 (t, 3H, J = 7.6 Hz), 1.21 (d, 3H, J = 6 Hz), 1.52-1.62 (m, 2H), 4.92 (sextet, 1H, J = 6 Hz), 5.95 (s, 1H), 7.33-7.44 (m, 5H), 9.13 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 9.6, 19.4, 28.7, 73.6, 97.5, 125.8, 128.6, 129.2, 130.6, 138.6, 152.3, 161.4, 166.5; IR (KBr, $cm^{-1}$): 3287, 2973, 1785,

1733, 1697, 1412, 1266, 772, 696; Anal. Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.66; H, 5.10; N, 10.18.

*4.2.6. (Z)-pentan-2-yl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3f**).* White solid, mp 112-113 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.55; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.93 (t, 3H, J = 7.3 Hz), 1.28 (d, 3H, J = 6.3 Hz), 1.30-1.40 (m, 2H), 1.49-1.55 (m, 1H), 1.61-1.66 (m, 1H), 5.06 (sextet, 1H, J = 6.2 Hz), 6.01 (s, 1H), 7.38-7.50 (m, 5H), 9.22 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 12.8, 17.5, 18.9, 36.9, 71.2, 96.5, 124.8, 127.6, 128.2, 129.5, 137.5, 151.3, 160.3, 165.4; IR (KBr, $cm^{-1}$): 3317, 2960, 1783, 1733, 1697, 1414, 1271, 772, 696; Anal. Calcd. for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.42; H, 5.19; N, 9.69.

*4.2.7. (Z)-isopentyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3g**).* White solid, mp 125-126 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.55; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.88-0.92 (m, 1H), 0.93-0.96 (m, 6H), 1.59 (q, 2H, J = 6.8 Hz), 4.26 (t, 2H, J = 6.8 Hz), 6.02 (s, 1H), 7.38-7.51 (m, 5H), 9.26 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 21.3, 23.9, 36.1, 63.0, 95.9, 124.8, 127.7, 128.2, 129.5, 137.6, 151.3, 160.3, 165.8; IR (KBr, $cm^{-1}$): 3266, 2958, 1785, 1736, 1699, 1416, 1263, 771, 695; Anal. Calcd. for $C_{16}H_{18}N_2O_4$: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.27; H, 5.82; N, 9.75.

*4.2.8. (Z)-2-ethylhexyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3h**).* White solid, mp 89-90 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.54; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.89-0.93 (m, 6H), 1.30-1.43 (m, 8H), 1.61 (septet, 1H, J = 6 Hz), 4.15 (dd, 2H, $J_1$ = 5.7 Hz, $J_2$ = 2.5 Hz), 6.04 (s, 1H), 7.39-7.51 (m, 5H), 9.26 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 9.9, 13.0, 21.9, 22.6, 27.8, 29.2, 37.6, 66.7, 96.0,124.8, 127.6, 128.2, 129.5, 137.6, 151.3, 160.3, 165.9; IR (KBr, $cm^{-1}$): 3272, 2961, 1785, 1736, 1678, 1417, 1264, 773, 697; Anal. Calcd. for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 65.87; H, 6.79; N, 7.91.

*4.2.9. (Z)-octyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3i**).* White solid, mp 119-120 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.58; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.89 (t, 3H, J = 7 Hz), 1.28-1.39 (m, 10H), 1.69 (quintet, 2H, J = 6.7 Hz), 4.22 (t, 2H, J = 6.7 Hz), 6.03 (s, 1H), 7.39-7.51 (m, 5H), 9.20 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 13.0, 21.6, 24.8, 27.5, 28.1, 30.7, 64.5, 96.0, 124.8, 127.6, 128.2, 129.5, 137.7, 151.3, 160.3, 165.8; IR (KBr, $cm^{-1}$): 3277, 2925, 1784, 1735, 1698, 1412, 1265, 772, 695; Anal. Calcd. for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.89; H, 6.12; N, 7.63.

*4.2.10. Didecyl 2-(3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl)succinate (**6j**).* White solid, mp 102-103 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.77; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 0.80 (t, 6H, J = 6.8 Hz), 1.16-1.22 (m, 28H), 1.53-1.56 (m, 4H), 2.92 (dd, 2H, $J_1$=16 Hz, $J_2$ = 7 Hz), 3.99-4.14 (m, 4H), 5.13 (dd, 1H, $J_1$ = 7.6, $J_2$ = 5.4 Hz), 7.28-7.45 (m, 5H), 8.32 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 13.0, 21.6, 24.6, 24.7, 27.3, 28.1, 28.1, 28.2, 28.2, 28.2, 28.2, 28.3, 28.4, 30.8, 33.3, 54.7, 64.7, 65.6, 75.6, 76.0, 76.3, 124.4, 127.2, 128.0, 130.0, 152.7, 153.0, 167.2, 169.3; IR (KBr, $cm^{-1}$): 3175, 2921, 1787, 1742, 1690, 1449, 1274, 764, 699; Anal. Calcd. for $C_{32}H_{51}N_3O_6$: C, 66.99; H, 8.96; N, 7.32. Found: C, 67.28; H, 8.31; N, 7.64.

*4.2.11. (Z)-2-methoxyethyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3k**).* White crystal, mp 123-124 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.11; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 3.42 (s, 3H), 3.66 (t, 2H, J = 4.6 Hz), 4.39 (t, 2H, J = 4.7 Hz), 6.06 (s, 1H), 7.39-7.51 (m, 5H), 9.27 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 58.0, 63.1, 69.0, 95.7, 124.8, 127.6, 128.2, 129.5, 137.9, 151.3, 160.2, 165.3; IR (KBr, $cm^{-1}$): 3313, 2931, 1783, 1734, 1692, 1415, 1269, 768, 693; Anal. Calcd. for $C_{14}H_{14}N_2O_5$: C, 57.93; H, 4.86; N, 9.65. Found: C, 58.12; H, 4.35; N, 9.22.

*4.2.12. (Z)-cyclohexyl 2-(2,5-dioxo-1-phenylimidazolidin-4-ylidene)acetate (**3l**).* White solid, mp 226-227 ˚C; $R_f$ (20% ethyl acetate/hexane) 0.42; $^1$H NMR (400 MHz, $CDCl_3$): δ ppm 1.25-1.58 (m, 6H), 1.74-1.90 (m, 4H), 4.90 (m, 1H), 6.02 (s, 1H), 7.33-7.62 (m, 5H), 9.20 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): 22.6, 24.2, 30.5, 72.9, 96.6, 124.8, 127.6, 128.2, 129.6, 137.4, 151.3, 160.4, 165.2; IR (KBr, $cm^{-1}$): 3267, 2932, 1785, 1733, 1699, 1414, 1261, 771, 695; Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 65.27; H, 5.42; N, 9.26.

In order to further investigation of product structures, the crystal structure of **3a** is shown in Fig. 1. For the crystal structure determination, the single crystal of the compound **3a** was used for data collection on a four-circle Rigaku R-AXIS RAPID-S diffractometer (equipped with a two dimensional area IP detector). The graphite-monochromatised Mo Kα radiation (λ = 0.71073 Å) and oscillation scans technique with Δω = 5° for one image were used for data collection. The lattice parameters were determined by the least-squares methods on the basis of all reflections with F2>2σ (F2). Integration of the intensities, correction for Lorentz and polarization effects and cell refinement was performed using Crystal Clear (Rigaku/MSC Inc., 2005) software.[25] The structures were solved by direct methods using *SHELXL2013*[26] and refined by a full-matrix least-squares procedure using the program *SHELXL2013*.[26] H-atoms were positioned geometrically and refined using a riding model. The final difference Fourier maps showed no peaks of chemical significance. Crystal packing diagram of **3a** are in sheet form across the intra- and inter-molecular H-bonds (Fig. 2). The crystallographic data and selected bond length, angles and torsion angles are summarized in Tables 3 and 4, respectively. Crystallographic data were deposited in CSD under CCDC-1435008 registration number and are available free of charge upon request to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033, *e-mail*: *deposit@ccdc.cam.ac.uk*).

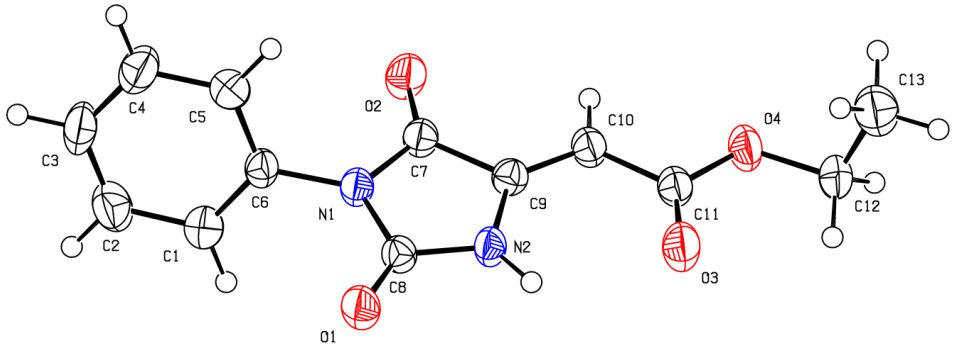



**Figure 1.** ORTEP diagram of **3a**.

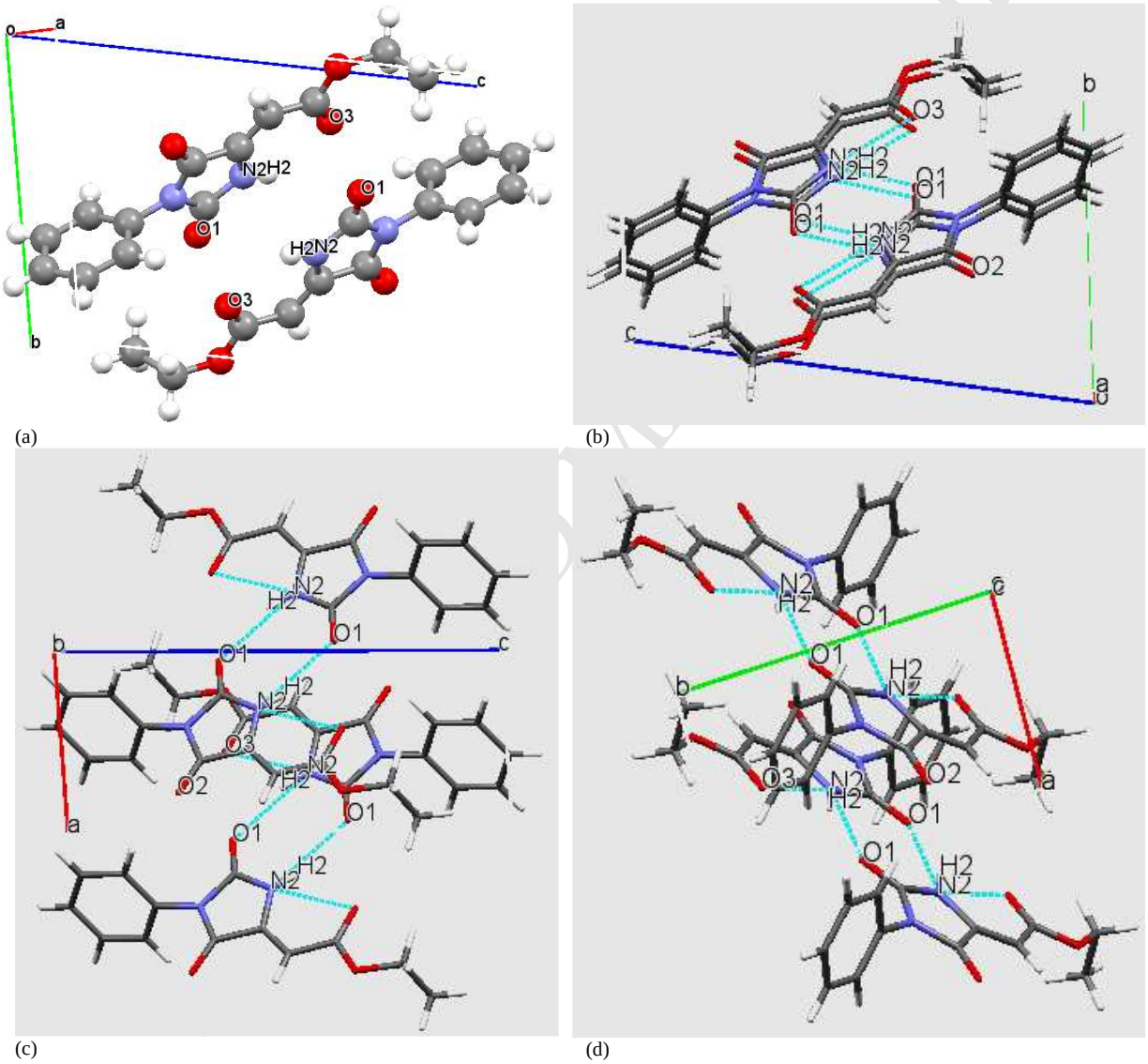



**Figure 2.** Crystal packing diagram of **3a** (a). View from the cell *a* axis (b), *b* axis (c) and *c* axis (d).

Compound **3a** show two type H-bonds. This compound formed a dimer form *via* two intermolecular H-bonds between N2–H2·····O1 atoms with $d_{(N\cdots O)}$ distance of 3.059 Å and made an eight-membered ring with centrosymmetric ($C_i$) form (Fig. 3). This compound also formed intramolecular H-bond N2–H2 and oxygen atom of carbonyl group in esteric moiety (N2–H2·····O3) with $d_{(N\cdots O)}$ distance of 2.817 Å. In other word, the H2 atom has a bifurcated inter- and intra-molecular H-bonds with both O1 and O3 atoms.

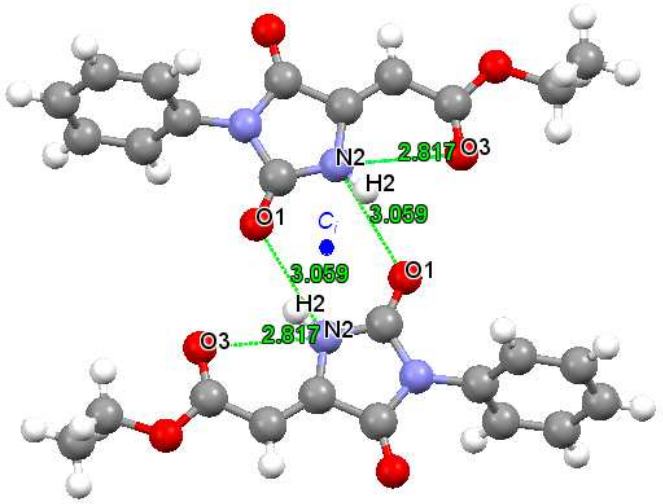



**Figure 3.** Inter- and intra-molecular H-bond distances in **3a**. Formation of eight-membered ring with centrosymmetric $C_i$ form and assigned with dense dot ( ● ).

**Table 3.** Crystallographic data for compound **3a**

| | |
|---|---|
| *Crystal data* | |
| $C_{13}H_{12}N_2O_4$ | γ = 85.669 (4)° |
| $M_r$ = 260.25 | $V$ = 596.88 (10) Å$^3$ |
| Triclinic, $P\bar{1}$ | $Z$ = 2 |
| $a$ = 5.3027 (5) Å | $F$(000) = 272 |
| $b$ = 8.6900 (9) Å | $D_x$ = 1.448 Mg m$^{-3}$ |
| $c$ = 13.2153 (12) Å | Mo $K\alpha$ radiation, λ = 0.71073 Å |
| α = 80.225 (4)° | μ = 0.11 mm$^{-1}$ |
| β = 85.234 (4)° | $T$ = 0 K |
| *Data collection* | |
| 13152 measured reflections | $\theta_{max}$ = 28.4°, $\theta_{min}$ = 3.1° |
| 2969 independent reflections | $h$ = −7→7 |
| 1579 reflections with $I > 2\sigma(I)$ | $k$ = −11→11 |
| $R_{int}$ = 0.105 | $l$ = −17→17 |
| *Refinement* | |
| $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, $S$ | 0.065, 0.155, 1.01 |
| Refinement on $F^2$ | 0 restraints |
| Least-squares matrix: full | Hydrogen site location: inferred from neighbouring sites |
| $\Delta\rho_{max}$ = 0.20 e Å$^{-3}$ | $\Delta\rho_{min}$ = −0.27 e Å$^{-3}$ |

**Table 4.** The selected bond length (Å), angle (°) and torsion angle ($\phi$) for **3a**

| | |
|---|---|
| C9—C10 | 1.325 (3) |
| C11—C10 | 1.458 (3) |
| O2—C7 | 1.206 (3) |
| O1—C8 | 1.207 (3) |
| O3—C11 | 1.207 (3) |
| N2—C8 | 1.365 (3) |
| N1—C7 | 1.378 (3) |

| | |
|---|---|
| N1—C8 | 1.408 (3) |
| C8—N2—H2 | 124.1 |
| C9—N2—H2 | 124.1 |
| O1—C8—N2 | 127.7 (2) |
| O3—C11—C10 | 123.7 (2) |
| C7—N1—C6—C5 | −67.0 (3) |
| C7—C9—C10—C11 | 178.6 (2) |
| C10—C9—C7—O2 | 1.2 (5) |
| O1—C8—N2—H2 | 0.64 |
| C7—C9—C10—H10 | −1.42 |
| N2—H2····O1—C8 | −14.05 |

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