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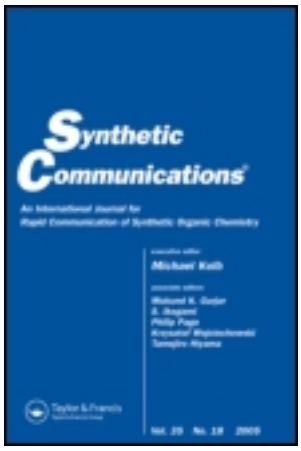

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# CHEMOSPECIFICITY IN ARYLATIONS OF δ- AND γ-KETOCARBOXYLIC ACIDS WITH $P_2O_5$-MsOH, TfOH, AND RELATED ACIDIC MEDIA

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# CHEMOSPECIFICITY IN ARYLATIONS OF δ- AND γ-KETOCARBOXYLIC ACIDS WITH $P_2O_5$–MsOH, TfOH, AND RELATED ACIDIC MEDIA

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## ABSTRACT

Remarkable contrast between chemospecificities in acid-mediated arylation of δ- and γ-ketocarboxylic acids was revealed: in the presence of $P_2O_5$–MsOH, TfOH, PPA, and MsOH, arylation of δ-ketocarboxylic acid **1A** with arenes takes place at the carboxycarbonyl carbon, while that of γ-ketocarboxylic acid **1B** takes place at the ketone carbonyl carbon, specifically.

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Electrophilic aromatic substitution of free carboxylic acids[1] using acidic medium such as PPA (polyphosphoric acid),[2] $P_2O_5$–MsOH (phosphorus pentoxide–methanesulfonic acid mixture),[3] MsOH,[4] and TfOH (triflic acid)[5] has attracted wide interest. In particular, TfOH-mediated aromatic substitution reactions have been widely investigated.[6] However, acid-promoted arylation of keto acids has been little known. Recently, we have revealed specific and chemoselective multi-α-arylation of α-alkoxy-[7a] and α-keto carboxylic acids.[7b]

In the course of this study, we happened to find the clear discrimination between regiospecificities in arylations of 5-ketohexanoic acid (δ-keto acid **1A**) and 4-ketopentanoic acid (γ-keto acid **1B**). There is no more than one carbon length difference between the two carboxylic acid substrates. However, the carbonyl carbons attacked by arenes were clearly distinguished. In this paper we report the striking contrast of chemospecific reaction behaviors in the acid-mediated arylations of δ-keto acid **1A** and γ-keto acid **1B**.

When acids **1A–B** were allowed to react with arenes in the presence of PPA, MsOH, $P_2O_5$–MsOH, and TfOH, δ-keto acid **1A** gave two types of products and γ-keto acid **1B** gave three types, respectively. That is, δ-keto acid **1A** yielded α,β-unsaturated cyclic ketones (cyclohexenones **3A**) and/or 1,5-diketones **4A**, while γ-keto acid **1B** yielded α,β-unsaturated cyclic ketones (cyclopentenones **3B**), γ-arylated phenones **5–7B**, and/or γ-lactones **8B** (Table 1). Among the products for the reactions of two keto acid substrates, only α,β-unsaturated cyclic ketones **3** (**3A** or **3B**) were observed in common.

In addition to the different reaction behaviors between the two keto acids, it was found that the product distributions varied drastically depending on the acidic medium used.

The $P_2O_5$–MsOH mediated arylation of δ-keto acid **1A** yielded cyclohexenones **3A** exclusively. On the other hand, the TfOH-mediated arylation of δ-keto acid **1A** gave 1,5-diketones **4A** solely. Still more, the arylation of δ-keto acid **1A** with PPA gave a mixture of compounds **3A** and **4A**, whereas that with MsOH yielded only cyclohexenones **3A** in a low yield.

The $P_2O_5$–MsOH mediated arylation of γ-keto acid **1B** efficiently produced cyclopentenones **3B**. At the same time, γ-arylated phenones **5–7Ba** were also obtained in the reaction with anisole (**2a**) and lactones **8** were produced in the reaction with bromoanisole (**2c**). On the contrary, the TfOH-mediated arylation of γ-keto acid **1B** yielded γ-lactones **8B** solely except for the reaction with toluene (**2b**). The arylation of γ-keto acid **1B** with PPA or MsOH gave a mixture of products **3B**, **5–7B**, and **8B**, depending on the kind of the arenes used.

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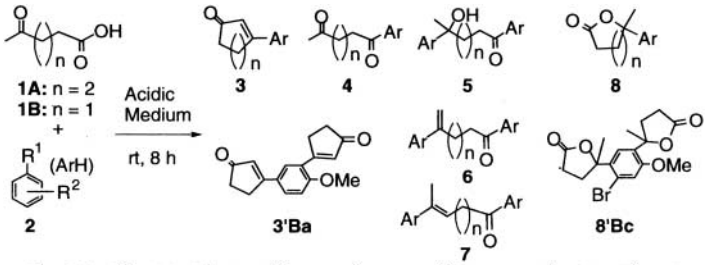
***Table 1.*** Reactions of δ- and γ-Keto Acid **1A–B** with Arenes **2a–e** in Several Acidic Media[a]




**a:** $R^1$ = OMe, $R^2$ = H; **b:** $R^1$ = Me, $R^2$ = H; **c:** $R^1$ = OMe, $R^2$ = *m*-Br; **d:** $R^1$ = OMe, $R^2$ = *o*-Br

| Substrate ArH | Product and Isolated Yield (%)[b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **1A** | | | | **1B** | | | |
| **2** | **3** | **4** | **5/6/7** | **8** | **3** | **4** | **5/6/7** | **8** |
| [$P_2O_5$-MsOH] | | | | | | | | |
| **2a** | 75 | 0 | 0/0/0 | 0 | 28[c] | 0 | 14/trace/trace | 0 |
| **2a**[d] | – | – | –/–/– | – | 49[e] | 0 | 11/11/23 | 0 |
| **2b** | 10 | 0 | 0/0/0 | 0 | 51 | 0 | 0/0/0 | 0 |
| **2c** | 69[f] | 0 | 0/0/0 | 0 | 51[g] | 0 | 0/0/0 | 29[h] |
| **2d** | 48 | 0 | 0/0/0 | 0 | 86 | 0 | 0/0/0 | 0 |
| [TfOH] | | | | | | | | |
| **2a** | 0 | 77 | 0/0/0 | 0 | 0 | 0 | 0/0/0 | 81 |
| **2b** | 0 | 81 | 0/0/0 | 0 | 0 | 0 | 0/0/0 | –[i] |
| **2c** | 0 | 68[j] | 0/0/0 | 0 | 0 | 0 | 0/0/0 | 84[k] |
| **2d** | 0 | 55 | 0/0/0 | 0 | 0 | 0 | 0/0/0 | 46 |
| [Polyphosphoric acid (PPA)] | | | | | | | | |
| **2a** | 23 | 25 | 0/0/0 | 0 | 23 | 0 | 50/0/0 | 0 |
| **2b** | 3 | 4 | 0/0/0 | 0 | 3 | 0 | 0/0/0 | 11 |
| [MsOH] | | | | | | | | |
| **2a** | 23 | 0 | 0/0/0 | 0 | 0 | 0 | 34/17/17 | 0 |
| **2b** | trace | 0 | 0/0/0 | 0 | 0 | 0 | 0/0/0 | 28[l] |

[a]Reaction conditions: keto acid 1 mmol, acidic medium 2 mL, arene 1 mmol, r.t., 8 h; [b]Yield based on the keto acid; [c]The yields of cyclopentenones **3Ba** and disubstituted arene **3′Ba** were 11 and 17%, respectively; [d]r.t., 24 h; [e]The yields of cyclopentenone **3Ba** and **3′Ba** were 36% and 13%, respectively; [f]*p*-Substituted product against methoxy group/*o*-substituted product against methoxy group = 42/24; [g]*p*-Substituted product against methoxy group/*o*-substituted product against methoxy group = 17/34; [h]*p*-Substituted product against methoxy group/*o*-substituted product against methoxy group = 13/16; [i]Unidentified products were obtained; [j]*p*-Substituted product against methoxy group/*o*-substituted product against methoxy group = 23/45; [k]The yields of lactones **8Bc** and disubstituted arene **8′Bc** were 42% (*p*-substituted lactone against methoxy group/*o*-substituted lactone against methoxy group = 19/23) and 42%, respectively; [l]The yields of lactones **8Bc** and disubstitued arene **8′Bc** were 7 and 21%, respectively.

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By comparing the structure of keto acids **1A–B** with products **4** and **8**, it is obvious that diketones **4** were formed through arylation at the carboxy carbon of δ-keto acid **1A** and that lactones **8** were produced through arylation at the γ-keto carbonyl carbon of acid **1B**. However, in case that α,β-unsaturated cyclic ketones **3A–B** and γ-arylated phenones **5–7** were obtained, whether the initial arylation occurred at the carboxy carbon or at the keto carbonyl carbon was still ambiguous.

On the basis of the reaction behavior, 1,5-diketones **4A** are considered to be the intermediates for the formation of cyclohexenones **3A** from δ-keto acid **1A**. The reasons are as follows: (1) diketones **4A** were obtained when δ-keto acid **1A** and arenes **2** were treated with TfOH or PPA, (2) δ-lactones **8A** were not isolated from any of the reaction mixtures of δ-keto acid **1A**, and 3) diketones **4A** were quantitatively converted into cyclohexenones **3A** when they were allowed to react in $P_2O_5$–MsOH or MsOH.

Accordingly, cyclohexenones **3A** are proved to be formed via Friedel–Crafts type acylation of δ-keto acid **1A** to arenes **2** followed by intramolecular aldol condensation of the resulting diketones (**4A**) (**4A→9→3A**).

On the other hand, γ-lactones **8B** or the ring-opened equivalents of γ-lactones **8B** are ascertained to be the intermediates for the formation of both cyclopentenones **3B** and γ-arylated phenones **5–7B** from γ-keto acid **1B**, on the basis of the following results: (1) every homologue of lactone **8B** corresponding to each arene used was isolated, (2) 1,4-diketones **4B** were not isolated from any of the reaction mixture of γ-keto acid **1B**, (3) lactones **8B** were quantitatively converted into cyclopentenones **3B** when lactones **8B** were allowed to react in $P_2O_5$–MsOH, and (4) when lactone **8Ba** was allowed to react with anisole (**2a**) in $P_2O_5$–MsOH, γ-arylated phenones **5–7Ba** were produced.

In consequence, cyclopentenones **3B** are ascertained to be produced via γ-arylated of acid **1B** to give intermediates **11** or lactones **8B** followed by conversion to olefins **12** and intramolecular acylation of olefins **12**. γ-Arylated intermediate **11** or lactone **8b** also yielded γ-arylated phenones **5–7B** via intermolecular Friedel–Crafts type acylation. γ-Arylated intermediate **11** would be converted to lactone **8** through cyclization during work-up process.

The results described above show that the initial arylations of δ- and γ-keto acids **1A–B** occur at the different carbonyl groups chemospecifically (Sch. 1). The arylation of δ-keto acid **1A** progress at the carboxy carbon, whereas the initial arylation of γ-keto acid **1B** proceeds at the keto carbonyl carbon, respectively.

The specificity in the arylation of δ- and γ-keto acids **1A–B** is rationally explained by the existence of different types of stable intermediates at the early stages (Sch. 2). The initial stable intermediate in the

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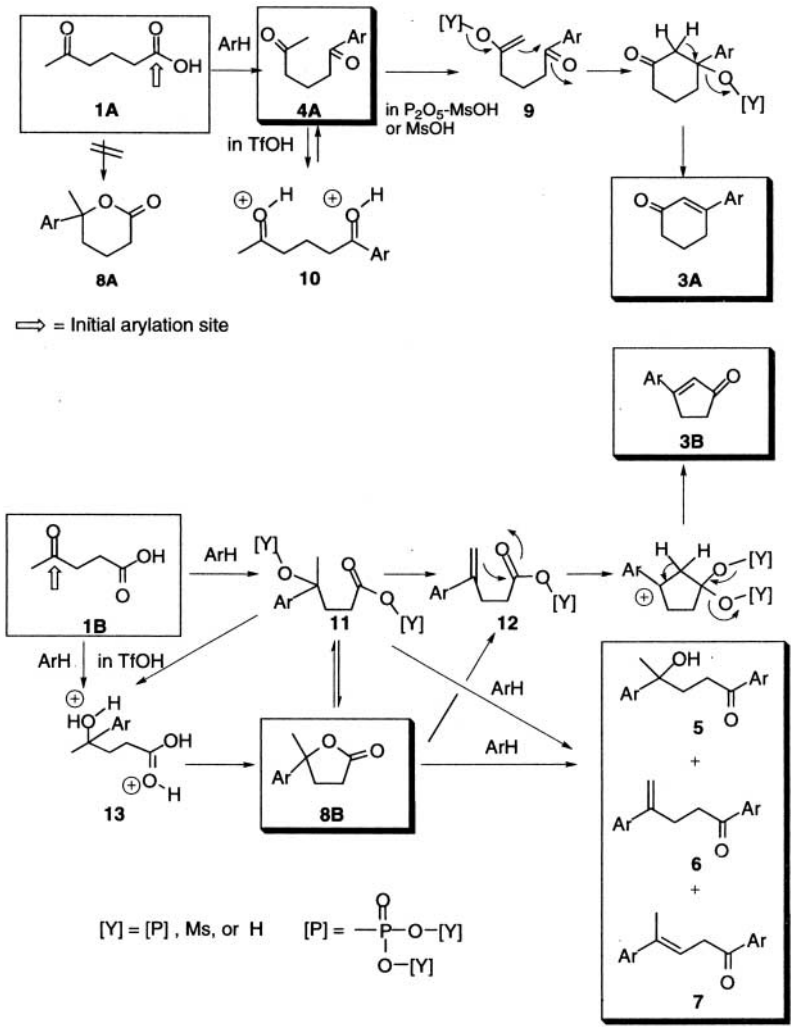


***Scheme 1.*** Plausible reaction mechanism in these reactions.

reaction of δ-keto acid **1A** is assumed to be an open-chain acylium ion equivalent (**1A′**), whereas that in the reaction γ-keto acid **1B** is suspected to be a cyclic oxonium ion equivalent (**1B′**).[8,9]

In this relation, acidic medium dependence in the reactions is interpreted as follows: formation of α,β-unsaturated cyclic ketones **3A** depends on the tendency for the intermediate, 1,5-diketones **4A**, toward

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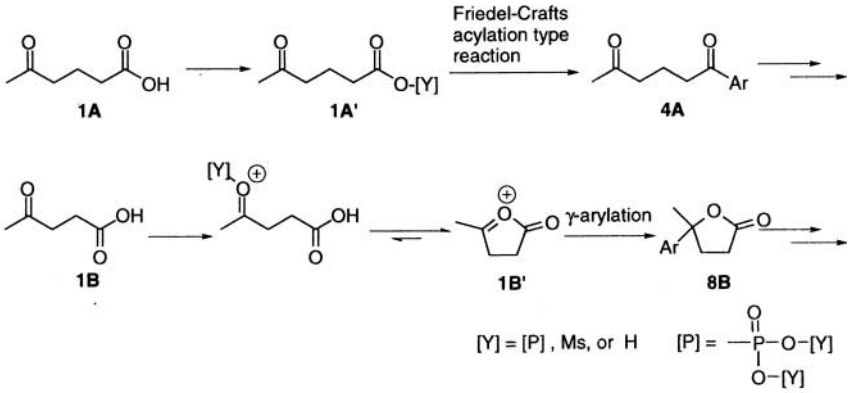


***Scheme 2.*** Difference between δ-keto acid **1A** and γ-keto acid **1B** in this reaction.

cyclizaiton. For the acid-mediated cyclization, enolization of diketones **4A** to intermediate **9** is needed. The exclusive formation of diketones **4A** in TfOH is supposed to be due to the predominant stability of the doubly protonated ketones (**10**) in such 'super acidic' circumstances.[6,10] Consequently, the repulsion of dication intermediates **10** should prevent further intramolecular reactions such as cyclization to give ketones **3A** in TfOH.

In the reaction γ-keto acid **1B**, lactone equivalents **11** are formed at the early stage owing to the equilibrium shown in Sch. 2. The selectivity is interpreted based on the relative susceptibilities of activated species formed from lactones **8** or their equivalents **11**. Then, these active intermediates cause further two types of reactions: one is the Friedel–Crafts type acylation (formation of compounds **5–7B**), and the other is olefin formation (olefin **12**), when arenes **2** have enough reactivities for ketone formation, diarylated compounds **5–7B** are formed. When reaction media have sufficient capability for formation of olefin **12**, simultaneous ring-closure reaction propagates (**12**→**3B**). On the other hand, γ-lactones **8B** are supposed to be stable enough to suppress further transformation in TfOH. Thus, the intermediates in TfOH are considered to exist as dication forms such as intermediates **13**.[6] Consequently, cyclization of dications **13** to lactones **8B** is supposed to be suppressed till aqueous work-up process.[11]

In conclusion, we examined the various reactions of δ- and γ-keto acids with several arenes in some acidic media such as $P_2O_5$–MsOH, PPA, MsOH, and TfOH. When δ-keto acid **1A** was treated with arenes, compounds **3A** and **4A** were mainly obtained. On the other hand, when γ-keto acid **1B** was treated with arenes, compounds **3B**, **5–7B**, and **8** were

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mainly obtained. Investigation on by-products distribution, it was cleared that arylation to δ- and γ-keto acids occurs at the different carbonyl carbons, carboxy carbon or ketone carbon, respectively. The observed discrimination in the reaction of these keto acids suggests a hitherto unclarified intramolecular effect in oxonium ion intermediate generated by strong to super acidic media.

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## EXPERIMENTAL

**General:** $^1$H and $^{13}$C NMR spectra were recorded on a JEOL JNM-A500 ($^1$H; 500 MHz, $^{13}$C; 125 MHz) spectrometer or a JEOL FX-200 ($^1$H; 200 MHz) spectrometer using $Me_4Si$ ($^1$H, δ 0.00) and $CDCl_2$ ($^{13}$C, δ 77.0) as internal standards. IR spectra were recorded on a JASCO FTIR-5300 spectrometer. $P_2O_5$-MeOH was prepared by stirring a 1/10 (w/w) mixture of $P_2O_5$ and MsOH at r.t. according to the method in literature.[3] Preparative TLC was performed using WAKO Wakogel B-5F. Column chromatography was performed using Merck silica gel 60-5B (particle size 0.063–0.200 mm).

**Typical reaction procedure for reaction of δ-and γ-keto acids 1A-B in acidic media: Reaction of δ-keto acid 1A with anisole (2a) in $P_2O_5$–MsOH:** $P_2O_5$–MsOH (2 mL) was added to an ice-cooled mixture of acid **1A** (130 mg, 1.0 mmol) with anisole (**2a**, 108 mg, 1.0 mmol) under vigorous stirring. The mixture was stirred at the prescribed temperature and for the prescribed time interval. Then the mixture was poured into ice water. The aqueous solution was extracted with chloroform (50 mL × 2). The combined organic layer was washed with saturated aqueous NaCl solution, dried over $MgSO_4$ overnight, and concentrated under reduced pressure. The residue was purified by preparative TLC to give 3-(4-methoxyphenyl)-2-cyclohexenone (**3Aa**).

**3-(4-Methoxyphenyl)-2-cyclohexenone (3Aa):**[12] $^1$H NMR ($CDCl_3$) $\delta$ 2.08–2.20 (2H, m), 2.48 (2H, t, $J = 6$ Hz), 2.70–2.80 (2H, m), 3.85 (3H, s), 6.43 (1H, t, $J = 2$ Hz), 6.95 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz), 7.54 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.6, 27.7, 37.0, 55.3, 114.2, 124.8, 127.7, 130.9, 159.3, 161.4, 200.0 ppm; IR (KBr) 1647 cm$^{-1}$.

**3-(4-Methylphenyl)-2-cyclohexenone (3Ab):**[13] $^1$H NMR ($CDCl_3$) $\delta$ 2.09–2.20 (2H, m), 2.39 (3H, s), 2.49 (2H, t, $J = 6$ Hz), 2.70–2.80 (2H, m), 6.41 (1H, t, $J = 2$ Hz), 7.22 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz), 7.46 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.2, 21.5, 29.8, 37.2, 42.5, 128.0, 129.2, 143.7, 158.7, 199.2, 208.3 ppm; IR (KBr) 1711, 1672 cm$^{-1}$.

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**3-(2-Bromo-4-methoxyphenyl)-2-cyclohexenone and 3-(4-bromo-2-methoxyphenyl)-2-cyclohexenone (3Ac):** These compounds were obtained as an inseparable mixture of regioisomers; IR (KBr) 1647, 1670 $cm^{-1}$. $^1$H-NMR signals are shown below.

**3-(4-Bromo-2-methoxyphenyl)-2-cyclohexenone:** $^1$H NMR ($CDCl_3$) $\delta$ 2.01–2.20 (2H, m), 2.43–2.51 (2H, m), 2.60–2.70 (2H, m), 3.81 (3H, s), 6.18 (1H, s), 6.84 (1H, d, $J = 2$ Hz), 7.01–7.20 (2H, m) ppm.

**3-(2-Bromo-4-methoxyphenyl)-2-cyclohexenone:** $^1$H NMR ($CDCl_3$) $\delta$ 2.01–2.20 (2H, m), 2.43–2.51 (2H, m), 2.60–2.70 (2H, m), 3.83 (3H, s), 6.00 (1H, s), 6.90 (1H, d, $J = 2$ Hz), 7.01–7.20 (2H, m) ppm.

**3-(3-Bromo-4-methoxyphenyl)-2-cyclohexenone (3Ad):** $^1$H NMR ($CDCl_3$) $\delta$ 2.02–2.24 (2H, m), 2.50 (2H, t, $J = 6$ Hz), 2.65–2.79 (2H, m), 3.93 (3H, s), 6.35–6.39 (1H, m), 6.93 (1H, d, $J = 9$ Hz), 7.50 (1H, dd, $J = 2$, 9 Hz), 7.75 (1H, d, $J = 2$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.6, 27.8, 37.1, 56.3, 111.7, 112.1, 124.5, 126.5, 131.2, 132.2, 157.2, 157.6, 199.6 ppm; IR (KBr) 1653 $cm^{-1}$.

**3-(4-Methoxyphenyl)-2-cyclopentenone (3Ba):**[14] $^1$H NMR ($CDCl_3$) $\delta$ 2.54–2.61 (2H, m), 2.98–3.06 (2H, m), 3.89 (3H, s), 6.49 (1H, t, $J = 2$ Hz), 6.95 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz), 7.63 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 28.4, 35.0, 55.0, 114.0, 125.1, 126.5, 128.3, 161.9, 173.6, 209.1 ppm; IR (KBr) 1672 $cm^{-1}$.

**3-(4-Methylphenyl)-2-cyclopentenone (3Bb):** $^1$H NMR ($CDCl_3$) $\delta$ 2.39 (3H, s), 2.52–2.57 (2H, m), 2.96–3.02 (2H, m), 6.51 (1H, t, $J = 2$ Hz), 7.23 (2H, pseudo d of AA′BB′ pattern, $J = 8$ Hz), 7.53 (2H, pseudo d of AA′BB′ pattern, $J = 8$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 20.4, 28.5, 35.1, 126.3, 126.8, 129.5, 131.1, 142.9, 174.0, 209.1 ppm; IR (KBr) 1674 $cm^{-1}$.

**3-(2-Bromo-4-methoxyphenyl)-2-cyclopentenone and 3-(4-Bromo-2-methoxyphenyl)-2-cyclopentenone (3Bc):** These compounds were obtained as an inseparable mixture of regioisomers; IR (KBr) 1672 $cm^{-1}$. $^1$H-NMR signals are shown below.

**3-(2-Bromo-4-methoxyphenyl)-2-cyclopentenone:** $^1$H NMR ($CDCl_3$) $\delta$ 2.54–2.64 (2H, m), 2.95–3.05 (2H, m), 3.96 (3H, s), 6.49 (1H, t, $J = 2$ Hz), 6.96 (1H, d, $J = 8$ Hz), 7.62 (1H, dd, $J = 8$, 2 Hz), 7.86 (1H, d, $J = 2$ Hz) ppm.

**3-(4-Bromo-2-methoxyphenyl)-2-cyclopentenone:** $^1$H NMR ($CDCl_3$) $\delta$ 2.42–2.53 (2H, m), 3.00–3.08 (2H, m), 3.93 (3H, s), 6.87 (1H, t, $J = 2$ Hz), 7.12 (1H, d, $J = 8$ Hz), 7.16 (1H, dd, $J = 8$, 2 Hz), 7.37 (1H, d, $J = 8$ Hz) ppm.

**3-(3-Bromo-4-methoxyphenyl)-2-cyclopentenone (3Bd):** $^1$H NMR ($CDCl_3$) δ 2.54–2.64 (2H, m), 2.95–3.05 (2H, m), 3.96 (3H, s), 6.49 (1H, t, $J = 2$ Hz), 6.96 (1H, d, $J = 8$ Hz), 7.62 (1H, dd, $J = 8$, 2 Hz), 7.86

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(1H, d, $J = 2$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 28.6, 35.2, 56.4, 111.7, 112.3, 126.5, 127.5, 128.1, 131.9, 158.1, 171.9, 208.8 ppm; IR (KBr) 1674 $cm^{-1}$.

**2,4-*Bis*(3-oxo-1-cyclopentenyl)anisole (3′Ba):** $^1$H NMR ($CDCl_3$) $\delta$ 2.44–2.63 (4H, m), 3.00–3.18 (4H, m), 3.95 (3H, s), 6.51 (1H, s), 6.89 (1H, s), 7.08 (1H, d, $J = 8$ Hz), 7.75 (1H, d, $J = 8$ Hz), 7.80 (1H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 28.5, 30.0, 34.0, 35.0, 55.5, 111.2, 123.3, 126.0, 126.5, 123.0, 130.1, 132.0, 160.3, 168.3, 172.0, 208.5, 210.0 ppm; IR (KBr) 1684 $cm^{-1}$.

**1-(4-Methoxyphenyl)-1,5-hexanedione (4Aa):** $^1$H NMR ($CDCl_3$) $\delta$ 1.90–2.09 (2H, m), 2.16 (3H, s), 2.58 (2H, t, $J = 7$ Hz), 2.97 (2H, t, $J = 7$ Hz), 3.88 (3H, s), 6.94 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz), 7.96 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.3, 29.8, 36.9, 42.5, 55.3, 113.6, 129.8, 130.0, 163.3, 198.1, 208.3 ppm; IR (KBr) 1709, 1669 $cm^{-1}$.

**1-(4-Methylphenyl)-1,5-hexanedione (4Ab):** $^1$H NMR ($CDCl_3$) $\delta$ 1.90–2.09 (2H, m), 2.16 (3H, s), 2.40 (3H, s), 2.57 (2H, t, $J = 7$ Hz), 2.99 (2H, t, $J = 7$ Hz), 7.26 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz), 7.87 (2H, pseudo dd of AA′BB′ pattern, $J = 8$, 2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.2, 22.7, 27.9, 37.2, 124.6, 125.9, 129.4, 135.7, 140.3, 159.4, 199.8 ppm; IR (KBr) 1661 $cm^{-1}$.

**1-(2-Bromo-4-methoxyphenyl)-1,5-hexanedione (4Ac):** $^1$H NMR ($CDCl_3$) $\delta$ 1.91–2.08 (2H, m), 2.17 (3H, s), 2.55 (2H, t, $J = 7$ Hz), 2.98 (2H, t, $J = 7$ Hz), 3.97 (3H, s), 6.86 (1H, dd, $J = 3$, 9 Hz), 7.13 (1H, d, $J = 3$ Hz), 7.49 (1H, d, $J = 9$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.4, 29.9, 40.8, 42.4, 55.7, 113.1, 119.5, 120.8, 130.8, 132.6, 161.6, 201.5, 208.5 ppm; IR (KBr) 1713, 1682 $cm^{-1}$.

**1-(4-Bromo-2-methoxyphenyl)-1,5-hexanedione (4Ac′):** $^1$H NMR ($CDCl_3$) $\delta$ 1.87–2.04 (2H, m), 2.16 (3H, s), 2.53 (2H, t, $J = 7$ Hz), 2.98 (2H, t, $J = 7$ Hz), 3.90 (3H, s), 7.09–7.20 (2H, m), 7.58 (1H, d, $J = 8$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.2, 29.9, 42.5, 42.7, 55.8, 115.1, 123.9, 126.8, 127.6, 131.5, 158.9, 200.7, 208.6 ppm; IR (KBr) 1713, 1670 $cm^{-1}$.

**1-(3-Bromo-4-methoxyphenyl)-1,5-hexanedione (4Ad):** $^1$H NMR ($CDCl_3$) $\delta$ 1.87–2.07 (2H, m), 2.16 (3H, s), 2.57 (2H, t, $J = 7$ Hz), 2.95 (2H, t, $J = 7$ Hz), 3.96 (3H, s), 6.95 (1H, d, $J = 9$ Hz), 7.91 (1H, dd, $J = 2$, 9 Hz), 8.16 (1H, d, $J = 2$ Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.0, 29.7, 42.3, 56.2, 56.3, 110.9, 111.7, 129.0, 130.6, 133.2, 159.3, 197.0, 208.2 ppm; IR (KBr) 1715, 1672 $cm^{-1}$.

**4-Hydroxy-1,4-*bis*(4-methoxyphenyl)pentanal (5Ba):** $^1$H NMR ($CDCl_3$) $\delta$ 1.60 (3H, s), 2.20–2.30 (2H, m), 2.82–2.97 (2H, m), 3.80 (3H, s), 3.85 (3H, s), 6.88 (4H, dd, $J = 8$, 2 Hz), 7.33–7.46 (2H, m), 7.87 (2H, dd, $J = 8$, 2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 31.5, 33.7, 38.2, 55.4, 55.7, 74.0, 113.7, 113.8, 126.3, 130.1, 130.6, 139.8, 158.4, 163.7, 200.0 ppm; IR (KBr) 1674 $cm^{-1}$.

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**1,4-*Bis*(4-methoxyphenyl)-4-penten-1-one (6Ba) and 1,4-*bis*(4-methoxyphenyl)-3-penten-1-one (7Ba):** These compounds were obtained as an inseparable mixture of isomers; IR (KBr) 1676, 1672 $cm^{-1}$. $^1H$ NMR signals are shown below.

**1,4-*Bis*(4-methoxyphenyl)-4-penten-1-one (6Ba):** $^1H$ NMR ($CDCl_3$) $\delta$ 2.83–3.16 (4H, m), 3.81 (3H, s), 3.85 (3H, s), 5.04 (1H, s), 5.25 (1H, s), 6.78–7.02 (4H, m), 7.38 (2H, dd, $J = 8$, 2 Hz), 7.90 (2H, dd, $J = 8$, 2 Hz) ppm.

**1,4-*Bis*(4-methoxyphenyl)-3-penten-1-one (7Ba):** $^1H$ NMR ($CDCl_3$) $\delta$ 2.11 (3H, d, $J = 1$ Hz), 3.79 (3H, s), 3.80–3.90 (5H, m), 5.95–6.09 (1H, m), 6.78–7.02 (4H, m), 7.37 (2H, dd, $J = 8$, 2 Hz), 7.99 (2H, dd, $J = 8$, 2 Hz) ppm.

**5-(4-Methoxyphenyl)-γ-valerolactone (8Ba):**[15] $^1H$ NMR ($CDCl_3$) $\delta$ 1.68 (3H, s), 2.27–2.75 (4H, m), 3.80 (3H, s), 6.89 (2H, d, $J = 8$ Hz), 7.28 (2H, d, $J = 8$ Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 28.9, 29.3, 36.0, 55.1, 86.9, 113.7, 125.3, 136.2, 158.9, 176.6 ppm; IR (KBr) 1772 $cm^{-1}$.

**5-(4-Methylphenyl)-γ-valerolactone (8Bb):**[16] $^1H$ NMR ($CDCl_3$) $\delta$ 1.70 (3H, s), 2.34 (3H, s), 2.34–2.76 (4H, m), 7.17–7.27 (4H, m) ppm; IR (KBr) 1779 $cm^{-1}$.

**5-(2-Bromo-4-methoxyphenyl)-γ-valerolactone and 5-(4-bromo-2-methoxyphenyl)-γ-valerolactone (8Bc):** These compounds were obtained as an inseparable mixture of isomers (19 : 23); IR (KBr) 1778 $cm^{-1}$. $^1H$ NMR signals are shown below.

**5-(2-Bromo-4-methoxyphenyl)-γ-valerolactone:** $^1H$ NMR ($CDCl_3$) $\delta$ 1.71 (3H, s), 2.36–2.67 (4H, m), 3.87 (3H, s), 7.05 (1H, d, $J = 2$ Hz), 7.10 (1H, dd, $J = 2$, 8 Hz), 7.34 (1H, d, $J = 8$ Hz) ppm.

**5-(4-Bromo-2-methoxyphenyl)-γ-valerolactone:** $^1H$ NMR ($CDCl_3$) $\delta$ 1.85 (3H, s), 2.49–2.85 (4H, m), 3.79 (3H, s), 6.85 (1H, dd, $J = 3$, 9 Hz), 7.18 (1H, d, $J = 3$ Hz), 7.57 (1H, d, $J = 9$ Hz) ppm.

**5-(3-Bromo-4-methoxyphenyl)-γ-valerolactone (8Bd):** $^1H$ NMR ($CDCl_3$) $\delta$ 1.71 (3H, s), 2.28–2.75 (4H, m), 3.90 (3H, s), 6.89 (1H, d, $J = 8$ Hz), 7.30 (1H, dd, $J = 2$, 8 Hz), 7.55 (1H, d, $J = 2$ Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 28.9, 29.3, 36.0, 56.2, 86.1, 111.7, 111.7, 124.3, 129.3, 137.7, 155.2, 176.2 ppm; IR (KBr) 1765 $cm^{-1}$.

**5-Bromo-2,4-*bis*(5-methyl-2-oxo-5-tetrahydrofuranyl)anisole (8′Bc):** This compound was obtained as an inseparable mixture of diastereomers. $^1H$ NMR ($CDCl_3$) $\delta$ 1.75 (3H, pseudo d, $J = 2$ Hz), 1.83 (3H, pseudo d, $J = 2$ Hz), 2.40–2.78 (8H, m), 3.88 (3H, pseudo s), 7.15 (1H, pseudo s), 7.69 (1H, pseudo d, $J = 4$ Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 26.7, 27.0, 28.7, 28.8, 34.0, 34.4, 55.8, 85.7, 85.8, 86.9, 87.0, 118.0, 118.1, 119.2, 123.9, 128.2, 131.5, 131.6, 134.7, 155.2, 155.3, 175.7, 176.2 ppm; IR (KBr) 1772 $cm^{-1}$.

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