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A Simple 1,5 → 1,3-Diketone Rearrangement

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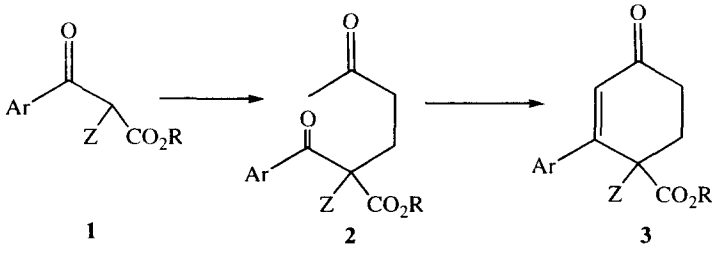
Abstract: 1-Aryl-1,3-diketones **4-7** were prepared by reaction of the corresponding 1-aryl-1,5-diketones **2b** with piperidinium acetate in refluxing C_6H_6. © 1998 Published by Elsevier Science Ltd. All rights reserved.

The construction of 2-cyclohexenones by the Michael addition of ketoactivated nucleophiles to methylvinyl ketone (MVK), followed by an intramolecular aldol-dehydration reaction of the intermediate 1,5 diketone, is a widely used method in organic synthesis (the Robinson annulation reaction).[2] The intramolecular aldol-dehydration step can be performed with dilute aqueous bases such as NaOH, but in some cases, the nearly neutral conditions of carboxylate salts of secondary amines (e.g. piperidinium or pyrrolidinium acetates) are advantageous.[3]

In a research which is currently underway in our laboratory, we required a series of 3-aryl-4,4-dialkoxycarbonyl-2-cyclohexenones **3b**. It has been reported[4] that the Robinson annulation of aroylacetates **1a** with MVK affords 2-cyclohexenones **3a** in good yields (scheme 1):

Scheme 1



a : Z = H

b : Z = CO_2R

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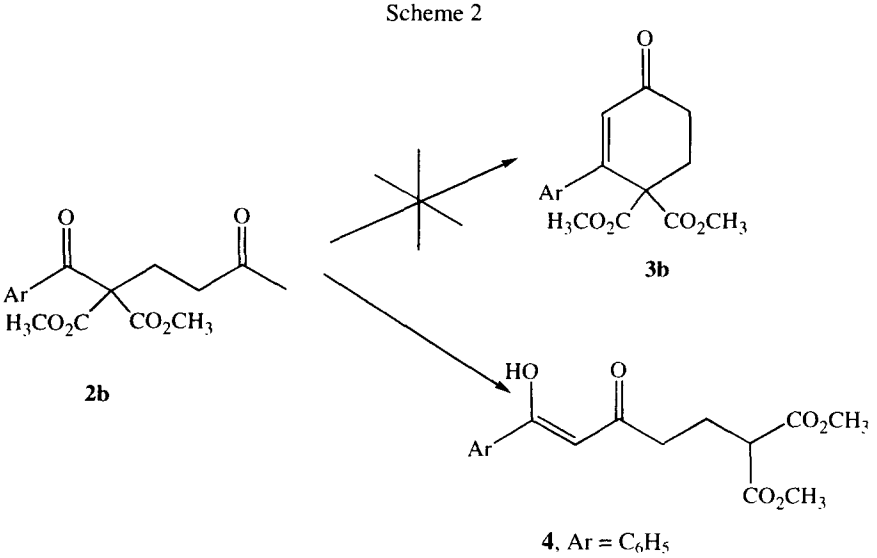
Hence, a logical extension of this route but applied to the aroylmalonates **1b**, in principle should fulfill our requirements.

The starting materials **1b** were prepared by C-benzoylation of the dimethyl malonate anion (NaH in THF) with the corresponding benzoyl chlorides (61-87 %). The Michael addition of the aroylmalonates **1b** to MVK proceeded without any incident in the presence of Triton B or Et_3N in THF, yielding the 1,5 diketones **2b** (64-80%). In order to avoid the base hydrolysis of the ester groups, we chose piperidinium acetate in refluxing C_6H_6 (24 h), as the catalyst to induce the intramolecular aldolization-dehydration reaction of **2b**. To our surprise, the products thus obtained in 50-60% yields were not the expected 2-cyclohexenones **3b**, but the strongly enolic ($FeCl_3$ test : red) 1,3-diketone malonates **4 - 7** (scheme 2):

Scheme 2



4, Ar = C_6H_5

5, Ar = p-BrC_6H_4

6, Ar = p-$NO_2C_6H_4$

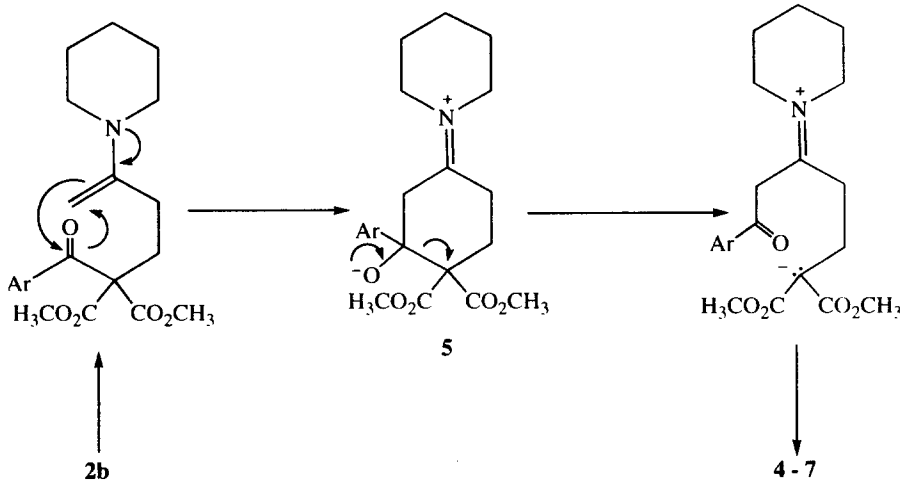
7, Ar = p-$OCH_3C_6H_4$

In the ^{1}H-NMR spectra, compounds **4-7** showed singlets at δ 15.88-16.10 (broad, enolic OH), 6.10-6.28 (vinyl H) and 3.75 (6H, 2 CO_2CH_3). The triplets at δ 3.50-3.52 (1H, J = 7.2-7.5 Hz) and 2.45-2.55 (2H, J= 7.1-8.0 Hz) have been assigned to the CH and CH_2-C=O groups, respectively.[5]

^{13}C-NMR spectra and EIMS were also in accord with the proposed structures and were further corroborated by appropriate DEPT, COSY, and HETCOR experiments.[6]

The formation of compounds **4-7** from **2b** can be explained as outlined in scheme 3 and involves a retroaldol type reaction in intermediate **5**. Undoubtedly, departure of the delocalized malonate anion is the driving force for this C-C bond cleavage.

Scheme 3



The reaction described herein is interesting both from mechanistic and preparative points of view, and the structural features of compounds **4-7** suggest their use as versatile synthetic intermediates.

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1. To whom correspondence should be addressed. Contribution No. 1637 of Instituto de Química.
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3. a) Nielsen, A. J.; Houlihan, W. J., *The Aldol Condensation* in : *Org. React.* **1968,** *16.* b) Plieninger, H.; Suchiro, T. *Chem. Ber.* **1956**, *89*, 2789.
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5. We have preferred enolization of the 1,3 diketone moiety as shown in **4-7**, based on the expected ^{1}H-NMR low field chemical shift for the CH_2-C=O as compared with CH_2-C=CH (the alternative enol).
6. Spectroscopic data for **4-7** are :

   Dimethyl 2-(3,5-dioxo-5-phenylpentyl) malonate 4: mp 40-42 °C; IR (KBr) ν (cm^{-1}) : 3460 (w, broad), 2958 (w), 1745 (s), 1604 (s), 1572 (s); ^{1}H-NMR δ (ppm) : 16.0 (broad s, 1H, OH enol), 7.88-7.84 (m, 2H,

o- H), 7.48-7.44 (m, 3H, m- and p- H), 6.16 (s, 1H, C***H***=COH), 3.75 (s, 6H, C***H***$_3$OCO), 3.51 (t, 1H, J =7.26 Hz, C***H***(COOCH$_3$)$_2$), 2.58-2.50 (t, 2H, COC***H***$_2$), 2.35-2.24 (q, 2H, COCH$_2$C***H***$_2$); ^{13}C-NMR δ (ppm) : 195.5 (***C***O), 182.61 (=***C***-OH), 169.40 (***C***OOCH$_3$), 134.57 (C ipso), 132.38 (p- C), 128.64 (m- C), 126.98 (o- C), 96.25 (=***C***H enol), 52.64 (***C***H$_3$OOC), 50.62 (***C***H(COOCH$_3$)$_2$), 36.44 (CO***C***H$_2$), 24.29 (COCH$_2$***C***H$_2$); MS (EI) m/e : M$^+$ 306, 288, 187, 175, 147, 105 (100 %).

Dimethyl 2-[5-(4-nitrophenyl)-3,5-dioxopentyl] malonate 5: mp 66-68 °C; IR (KBr) ν (cm^{-1}) : 3111(w), 2954(m), 1732(s), 1607(s), 1520(s), 1346(s); ^{1}H-NMR δ (ppm) : 8.28-8.33 (d, 9.04 Hz, 2H, m- H), 8.02-8.07 (d, 2H, 9.04 Hz, o- H), 6.28 (s, 1H, C***H***=COH), 3.76 (s, 6H, C***H***$_3$OCO), 3.52 (t, 1H, J =7.3 Hz, C***H***(COOCH$_3$)$_2$), 2.62-2.52 (t, 2H, COC***H***$_2$), 2.33-2.26 (q, 2H, COCH$_2$C***H***$_2$); ^{13}C-NMR δ (ppm) : 197.75 (***C***O), 177.10 (=***C***-OH), 168.71 (***C***OOCH$_3$), 149.16 (C-NO$_2$), 139.41 (C ipso), 127.31 (o- C), 123.21 (m-C), 97.20 (=***C***H enol), 52.06 (***C***H(COOCH$_3$)$_2$), 49.87 (***C***H$_3$OOC), 36.45 (CO***C***H$_2$), 23.26 (COCH$_2$***C***H$_2$); MS (EI) m/e : M$^+$ 351, 220, 192, 150 (100 %).

Dimethyl 2-[5-(4-bromophenyl)-3,5-dioxopentyl] malonate 6: mp 60-62 °C; IR (KBr) ν (cm^{-1}) 3445 (w, broad), 2961 (w), 2902 (w), 1752 (s),1733(s), 1615 (s); ^{1}H-NMR δ (ppm) : 15.88 (broad s, 1H, OH enol), 7.71-7.75 (d, 8.7 Hz, 2H, o- H), 7.57 -7.60 (d, 2H, 8.7 Hz, m- H), 6.12 (s, 1H, C***H***=COH), 3.76 (s, 6H, C***H***$_3$OCO), 3.50 (t, 1H, J =7.5 Hz, C***H***(COOCH$_3$)$_2$), 2.56-2.51 (t, 2H, COC***H***$_2$), 2.33-2.25 (q, 2H, COCH$_2$C***H***$_2$); ^{13}C-NMR δ (ppm) : 195.68 (***C***O), 181.46 (=***C***-OH), 169.37 (***C***OOCH$_3$), 133.50 (C-Br), 127.20 (C ipso), 131.95 (o- C), 128.50 (m- C), 96.20 (=***C***H enol), 52.61 (***C***H$_3$OOC), 50.61 (***C***H(COOCH$_3$)$_2$), 36.45 (CO***C***H$_2$), 24.27 (COCH$_2$***C***H$_2$); MS (EI) m/e : M$^+$ 384, M$^+$ + 2= 386, 253, 255, 225, 227, 183 (97%), 185 (100 %).

Dimethyl 2-[5-(4-methoxyphenyl)-3,5-dioxopentyl] malonate 7: mp 36-38 °C; IR (KBr) ν (cm^{-1}) : 3434 (w, broad), 2960 (w), 2845 (w), 1750 (s), 1724 (s), 1606 (s), 1512 (m), 1258 (s), 1151 (s); ^{1}H-NMR δ (ppm) : 16.10 (broad s, 1H, OH enol), 7.88-7.83 (d, 9.1 Hz, 2H, m- H), 6.97-6.92 (d, 2H, 9.1 Hz, o- H), 6.10 (s, 1H, C***H***=COH), 3.87 (s, 3H, CH$_3$OPh), 3.75 (s, 6H, C***H***$_3$OCO), 3.51 (t, 1H, J =7.17 Hz, C***H***(COOCH$_3$)$_2$), 2.54-2.46 (t, 2H, COC***H***$_2$), 2.34-2.27 (q, 2H, COCH$_2$C***H***$_2$); ^{13}C-NMR δ (ppm) : 193.22(***C***O), 183.58 (=***C***-OH), 169.43 (***C***OOCH$_3$), 163.16(C- OCH$_3$), 127.24 (C ipso), 129.12 (o- C), 113.95 (m- C), 95.31 (=***C***H enol), 55.45 (***C***H$_3$OPh), 53.67 (***C***H$_3$OOC), 52.60 (***C***H(COOCH$_3$)$_2$), 35.98 (CO***C***H$_2$), 24.55 (COCH$_2$***C***H$_2$); MS (EI) m/e : M$^+$ 336, 318, 205, 177, 135 (100 %).