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UNEXPECTED TANDEM REACTION OF NEW TYPE MORITA-BAYLIS-HILLMAN ADDUCTS PROMOTED BY [HMIM]HSO₄/NaNO₃ SYSTEM

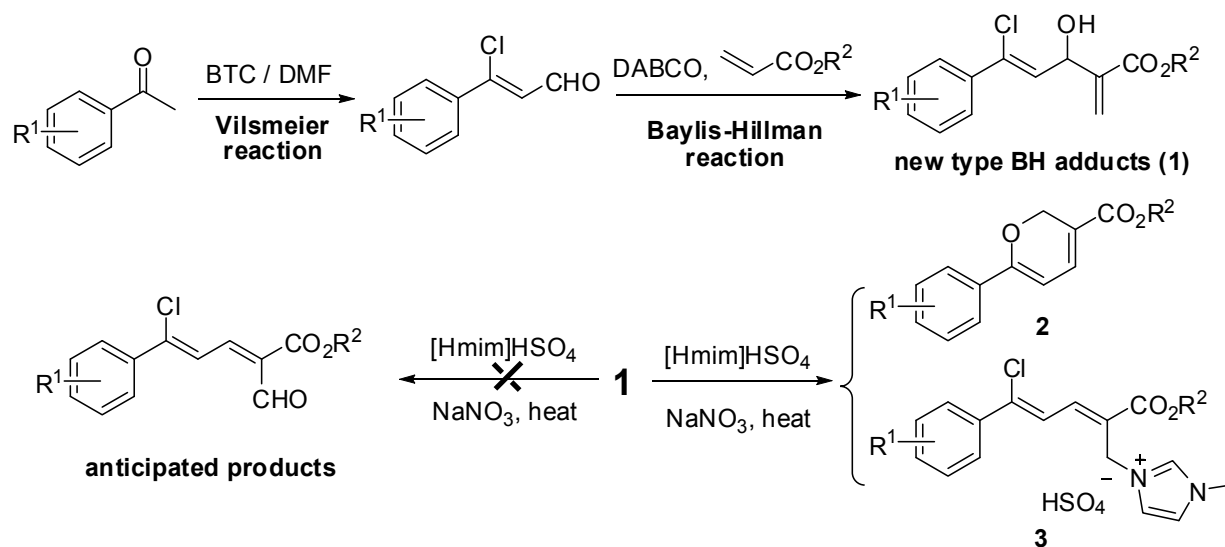
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Abstract – A tandem reaction of new type Baylis-Hillman adducts **1** was prompted by ionic liquid [Hmim]HSO₄/NaNO₃ system and the unexpected products 6-aryl-2*H*-pyran-3-carboxylates **2** and imidazolium salts **3** were efficiently formed *via* the rearrangement and substitution reaction. While mediated by [Emim]HSO₄/NaNO₃ system, the key intermediates **4** were isolated. A plausible mechanism for the transformation was given.

INTRODUCTION

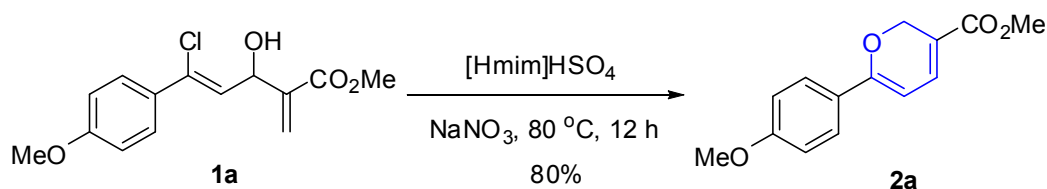
Tandem reactions are of great importance in organic synthesis due to generation of some important products in a single operation with high atom economy and bond-forming efficiency. Recently, more and more novel types of tandem reactions, including tandem Michael addition,¹ substitution,² cyclization³⁻⁵ and rearrangement reaction,⁶ were extensively applied to organic synthesis, especially the synthesis of natural optically active products⁷ and heterocyclic compounds. The Baylis-Hillman reaction is a synthetically useful method for carbon-carbon bond-forming reactions to yield functionalized allylic alcohols,⁸ thereby providing handles for further manipulation in a multitude of synthetic organic transformations.⁹ In continuation of our research on new type Baylis-Hillman adducts **1** prepared from aryl methyl ketones *via* a combination of the Vilsmeier and the Baylis-Hillman reactions,¹⁰⁻¹³ we investigated the tandem reaction of new type Baylis-Hillman adduct **1** under the [Hmim]HSO₄/NaNO₃ system¹⁴ (Scheme 1). To our surprise, the unexpected products 6-aryl-2*H*-pyran-3-carboxylates **2** and/or imidazolium salt **3** were isolated.



Scheme 1

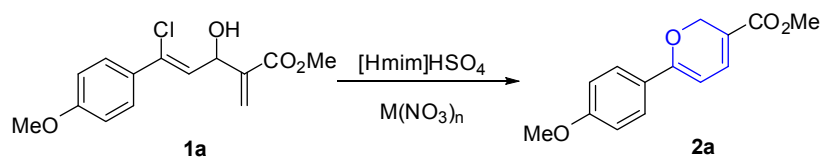
RESULTS AND DISCUSSION

Initially, we mixed 1.0 mmol of (*Z*)-methyl 5-chloro-3-hydroxy-5-(4-methoxyphenyl)-2-methylenepent-4-enoate **1a** with 1.1 mmol of NaNO₃ in ionic liquid [Hmim]HSO₄ at 80 °C for 12 h, the unexpected product methyl 6-(4-methoxyphenyl)-2*H*-pyran-3-carboxylate **2a** was isolated in 80% yield (Scheme 2).



Scheme 2

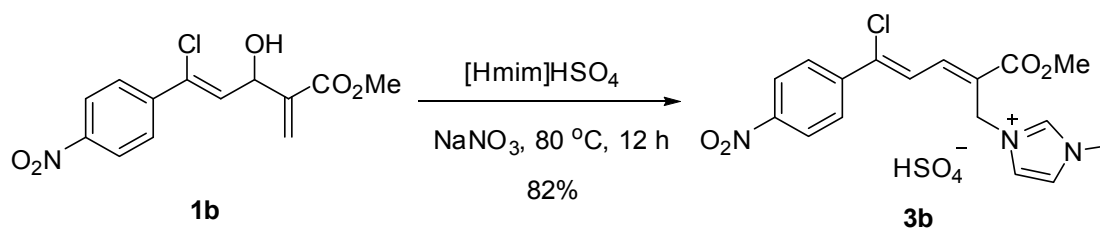
Encouraged by this result, several other nitrate salts have been used to investigate the above reaction and the results were summarized in Table 1. No desired product **2a** was detected using NH₄NO₃-[Hmim]HSO₄ system at 80 °C for 12 h (Table 1, entry 2). Zn(NO₃)₂-[Hmim]HSO₄ system could produce **2a** with only 10% yield (Table 1, entry 3). Compared to the NaNO₃-[Hmim]HSO₄ system, a slightly lower yield was found using KNO₃-[Hmim]HSO₄ system (Table 1, entry 4). The highest yield (80%) of **2a** was obtained in NaNO₃-[Hmim]HSO₄ system at 80 °C for 12 h (Table 1, entry 1). Moreover, proper temperature was found to be essential to this reaction and the system showed homogeneous at 80 °C. At lower temperatures, **2a** was obtained in lower yield even with longer reaction time (Table 1, entries 5 and 6), while higher temperatures led to unknown side reactions and very complicated results (Table 1, entries 7 and 8).

Table 1. Reaction of **1a** with $M(\text{NO}_3)_n\text{-}[\text{Hmim}]\text{HSO}_4$ 

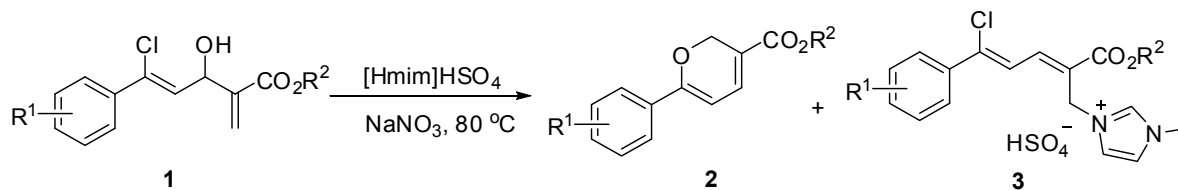
| Entry | $M(\text{NO}_3)_n$ | Temp.(°C) | Time (h) | Yield ^a of 2a (%) |
|-------|----------------------------|------------|----------|-------------------------------------|
| 1 | NaNO_3 | 80 | 12 | 80 |
| 2 | NH_4NO_3 | 80 | 12 | 0 |
| 3 | $\text{Zn}(\text{NO}_3)_2$ | 80 | 12 | 10 |
| 4 | KNO_3 | 80 | 12 | 78 |
| 5 | NaNO_3 | 40 | 72 | 0 |
| 6 | NaNO_3 | 60 | 48 | 34 |
| 7 | NaNO_3 | 100 | 10 | 67 |
| 8 | NaNO_3 | 120 | 10 | 46 |

^a Isolated yield based on **1a**.

Another type BH adduct **1b** with a *para*-nitro group on the aromatic ring was also investigated under the similar conditions. To our surprise, when substrate **1b** was mixed with the $\text{NaNO}_3\text{-}[\text{Hmim}]\text{HSO}_4$ system at 80 °C for 12h, only imidazolium salt **3b** was isolated in 82%, which was confirmed by ¹H-NMR, ¹³C-NMR and MS spectra (Scheme 3). This interesting result indicated that the different type of the substituted groups on the aromatic ring had evident influence on the products.

**Scheme 3**

In order to confirm our presumption, various new type Baylis-Hillman adducts **1** were used for the tandem rearrangement-substitution reaction under similar conditions and the full results are summarized in Table 2. It was found that the substrates **1** with electron-donating groups on the aromatic ring gave the corresponding 2*H*-pyrans **2** in good yields (80-75%) (Table 2, entries 1, 3 and 4), while those with electron-withdrawing groups produced the corresponding imidazolium salts **3** in good yields (98-78%) (Table 2, entries 2, 6-9). Interestingly, the substrates **1e** could give both of the products with the ratio of **2e** : **3e** = 1 : 2. In addition, when 2.2 equivalents of NaNO_3 was added to this reaction, the ratio of these two products was not obviously changed (Table 2, entry 5).

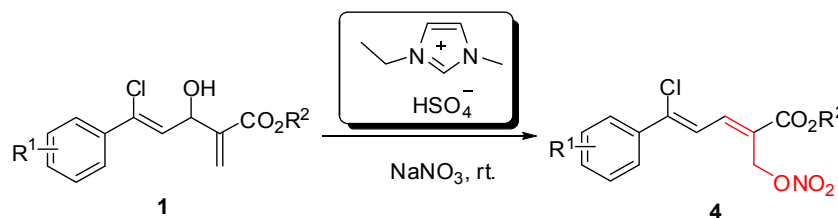
Table 2. Reaction of new type BH adducts **1** with NaNO₃-[Hmim]HSO₄

| Entry | Substrates | R ¹ | R ² | Time (h) | Yield of products ^a | |
|----------------|------------|---------------------------|----------------|----------|--------------------------------|----------------|
| | | | | | 2 | 3 |
| 1 | 1a | <i>p</i> -MeO | Me | 12 | 2a (80) | - |
| 2 | 1b | <i>p</i> -NO ₂ | Me | 12 | - | 3b (82) |
| 3 | 1c | <i>p</i> -Me | Me | 13 | 2c (78) | - |
| 4 | 1d | <i>p</i> -MeO | Et | 13 | 2d (75) | - |
| 5 ^b | 1e | H | Me | 12 | 2e (25) | 3e (50) |
| 6 | 1f | <i>m</i> -Cl | Me | 11 | - | 3f (80) |
| 7 | 1g | <i>p</i> -NO ₂ | Et | 13 | - | 3g (78) |
| 8 | 1h | <i>p</i> -F | Me | 11 | - | 3h (98) |
| 9 | 1i | <i>p</i> -F | Et | 12 | - | 3i (83) |

^a Isolated yield based on **1**.

^b The ratio of **2e** and **3e** was not obviously changed when 2.2 mmol of NaNO₃ was added.

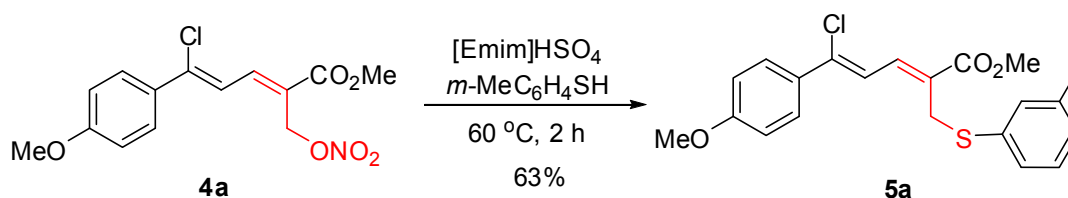
In order to clarify the formation mechanism of these products, ionic liquid [Emim]HSO₄ was prepared,¹⁵ which could avoid theoretical formation of imidazolium salts **3**. As we anticipated, the reactions of the Baylis-Hillman adducts **1** under the ionic liquid [Emim]HSO₄/NaNO₃ system gave S_N2' products (2*E*,4*Z*)-5-chloro-2-(nitrooxymethyl)-5-arylpenta-2,4-dienoates **4** with satisfactory yields (Table 3).

Table 3. Reactions of new type BH adducts **1** with NaNO₃-[Emim]HSO₄

| Entry | Substrates | R ¹ | R ² | Time (h) | Yield of 4 ^a (%) |
|-------|------------|----------------|----------------|----------|------------------------------------|
| 1 | 1a | <i>p</i> -MeO | Me | 3 | 4a (65) |
| 2 | 1f | <i>m</i> -Cl | Et | 2 | 4b (76) |
| 3 | 1h | <i>p</i> -F | Me | 2 | 4c (83) |

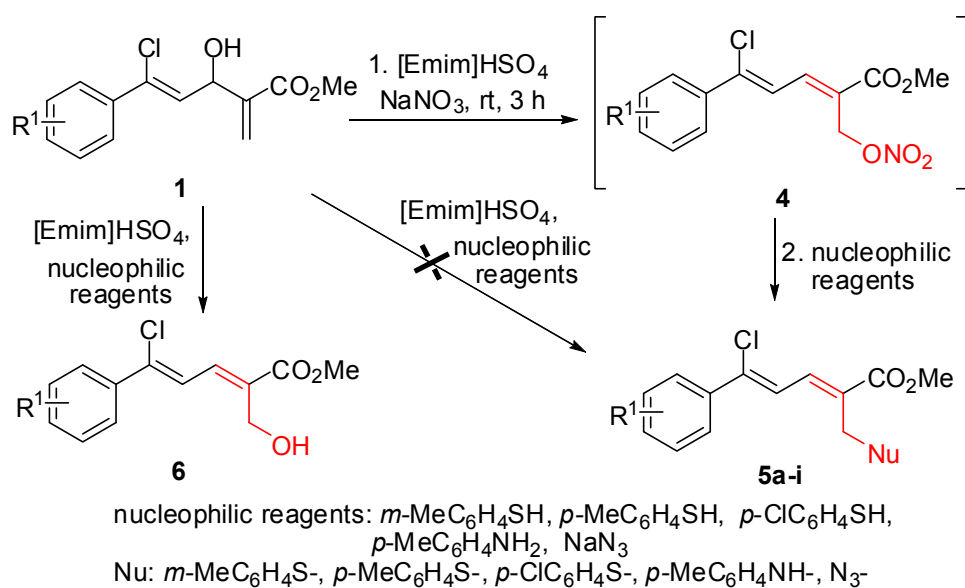
^a Isolated yield based on **1**.

However, these intermediates **4a-c** were unstable at high temperature. Treatment of this intermediate **4a** with 3-methylbenzenethiol afforded the desired product (2*Z*,4*Z*)-methyl 5-chloro-5-(4-methoxyphenyl)-2-(*m*-tolylthiomethyl)penta-2,4-dienoate **5a** in 63% yield (Scheme 4).



Scheme 4

To confirm the regularity, we used various of nucleophilic reagents to react with the Baylis-Hillman adducts **1** under the ionic liquid [Emim]HSO₄/NaNO₃ system in one pot, and afforded the compounds **5a-i** in good yields (Scheme 5, Table 4). During our experiments, we found without addition of NaNO₃, not desired compounds **5**, but the rearranged compound **6** (R¹= *p*-Cl) was isolated and conformed by NMR and MS, which demonstrated the NaNO₃ play an important role in the reactions, and the intermediates **4** were existed in the reaction paths (Scheme 5). It was also found from Table 4 that the substrates **1** with electron-donating groups on the aromatic ring gave the higher yields than those with electron-withdrawing groups. In other words, the more stable the intermediates **4** with electron-donating groups are, the more possible to form the 2*H*-pyrans **2** in [Hmim]HSO₄/NaNO₃ system.



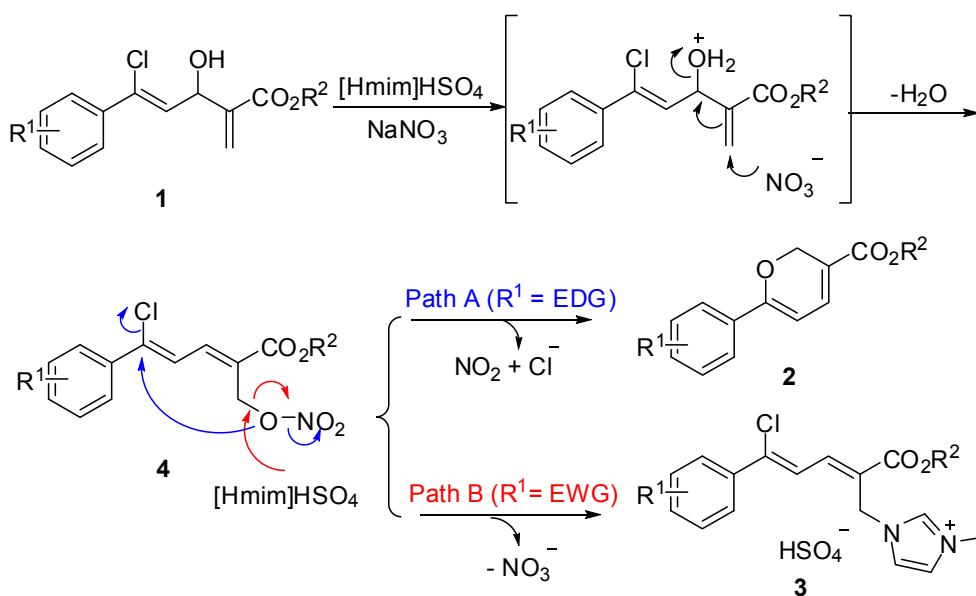
Scheme 5

Table 4. Reactions of new type BH adducts **1** with NaNO₃-[Emim]HSO₄ and nucleophilic reagents

| Entry | Substrates | R ¹ | Nu | Yield of 5 ^a (%) |
|----------------|------------|----------------|--|------------------------------------|
| 1 | 1a | <i>p</i> -MeO | <i>m</i> -MeC ₆ H ₄ S | 5a (63) ^b |
| 2 | 1a | <i>p</i> -MeO | <i>p</i> -MeC ₆ H ₄ S | 5b (83) |
| 3 | 1a | <i>p</i> -MeO | <i>p</i> -ClC ₆ H ₄ S | 5c (81) |
| 4 | 1a | <i>p</i> -MeO | <i>p</i> -MeC ₆ H ₄ NH | 5d (78) |
| 5 ^c | 1a | <i>p</i> -MeO | N ₃ | 5e (76) |
| 6 | 1h | <i>p</i> -F | <i>p</i> -MeC ₆ H ₄ S | 5f (74) |
| 7 | 1h | <i>p</i> -F | <i>p</i> -ClC ₆ H ₄ S | 5g (76) |
| 8 | 1h | <i>p</i> -F | <i>p</i> -MeC ₆ H ₄ NH | 5h (67) |
| 9 ^c | 1h | <i>p</i> -F | N ₃ | 5i (70) |

^a Isolated yield based on **1**.^b This reaction was carried out in two step and intermediate **4a** was isolated.^c NaN₃ was added dissolved in DMF.

According to the above results, a plausible mechanism¹⁶ for the formation of products **2**, **3** and **4** was shown in Scheme 6. Firstly, the BH adduct **1** was attacked by nitrate anion in ionic liquid to give S_N2' products **4**, where [Hmim]HSO₄ played a dual role of Brønsted acid catalyst and solvent for both rearrangement and substitution.¹² Intermediates **4** are unstable at high temperature and could be readily converted into **2** and **3** via path A or path B dependent on the activities of substrates.

**Scheme 6**

In summary, the present study investigated the tandem reaction of new type Morita-Baylis-Hillman adducts in ionic liquids/ NaNO_3 system, which provided a new and efficient way for the synthesis of 2*H*-pyrans and imidazolium salts. The new applications of ionic liquids/ NaNO_3 system are now being investigated in our lab.

EXPERIMENTAL

Unless otherwise indicated, chemicals and solvents were purchased from commercial suppliers and without further purification. Flash column chromatography was performed using silica gel (200-400 mesh). IR spectra were recorded on a Nicolet Avatar-370 instrument. Mass spectra were measured with Thermo Finnigan LCQ-Advantage. ^1H NMR and ^{13}C NMR spectra were recorded at VARAIN-400 or BRUKER AVANCE III-500 using CDCl_3 or DMSO as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts were given in δ relative to TMS, the coupling constants J were given in Hertz. The low-resolution mass spectra were obtained with the Thermo Trace GC Ultra-DSQ II and Agilent 6120 (Quadrupole LC-MS) mass spectrometer. High resolution mass spectra (HRMS) analyze were measured on an Agilent 6210 TOF LC/MS using ESI or EI (electrospray ionization) techniques.

General procedure for the synthesis of 2*H*-pyrans **2** and/or imidazolium salts **3**

A mixture of Baylis-Hillman adducts **1** (1 mmol) and NaNO_3 (1.1 mmol) was stirred in 2 mL of [Hmim]HSO₄ at 80 °C for 12 h. The reaction mixture was cooled to rt. After completion of the reaction (monitored by TLC), the product was extracted with EtOAc (3 × 10 mL). The combined extract was dried over Na_2SO_4 , filtered, concentrated under reduced pressure, and purified by silica gel column chromatography (CH_2Cl_2 -MeOH, 16 : 1) to afford the products **2** and **3**.

General procedure for the synthesis of (2*E*,4*Z*)-5-chloro-2-(nitrooxymethyl)-5-arylpenta-2,4-dienoates **4**

A mixture of Baylis-Hillman adducts **1** (1 mmol) and NaNO_3 (1.1 mmol) was stirred in 2 mL of [Emim]HSO₄ at rt for 3 h. After completion of the reaction (monitored by TLC), the product was extracted with EtOAc (3 × 10 mL). The combined extract was dried over Na_2SO_4 , filtered, concentrated under reduced pressure, and purified by silica gel column chromatography (hexane-EtOAc, 8 : 1) to afford the desired products **4**.

General procedure for the synthesis of compounds **5**

A mixture of Baylis-Hillman adducts **1** (1 mmol) and NaNO_3 (1.1 mmol) was stirred in 2 mL of

[Emim]HSO₄ at rt for 3 h. The reaction mixture was heat to 60 °C and *o*-MeC₆H₄SH (1.1 mmol) was added. The mixture was further stirred at rt for 2-3 h. After completion of the reaction (monitored by TLC), the product was extracted with EtOAc (3 × 10 mL). The combined extract was dried over Na₂SO₄, filtered, concentrated under reduced pressure, and purified by silica gel column chromatography (hexane-EtOAc, 8: 1) to afford the desired product **5**.

Methyl 6-(4-methoxyphenyl)-2*H*-pyran-3-carboxylate (**2a**)

White solid. Mp 166-169 °C. IR (KBr) (ν_{\max} , cm⁻¹): 3188, 2936, 1670. ¹H NMR (400 MHz, DMSO-*d*₆) δ_{H} : 3.75 (3H, s, COOCH₃), 3.82 (3H, s, Ar-OCH₃), 4.66 (2H, s, O-CH₂-C=C), 7.04-7.79 (4H, m, ArH), 7.61 (1H, d, *J* = 11.2 Hz, O-C=CH-C), 7.73 (1H, d, *J* = 11.2 Hz, CH=C-COOMe). ¹³C NMR (100 MHz, DMSO-*d*₆) δ_{C} : 52.1, 55.5, 59.8, 92.2, 104.5, 114.3(2C), 119.1, 128.4, 128.7, 137.5, 139.8, 161.0, 166.6; MS (CI) 246.0 [M]⁺. HRMS (CI) calcd for [C₁₄H₁₄O₄]: 246.0892; found: 246.0895.

Methyl 6-*p*-tolyl-2*H*-pyran-3-carboxylate (**2c**)

White solid. Mp 166-169 °C. IR (KBr) (ν_{\max} , cm⁻¹): 3183, 2943, 1674. ¹H-NMR (400 MHz, DMSO-*d*₆) δ_{H} : 2.36 (3H, s, Ar-CH₃), 3.76 (3H, s, COOCH₃), 4.67 (2H, s, OCH₂C), 7.30 (1H, d, *J* = 8.0, O-C=CH), 7.64-7.71 (4H, m, ArH), 7.74 (1H, d, *J* = 2.8, MeOOC-C=CH); ¹³C NMR (100 MHz, DMSO-*d*₆) δ_{C} : 20.8, 52.1, 59.8, 120.2, 126.6(2C), 129.4(2C), 129.5, 133.2, 137.1, 139.9, 140.4, 166.6; MS (CI) 231.3 [M+1]⁺. HRMS (CI) calcd for [C₁₄H₁₄O₃]: 230.0943; found: 230.0939.

Ethyl 6-(4-methoxyphenyl)-2*H*-pyran-3-carboxylate (**2d**)

White solid. Mp 166-169 °C. IR (KBr) (ν_{\max} , cm⁻¹): 3176, 2945, 1665. ¹H NMR (400 MHz, DMSO-*d*₆) δ_{H} : 1.27 (3H, t, *J* = 7.2, CH₂CH₃), 3.82 (3H, s, Ar-OCH₃), 4.42 (2H, q, *J* = 7.2, CH₂CH₃), 4.66 (2H, s, OCH₂), 7.04 (2H, m, ArH), 7.62 (1H, d, *J* = 11.2, C=CH-CH=C-O), 7.73 (1H, d, *J* = 11.2, C=CH-CH=C-O), 7.78-7.80 (2H, m, ArH); ¹³C NMR (100 MHz, DMSO-*d*₆) δ_{C} : 14.1, 55.4, 59.8, 60.6, 144.2(2C), 119.1, 128.3(2C), 128.9, 137.2, 139.5, 160.9, 166.1(2C); MS (CI) 261.3 [M+1]⁺. HRMS (CI) calcd for [C₁₅H₁₆O₄]: 260.1049; found: 260.1045.

Methyl 6-phenyl-2*H*-pyran-3-carboxylate (**2e**)

White solid. Mp 163-165 °C. IR (KBr) (ν_{\max} , cm⁻¹): 3163, 2959, 1660. ¹H NMR (400 MHz, DMSO-*d*₆) δ_{H} : 3.87 (3H, s, COOCH₃), 4.42 (2H, s, OCH₂C), 7.30 (1H, d, *J* = 11.2, O-C=CH), 7.24 (H, s, ArH), 7.42 (2H, d, *J* = 3.6, ArH), 7.73 (2H, d, *J* = 3.6, ArH), 7.42 (2H, d, *J* = 11.2, MeOOC-C=CH); ¹³C NMR (100 MHz, DMSO-*d*₆) δ_{C} : 52.1, 59.8, 121.0, 126.6(2C), 128.8(2C), 129.9, 130.3, 135.9, 136.9, 139.7, 166.5; MS (ESI) 217.1 [M+1]⁺. HRMS (ESI) calcd for [C₁₃H₁₂O₃]: 216.0786; found: 216.0780.

1-((2E,4Z)-5-Chloro-2-(methoxycarbonyl)-5-(4-nitrophenyl)penta-2,4-dienyl)-3-methyl-1H-imidazol-3-iumhydrogensulfate (3b)

Yellow solid. Mp 260-262 °C. IR (KBr) (ν_{\max} , cm^{-1}): 3442, 2945, 1694. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} : δ (ppm) 3.77 (3H, s, N- CH_3), 3.86 (3H, s, COOCH_3), 5.43 (2H, s, N- CH_2), 7.36-7.40 (2H, m, ArH), 7.77 (1H, d, $J = 5.6$ Hz, Cl-C=CH), 7.86 (1H, d, $J = 11.2$ Hz, Me-N-CH=C), 7.95 (1H, d, $J = 11.2$ Hz, N-CH=C), 8.06 (1H, d, $J = 5.6$ Hz, ClC=C-CH=C), 8.07-8.09 (2H, m, ArH), 9.21 (1H, s, N=CH-C). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} : 36.8, 52.1, 59.8, 121.0, 126.7(2C), 128.8(2C), 129.9, 130.3, 135.9, 136.9, 139.6, 141.8, 147.4, 148.0, 166.5; MS (ESI) 362.1 $[\text{M}]^+$. HRMS (ESI) calcd for $[\text{C}_{17}\text{H}_{17}\text{ClN}_3\text{O}_4]^+$: 362.0908; found: 362.0900.

3-((2E,4Z)-5-Chloro-2-(methoxycarbonyl)-5-phenylpenta-2,4-dienyl)-1-methyl-1H-imidazol-3-iumhydrogensulfate (3e)

White solid. Mp 260-262 °C. IR (KBr) (ν_{\max} , cm^{-1}): 3443, 2942, 1699. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} : 3.76 (3H, s, N- CH_3), 3.86 (3H, s, COOCH_3), 4.67 (2H, s, N- CH_2), 7.29 (2H, d, $J = 8.8$ Hz, ArH), 7.65 (2H, d, $J = 3.2$ Hz, Cl-C=CH, ClC=C-CH=C), 7.66 (2H, d, $J = 6.4$ Hz, Me-N-CH=C, N-CH=C), 7.70 (2H, d, $J = 8.8$ Hz, ArH), 7.74 (H, d, $J = 3.2$ Hz, ArH), 9.03 (1H, s, N=CH-C). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} : 35.8, 44.8, 61.2, 118.7, 122.7, 123.5, 125.7, 127.3(2C), 129.3(2C), 133.0, 136.7, 139.1, 141.0, 143.1, 165.4; MS (ESI) 317.1 $[\text{M}]^+$. HRMS (ESI) calcd for $[\text{C}_{17}\text{H}_{18}\text{ClN}_2\text{O}_2]^+$: 317.1057; found: 317.1062.

3-((2E,4Z)-5-Chloro-5-(3-chlorophenyl)-2-(methoxycarbonyl)penta-2,4-dienyl)-1-methyl-1H-imidazol-3-iumhydrogensulfate (3f)

White solid. Mp 265-268 °C. IR (KBr) (ν_{\max} , cm^{-1}): 3456, 2938, 1676. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} : 3.77 (3H, s, N- CH_3), 3.87 (3H, s, COOCH_3), 5.44 (2H, s, N- CH_2), 7.54-7.58 (2H, m, ArH), 7.59-7.61 (2H, m, ArH), 7.73 (1H, d, $J = 13.6$ Hz, Me-N-CH=C), 7.75 (1H, d, $J = 8.8$ Hz, Cl-C=CH), 7.94 (1H, d, $J = 13.6$ Hz, N-CH=C), 7.95 (1H, d, $J = 8.8$ Hz, ClC=C-CH=C), 9.20 (1H, s, N=CH-C). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ_{C} : 35.9, 44.7, 52.6, 121.1, 122.7, 123.5, 126.2, 126.7, 126.9, 130.5, 130.7, 133.7, 136.8, 137.7, 138.6, 140.8, 165.8; MS (ESI) 351.0 $[\text{M}]^+$. HRMS (ESI) calcd for $[\text{C}_{17}\text{H}_{17}\text{Cl}_2\text{N}_2\text{O}_2]^+$: 351.0667; found: 351.0653.

3-((2E,4Z)-5-Chloro-2-(ethoxycarbonyl)-5-(4-nitrophenyl)penta-2,4-dienyl)-1-methyl-1H-imidazol-3-iumhydrogensulfate (3g)

Yellow solid. Mp 272-273 °C. IR (KBr) (ν_{\max} , cm^{-1}): 3469, 2934, 1689. ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ_{H} : 1.24 (3H, t, $J = 7.2$, $\text{COOCH}_2\text{CH}_3$), 3.86 (3H, s, N- CH_3), 4.22 (2H, q, $J = 7.2$, $\text{COOCH}_2\text{CH}_3$), 5.48 (2H, s, N- CH_2), 7.73-7.78 (2H, m, N-HC=CH-N), 7.95 (1H, d, $J = 11.6$, ClC=C-CH=C), 8.12 (1H, d, $J = 11.2$, ClC=HC-C=C), 8.29-8.34 (4H, m, ArH), 9.24 (1H, s, N=CH-N); ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$)

δ_C : 13.9, 35.8, 44.8, 61.5, 122.8, 123.5, 123.8(2C), 128.3, 128.7(2C), 136.9, 138.1, 139.9, 141.5, 148.2(2C), 165.1; MS (ESI) 376.1 $[M]^+$. HRMS (ESI) calcd for $[C_{18}H_{19}ClN_3O_4]^+$: 376.1064; found: 376.1067.

1-((2E,4Z)-5-Chloro-5-(4-fluorophenyl)-2-(methoxycarbonyl)penta-2,4-dienyl)-3-methyl-1H-imidazol-3-ium hydrogensulfate (3h)

White solid. Mp 257-258 °C. IR (KBr) (ν_{max} , cm^{-1}): 3455, 2940, 1705. 1H NMR (400 MHz, DMSO- d_6) δ_H : 3.77 (3H, s, N- CH_3), 3.86 (3H, s, $COOCH_3$), 5.43 (2H, s, N- CH_2), 7.38 (2H, t, $J = 8.8$ Hz, ArH), 7.23 (1H, d, $J = 3.6$ Hz, Cl-C=CH), 7.64 (1H, d, $J = 3.6$ Hz, ClC=C-CH=C), 7.86 (1H, d, $J = 11.2$ Hz, Me-N-CH=C), 7.95 (1H, d, $J = 11.2$ Hz, N-CH=C), 8.06-8.09 (2H, m, ArH), 9.21 (1H, s, N=CH-C). ^{13}C NMR (100 MHz, DMSO- d_6) δ_C : 35.8, 44.8, 52.6, 115.8 ($J = 22$ Hz, 2C), 119.7, 122.6, 123.5, 126.1, 130.0 ($J = 9$ Hz, 2C), 132.3, 136.8, 139.0, 141.7, 162.2, 165.9; MS (ESI) 335.0 $[M]^+$. HRMS (ESI) calcd for $[C_{17}H_{17}ClFN_2O_2]^+$: 335.0963; found: 335.0962.

3-((2E,4Z)-5-Chloro-2-(ethoxycarbonyl)-5-(4-fluorophenyl)penta-2,4-dienyl)-1-methyl-1H-imidazol-3-ium hydrogensulfate (3i)

White solid. Mp 263-266 °C. IR (KBr) (ν_{max} , cm^{-1}): 3449, 2966, 1673. 1H NMR (400 MHz, DMSO- d_6) δ_H : 1.24 (3H, t, $J = 7.2$, $COOCH_2CH_3$), 3.72 (3H, s, N- CH_3), 4.20 (2H, q, $J = 7.2$ Hz, $COOCH_2CH_3$), 5.37 (2H, s, N- CH_2), 7.39 (2H, t, $J = 8.8$ Hz, ArH), 7.68 (1H, t, $J = 1.6$ Hz, N-HC=CH-N), 7.72 (1H, t, $J = 1.6$ Hz, N-HC=CH-N), 7.77 (1H, d, $J = 11.6$, ClC=HC-C=C), 7.95 (1H, d, $J = 11.6$ Hz, ClC=C-CH=C), 8.02 (2H, m, $J_1 = 5.6$ Hz, $J_2 = 9.2$ Hz, ArH), 9.10 (1H, s, N=CH-N); ^{13}C NMR (100 MHz, DMSO- d_6) δ_C : 14.1, 36.0, 44.9, 61.5, 115.9 ($J = 22$ Hz, 2C), 119.7, 122.8, 123.6, 126.3, 130.0 ($J = 9$ Hz, 2C), 132.5, 136.8, 138.9, 141.8, 163.7 ($J = 226$ Hz), 165.5; MS (ESI) 349.1 $[M]^+$. HRMS (ESI) calcd for $[C_{18}H_{19}ClFN_2O_2]^+$: 349.1119; found: 349.1102.

(2E,4Z)-Methyl-5-chloro-5-(4-methoxyphenyl)-2-(nitrooxymethyl)penta-2,4-dienoate(4a)

Yellow solid. Mp 78-80 °C. IR (KBr) (ν_{max} , cm^{-1}): 3157, 2925, 1656. 1H -NMR ($CDCl_3$, 400 MHz): δ (ppm) 3.84 (3H, s, CH_3), 3.85 (3H, s, CH_3), 4.42 (2H, s, CH_2), 6.91-6.93 (2H, m, ArH), 6.99 (1H, d, $J = 11.6$ Hz, CH=CH), 7.67-7.70 (2H, m, ArH), 7.87 (1H, d, $J = 11.6$ Hz, CH=CH). ^{13}C -NMR (100 MHz, $CDCl_3$) δ (ppm) 25.3, 52.8, 55.8, 114.3(2C), 118.0, 128.6, 128.8(2C), 129.6, 137.9, 143.2, 161.5, 166.3. MS (EI): m/z (%) = 265(69, M-62), 223(71), 205(92), 179(100). HRMS (EI) calcd for $[C_{14}H_{14}ClNO_6]$: 327.0510; found: 327.0515.

(2E,4Z)-Ethyl-5-chloro-5-(3-chlorophenyl)-2-(nitrooxymethyl)penta-2,4-dienoate(4b)

White solid. Mp 80-83 °C. IR (KBr) (ν_{max} , cm^{-1}): 3139, 2921, 1671. 1H -NMR ($CDCl_3$, 400 MHz): δ

(ppm) 1.37 (3H, t, $J = 7.2$ Hz, CH_2CH_3), 4.32 (2H, q, $J_1 = 7.2$ Hz, $J_2 = 14.4$ Hz, CH_2CH_3), 4.41 (2H, s, CH_2), 7.06 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$), 7.33-7.38 (2H, m, ArH), 7.58-7.69 (2H, m, ArH), 7.82 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$). ^{13}C -NMR (100 MHz, CDCl_3) δ (ppm) 29.7, 37.4, 52.5, 119.8, 123.7, 128.3, 128.9, 129.7, 130.7, 135.3, 136.5, 137.4, 141.9, 166.2. MS (EI): m/z (%) = 329 (5, $[\text{M}-16]^+$), 283(32), 237(100). HRMS (EI) calcd for $[\text{C}_{14}\text{H}_{13}\text{Cl}_2\text{NO}_5]$: 345.0171; found: 345.0175.

(2E,4Z)-Methyl-5-chloro-5-(4-fluorophenyl)-2-(nitrooxymethyl)penta-2,4-dienoate(4c)

White solid. Mp 85-87 °C. IR (KBr) (ν_{max} , cm^{-1}): 3148, 2959, 1668. ^1H -NMR (CDCl_3 , 400 MHz): δ (ppm) 3.86 (3H, s, CH_3), 4.40 (2H, s, CH_2), 7.01 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$), 7.13-7.08 (2H, m, ArH), 7.82-7.70 (2H, m, ArH), 7.84 (1H, d, $J = 11.6$ Hz, $\text{CH}=\text{CH}$). ^{13}C -NMR (100 MHz, CDCl_3) δ (ppm) 24.5, 52.5, 115.7 ($J = 22$ Hz, 2C), 119.4, 128.9 ($J = 8$ Hz, 2C), 129.6, 133.1, 136.9, 141.6, 163.6 ($J = 250$ Hz), 165.8. MS (EI): m/z (%) = 299 (12, $[\text{M}-16]^+$), 253(37), 221(100), 193(77), 157(32). HRMS (EI) calcd for $[\text{C}_{13}\text{H}_{11}\text{ClFNO}_5]$: 315.0310; found: 315.0308.

(2Z,4Z)-Methyl-5-chloro-5-(4-methoxyphenyl)-2-(*m*-tolylthiomethyl)penta-2,4-dienoate (5a)

Yellow liquid. IR (KBr) (ν_{max} , cm^{-1}): 3134, 2955, 1661. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.24 (3H, s, CH_3), 3.82 (3H, s, CO_2CH_3), 3.83 (3H, s, OCH_3), 3.91 (2H, s, SCH_2), 6.44 (1H, d, $J = 12$ Hz, $\text{CH}=\text{CH}$), 6.84 (2H, dd, $J_1 = 2$ Hz, $J_2 = 4.4$ Hz, ArH), 6.95 (1H, d, $J = 4.0$ Hz, ArH), 7.13-7.09 (1H, m, ArH), 7.27-7.24 (2H, m, ArH), 7.41-7.39 (2H, dd, $J_1 = 2$ Hz, $J_2 = 3.2$ Hz, ArH), 7.73 (1H, d, $J = 11.6$ Hz, $\text{CH}=\text{CH}$). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.3, 32.8, 52.3, 55.5, 113.6(2C), 118.3, 128.2(2C), 128.4, 128.6, 129.5, 129.9, 130.8, 133.3, 134.9, 135.5, 138.6, 140.4, 160.7, 167.1; MS (EI): m/z (%) = 388 (5, M^+), 265(100), 233(80), 205(55), 179(52). HRMS (EI) calcd for $[\text{C}_{21}\text{H}_{21}\text{ClO}_3\text{S}]$: 388.0900; found: 388.0904.

(2Z,4Z)-Methyl 5-chloro-5-(4-methoxyphenyl)-2-(*p*-tolylthiomethyl)penta-2,4-dienoate (5b)

Yellow liquid. IR (KBr) (ν_{max} , cm^{-1}): 3135, 2942, 1689. ^1H -NMR (CDCl_3 , 400 MHz): δ (ppm) 2.24 (3H, s, CH_3), 3.67 (3H, s, CH_3), 3.82 (3H, s, CH_3), 3.91 (2H, s, CH_2), 6.40 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$), 6.58 (2H, d, $J = 8.8$ Hz, ArH), 6.73-6.86 (4H, m, ArH), 7.38 (2H, d, $J = 8.8$ Hz, ArH), 7.73 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$). ^{13}C -NMR (100 MHz, CDCl_3) δ (ppm) 21.2, 39.1, 52.2, 56.0, 114.8(2C), 126.6, 126.9, 128.8(2C), 129.3(2C), 130.1(2C), 131.8, 132.9, 136.7, 136.8, 136.9, 161.5, 163.4. MS (ESI) 389.9 $[\text{M}+1]^+$. HRMS (ESI) calcd for $[\text{C}_{21}\text{H}_{21}\text{ClO}_3\text{S}]$: 388.9076; found: 388.9082.

(2Z,4Z)-Methyl-5-chloro-2-((4-chlorophenylthio)methyl)-5-(4-methoxyphenyl)penta-2,4-dienoate (5c)

Yellow liquid. IR (KBr) (ν_{max} , cm^{-1}): 3157, 2925, 1656. ^1H -NMR (CDCl_3 , 400 MHz): δ (ppm) 3.87 (3H, s,

*CH*₃), 3.90 (3H, s, *CH*₃), 3.95(2H, s, *CH*₂), 6.94 (1H, d, *J* = 11.2 Hz, *CH=CH*), 7.26-7.54 (8H, m, *ArH*), 7.7 7(1H, d, *J* = 11.2 Hz, *CH=CH*). ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 39.1, 52.1, 56.0, 114.8(2C), 126.5, 126.9, 128.9(2C), 129.3(2C), 131.6(2C), 131.8, 133.1, 134.3, 136.7, 136.9, 161.5, 163.4. MS (ESI) 410.2 [M+1]⁺. HRMS (ESI) calcd for [C₂₀H₁₈Cl₂O₃S]: 409.3261; found: 409.3269.

(2*E*,4*Z*)-Methyl-5-chloro-5-(4-methoxyphenyl)-2-(*p*-tolylamino)methyl)penta-2,4-dienoate (5d)

Yellow liquid. IR (KBr) (ν_{\max} , cm⁻¹): 3457, 3130, 2931, 1650. ¹H-NMR (CDCl₃, 400 MHz): δ (ppm) 2.21 (3H, s, *CH*₃), 3.60 (3H, s, *CH*₃), 3.84 (3H, s, *CH*₃), 4.14 (2H, s, *CH*₂), 6.48 (1H, d, *J* = 11.2 Hz, *CH=CH*), 6.65 (2H, d, *J* = 8.8 Hz, *ArH*), 6.73-6.80 (4H, m, *ArH*), 7.28 (2H, d, *J* = 8.8 Hz, *ArH*), 7.74 (1H, d, *J* = 11.2 Hz, *CH=CH*). ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 21.1, 41.8, 52.0, 56.0, 114.3(2C), 114.8(2C), 126.5, 126.7, 128.9(2C), 130.0(2C), 131.8, 135.1, 136.7, 140.7, 144.9, 161.5, 166.7. MS (ESI) 372.9 [M+1]⁺. HRMS (ESI) calcd for [C₂₁H₂₂ClNO₃]: 371.8573; found: 371.8564.

(2*E*,4*Z*)-Methyl-2-(azidomethyl)-5-chloro-5-(4-methoxyphenyl)penta-2,4-dienoate (5e)

Yellow liquid. IR (KBr) (ν_{\max} , cm⁻¹): 3154, 2922, 1956, 1658. ¹H-NMR (CDCl₃, 400 MHz): δ (ppm) 3.81 (3H, s, *CH*₃), 3.83 (3H, s, *CH*₃), 4.23 (2H, s, *CH*₂), 6.91-6.93 (2H, m, *ArH*), 7.01 (1H, d, *J* = 11.2 Hz, *CH=CH*), 7.77-7.80 (2H, m, *ArH*), 7.88 (1H, d, *J* = 11.2 Hz, *CH=CH*). ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 49.4, 52.0, 56.0, 114.8(2C), 126.5, 128.9(2C), 131.8, 135.8, 136.7, 138.1, 161.5, 167.2. MS (ESI) 308.7 [M+1]⁺. HRMS (ESI) calcd for [C₁₄H₁₄ClN₃O₃]: 307.7323; found: 307.7326.

(2*Z*,4*Z*)-Methyl-5-chloro-5-(4-fluorophenyl)-2-(*p*-tolylthiomethyl)penta-2,4-dienoate (5f)

Yellow liquid. IR (KBr) (ν_{\max} , cm⁻¹): 3149, 2933, 1641. ¹H-NMR (CDCl₃, 400 MHz): δ (ppm) 2.47 (3H, s, *CH*₃), 3.82 (3H, s, *CH*₃), 3.91 (2H, s, *CH*₂), 7.01 (1H, d, *J* = 11.2 Hz, *CH=CH*), 7.35-7.37 (4H, m, *ArH*), 7.49-7.83 (4H, m, *ArH*), 7.84 (1H, d, *J* = 11.2 Hz, *CH=CH*). ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 21.3, 32.1, 52.3, 115.4(2C), 119.8, 128.0(2C), 129.2(2C), 131.6, 131.7(2C), 133.1 (*J* = 61 Hz), 137.5, 140.3, 146.4, 147.9 (*J* = 37 Hz), 162.1, 167.2. MS (ESI) 377.9 [M+1]⁺. HRMS (ESI) calcd for [C₂₀H₁₈ClFO₂S]: 376.8721; found: 376.8719.

(2*Z*,4*Z*)-Methyl-5-chloro-2-((4-chlorophenylthio)methyl)-5-(4-fluorophenyl)penta-2,4-dienoate (5g)

Yellow liquid. IR (KBr) (ν_{\max} , cm⁻¹): 3174, 2934, 1689. ¹H-NMR (CDCl₃, 400 MHz): δ (ppm) 3.88 (3H, s, *CH*₃), 3.94 (2H, s, *CH*₂), 7.00 (1H, d, *J* = 11.2 Hz, *CH=CH*), 7.21-7.31 (4H, m, *ArH*), 7.47-7.63 (4H, m, *ArH*), 7.84 (1H, d, *J* = 11.2 Hz, *CH=CH*). ¹³C-NMR (100 MHz, CDCl₃) δ (ppm) 32.1, 52.3, 115.4(2C), 119.8, 128.0(2C), 129.0(2C), 130.7, 131.2(2C), 132.2 (*J* = 123 Hz), 134.5, 140.3, 146.3, 147.9 (*J* = 32 Hz), 162.1, 167.2. MS (ESI) 398.3 [M+1]⁺. HRMS (ESI) calcd for [C₁₉H₁₅Cl₂FO₂S]: 397.2906; found: 397.2914.

(2E,4Z)-Methyl-5-chloro-5-(4-fluorophenyl)-2-[(p-tolylamino)methyl]penta-2,4-dienoate (5h)

Yellow liquid. IR (KBr) (ν_{\max} , cm^{-1}): 3467, 3199, 2913, 1687. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ (ppm) 2.43 (3H, s, CH_3), 3.85 (3H, s, CH_3), 4.12 (2H, s, CH_2), 7.01 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$), 7.31-7.37 (4H, m, ArH), 7.64-7.74 (4H, m, ArH), 7.84 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm) 21.3, 48.5, 52.3, 113.4 (2C), 115.4 (2C), 119.8, 128.0 (2C), 129.6, 130.7 ($J = 180$ Hz, 2C), 134.4, 139.3, 144.6, 146.2, 147.9 ($J = 30$ Hz), 162.1, 167.1. MS (ESI) 360.8 $[\text{M}+1]^+$. HRMS (ESI) calcd for $[\text{C}_{20}\text{H}_{19}\text{ClFNO}_2]$: 359.8218; found: 359.8215.

(2E,4Z)-Methyl-2-(azidomethyl)-5-chloro-5-(4-fluorophenyl)penta-2,4-dienoate (5i)

Yellow liquid. IR (KBr) (ν_{\max} , cm^{-1}): 3145, 2911, 1949, 1662. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ (ppm) 3.84 (3H, s, CH_3), 4.22 (2H, s, CH_2), 7.01 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$), 7.13-7.18 (2H, m, ArH), 7.67-7.69 (2H, m, ArH), 7.87 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm) 49.4, 52.0, 115.0 (2C), 126.5, 130.9 ($J = 132$ Hz, 2C), 134.0, 136.3 ($J = 89$ Hz), 138.1, 141.6, 162.9 ($J = 101$ Hz), 167.2. MS (ESI) 296.7 $[\text{M}+1]^+$. HRMS (EI) calcd for $[\text{C}_{13}\text{H}_{11}\text{ClFN}_3\text{O}_2]$: 295.6967; found: 295.6959.

(2E,4Z)-Methyl-5-chloro-5-(4-chlorophenyl)-2-(hydroxymethyl)penta-2,4-dienoate (6)

Yellow liquid. IR (KBr) (ν_{\max} , cm^{-1}): 3644, 2953, 1648. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ (ppm) 3.87 (3H, s, CH_3), 4.51 (2H, s, CH_2), 7.09 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$), 7.09-7.41 (2H, m, ArH), 7.65-7.68 (2H, m, ArH), 7.89 (1H, d, $J = 11.2$ Hz, $\text{CH}=\text{CH}$). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ (ppm) 37.4, 52.5, 119.8, 123.7, 128.3 (2C), 128.9 (2C), 129.7, 130.7, 135.4, 136.5, 166.2. MS (ESI) 288.4 $[\text{M}+1]^+$. HRMS (ESI) calcd for $[\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{O}_3]$: 287.1386; found: 287.1380.

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