($CDCl_3$, $T$ = −33 °C) δ 7.33 (br s, 2, $H_{bv}$), 6.87 (s, 2 $H_c$), 6.66 (s, 2, $H_c$), 5.88 (s, 2, $H_{bh}$), 4.25 (br s, 4, CH), 2.66 (q, 8, $J$ = 7 Hz, $COCH_2$), 2.31 (q, 8, $J$ = 7 Hz, $COCH_2$), 1.48 (br s, 12, $CHCH_3$), 1.29 (t, 12, $J$ = 7 Hz, $CH_2CH_3$), 1.06 (t, 12, $J$ = 7 Hz, $CH_2CH_3$); ($T$ = 32 °C) δ 7.30 (vbr s, 2 $H_{bv}$), 6.86 (br s, 4, $H_c$), 5.95 (vbr s, 2, $H_{bh}$), 4.22 (q, 4, $J$ = 7 Hz, CH), 2.42 (vbr s, 16, $COCH_2$), 1.35 (d, 12, $J$ = 7 Hz, $CHCH_3$), 1.12 (br t, 24, $CH_2CH_3$); ($T$ = 150 °C)[15b] δ 7.16 (s, 4, $H_c$), 6.98 (s, 4, $H_b$), 4.42 (q, 4, $J$ = 7 Hz, CH), 2.44 (q, 16, $J$ = 7 Hz, $COCH_2$), 1.40 (d, 12, $J$ = 7 Hz, $CHCH_3$), 1.08 (t, 24, $J$ = 7 Hz, $CH_2CH_3$); mass spectrum, $m/z$ (relative intensity) 992 (6, molecular ion), 936 (47), 880 (100), 824 (49), 768 (24), 712 (14), 656 (9), 600 (4), 544 (1). Anal. Calcd for $C_{56}H_{64}O_{16}$: C, 67.73; H, 6.50. Found: C, 67.76; H, 6.45.

**Condensation of Resorcinol and Acetaldehyde in Solutions Containing Ethanol.** (1) The experiment was performed as in method A, but a solvent mixture (50 mL) of ethanol, water, and concentrated hydrochloric acid (2:2:1) was used. After an induction period of 15 min the gradual crystallization of a yellow compound occurred. The crystals 8.2 g) were collected by filtration. The filtrate was poured into water to give a second precipitate. Acetylation of the combined precipitates gave *only* octaacetate **2b** in 57% yield. No octaacetate **2a** could be detected (TLC, NMR).

(2) The experiment was performed as in method A, but a solvent mixture of ethanol (40 mL) and concentrated hydrochloric acid (10 mL) was used. No precipitation was observed. After 1 h the reaction mixture was cooled, neutralized with concentrated aqueous ammonia, and poured into water. A phenolic product (4.7 g) precipitated. On acetylation it gave only octaacetate **2b** (yield 12%).

**Condensation of Resorcinol and Acetaldehyde in Water. Method B.** When the procedure given by Niederl and Vogel[6] was followed (dilute sulfuric acid, three days reaction time), 48.9 g (79.1%) of phenolic products was obtained. This material (20.4 g) was warmed in a mixture of 60 mL of propionic anhydride and 10 mL of pyridine at 110 °C for 1 h. Cooling in the refrigerator overnight resulted in the crystallization of 9.55 g (25.7%) of the octapropionate **3a** (after washing with methanol). Evaporation of the combined mother liquor and washings and treatment of the semicrystalline residue with 50 mL of methanol gave 22.24 g (59.8%) of the octapropionate **3b**. After recrystallization (**3a** from a mixture of 50 mL of acetonitrile and 100 mL of ethanol and **3b** from 100 mL of ethanol), the two octapropionates, 8.48 g (22.8%) and 21.10 g (56.7%), respectively, exhibited melting points and spectral data identical with those of the analytically pure samples.

**Phenol 1a.**[2] To a slurry of 2.0 g (2 mmol) of octabutyrate **3a** in a mixture of 5 mL of acetonitrile and 15 mL of ethanol at 60 °C under nitrogen was rapidly added a solution of 2 g of potassium hydroxide in 25 mL of ethanol. After 30 min the mixture was acidified with 2 mL of acetic acid. The homogeneous solution was concentrated on a rotary evaporator, 50 mL of water was added, and the mixture was allowed to stand in the refrigerator overnight. The phenol **1a** (1.04 g, 95%) was then collected by filtration, washed thoroughly with water, and dried at 70 °C under vacuum (1 Pa): mp >350 dec; IR (KBr) 3700–2500 (OH) $cm^{-1}$; NMR (0.5 M NaOD in $D_2O$, with sodium 3-(trimethylsilyl)-propanesulfonate as an internal reference) δ 7.00 (s, 2, $H_{bv}$), 6.33 (s, 2, $H_{bh}$), 6.01 (s, 2, $H_c$), 5.92 (s, 2, $H_c$), 4.27 (br q, 4, $J$ = 7 Hz, CH), 1.20 (br d, 12, $J$ = 7 Hz, $CH_3$). Anal. Calcd for $C_{32}H_{32}O_8$: C, 70.57; H, 5.92. Found: C, 70.36; H, 5.88.

**Phenol 1b.**[2] A solution of 2.0 g (2 mmol) of octabutyrate **3b** in 25 mL of ethanol was hydrolyzed in the same way as described above. However, when the warm slurry of the potassium salt of the phenol **1b** was acidified with acetic acid, a homogenous solution first formed from which the phenol **1b** rapidly crystallized and could be collected by filtration: yield 1.05 g (96%) after drying at 70 °C (1 Pa); mp >350 °C dec; IR (KBr) 3700–2500 (OH) $cm^{-1}$; NMR (0.5 M NaOD in $D_2O$, with sodium 3-(trimethylsilyl)-propanesulfonate as an internal reference) δ 7.02 (br s, 4, $H_b$), 5.88 (s, 4, $H_c$), 4.38 (br q, 4, $J$ = 7 Hz, CH), 1.42 (br d, 12, $J$ = 7 Hz, $CH_3$). Anal. Calcd for $C_{32}H_{32}O_8$: C, 70.57; H, 5.92. Found: C, 70.40; H, 5.87.

**Acknowledgment.** The author thanks Professor Holger Erdtman for many discussions in connection with this work. The dynamic NMR measurements were performed by Ms. Gurli Hammarberg.

**Registry No. 1a**, 74645-05-9; **1b**, 74708-10-4; **2a**, 74629-75-7; **2b**, 74708-70-6; **3a**, 74629-76-8; **3b**, 74708-11-5; resorcinol, 108-46-3; acetaldehyde, 75-07-0.

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## A Rapid and Efficient Route to 4- and 5-Amino-3-oxocyclopentene Derivatives

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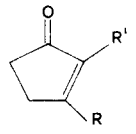
The conversion of open-chain 1,4-diketones to cyclopentenones of type 1 via intramolecular aldol reaction is a common final step in a number of synthetic schemes.[1]

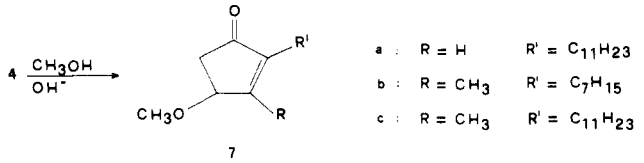


1

Only occasionally have ene dicarbonyl compounds (**3**) been employed as intermediates in the synthesis of cyclopentenone derivatives **5** (and **6**), due to their difficult preparation in the necessary cis configuration and, most of all, their easy cis–trans isomerization that prevented any efficient cyclization to **5**.[2,3]

In fact, compounds **3** were achievable only by hydrolysis of 2,5-dihydro-2,5-dimethoxyfuran derivatives (**2**), which afforded a mixture of cis–trans stereoisomers (Scheme I). The double-bond isomerization, leading to the undesired trans byproduct, was further favored in the course of the subsequent aldol condensation, usually carried out under acid-catalysis conditions. Of course, this procedure allowed only 5-hydroxy derivatives of the type either **5** or **6** to be prepared.[2,3]

Recently, instead, we have shown that trans ene dicarbonyl compounds **4**, easily obtained by reaction of pyridinium chlorochromate (PCC) with 2,5-dialkylfurans (>90%), could be converted in high yield into 5-methoxy-3-oxocyclopentene derivatives **7**.[4]




7

This result demonstrated the potential synthetic value of **4** as intermediates in the preparation of variously functionalized cyclopentenones.

In this paper we report that trans ene dicarbonyl compounds can be easily changed into 4-amino- and 5-amino-3-oxocyclopentene derivatives; in fact, by reaction

(1) R. A. Ellison, *Synthesis*, 397 (1973).
(2) T. Shono, Y. Matsumura, H. Hamaguchi and K. Nakamura, *Chem. Lett.*, 1249 (1976).
(3) M. B. Floyd, *J. Org. Chem.*, **43**, 1641 (1978).
(4) G. Piancatelli, A. Scettri, and M. D'Auria, *Tetrahedron*, **36**, 661 (1980).

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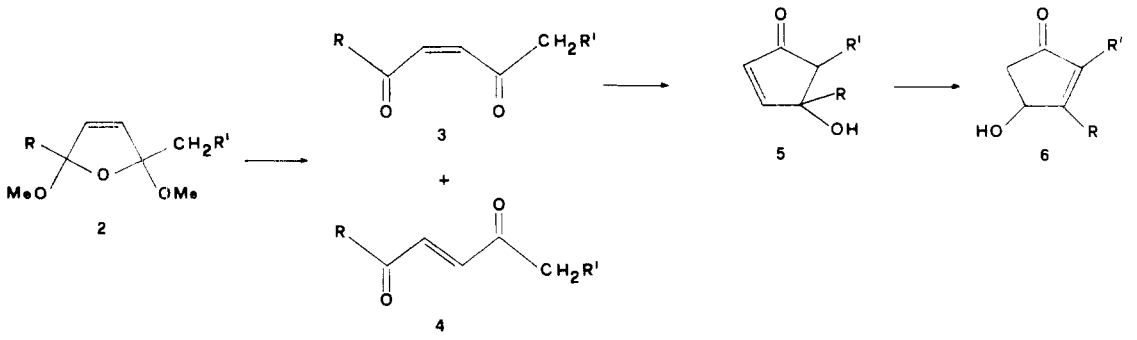
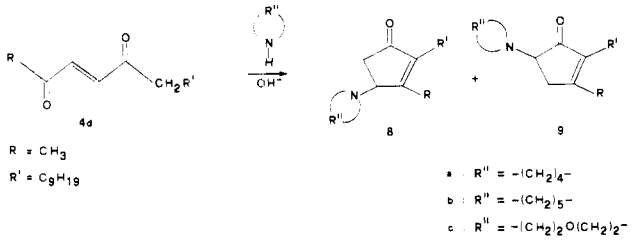
Scheme I



of the starting material **4d** with cyclic secondary amines in basic medium, two new classes of products, **8** and **9**, were obtained in high yield under mild and simple conditions.



The analytical and spectroscopic data of **8** and **9** were in agreement with those reported for similar compounds and with the proposed structures.[4]

The reaction mechanism was easily explained through a two-step sequence involving first the formation of the two possible regioisomeric Michael adducts (very fast), followed by their base-catalyzed cyclization to **8** and **9**.

Aqueous dilute base was generally employed as catalyst. Various water-miscible solvents were tested with unsatisfactory results; in fact, they were either unsuitable (tetrahydrofuran, dioxane)[5] or interfered in an undesired way with the reaction path (methanol, ethanol).

However, the procedure proved to be fully successful with an excess of liquid cyclic secondary amines, which, acting as solvent too, were able to ensure the necessary homogeneity of the reaction medium.

In the case of aliphatic amines, such as $Et_2NH$, the initial Michael addition proceeded satisfactorily; however, the adducts, when subjected to the more drastic conditions needed for the aldol cyclization, yielded only very complex mixtures of products.

In conclusion, although many synthetic sequences leading to 3-oxocyclopentenes, or to the corresponding 5-hydroxy derivatives, have been developed in recent years, this route represents the first approach to 4- and 5-aminocyclopentenones. Furthermore, the addition of different types of nucleophilic reagents to the activated double bond of **4** can afford variously functionalized 1,4-diketones, key intermediates in the synthesis of new classes of cyclopentenone derivatives.

## Experimental Section

Melting points were determined on a Kofler block and are uncorrected. $^1H$ NMR spectra were taken with a Perkin-Elmer R32 spectrometer, using usually $CCl_4$ solutions. Chemical shifts are given in parts per million from $Me_4Si$ as an internal standard. IR spectra were taken with a Perkin-Elmer 257 Infracord spectrometer. Mass spectra were obtained with an AEI MS-12 spectrometer at 70 eV by using direct insertion at source temperature of 150 °C. Commercial Woelm alumina was used for column chromatography. Merck precoated silica gel plates were used for TLC. The chromatograms were detected with iodine vapors.

**trans-3-Pentadecene-2,5-dione (4d).** 2-Methyl-5-decylfuran[4] (1.1 g), diluted with 10 mL of anhydrous $CH_2Cl_2$, was added to a suspension of PCC (4 g) in 50 mL of anhydrous $CH_2Cl_2$. The mixture was refluxed for 24 h and then it was filtered on Florisil, and the crude product obtained after the removal of the solvent was chromatographed on $SiO_2$. Elution with *n*-hexane yielded 1.060 g (90%) of **4d**: plates from ethanol; mp 68–69 °C; IR ($CCl_4$) $\nu_{max}$ 2970, 2872, 1680, 1620, 1360, 980 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$ 6.77 (s, 2 H), 2.60 (t, 2 H, $J$ = 8 Hz), 2.31 (s, 3 H), 1.31 (s, 17 H), 0.92 (m, 3 H); mass spectrum, *m/e* 238 ($M^+$). Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.44; H, 11.09.

**General Procedure for Preparation of 8 and 9.** A solution of **4d** (1 mmol), cyclic amine (2 mL) and aqueous 0.1 N NaOH (1 mL) was stirred at room temperature for 2 h. Then, it was diluted with $Et_2O$ and washed several times with water. The neutral organic phase was dried over $Na_2SO_4$ and, after the removal of the solvent in vacuo, the crude product was chromatographed on $Al_2O_3$ (Brockmann grade III, neutral); elution with $C_6H_6$ or $C_6H_6$–$Et_2O$ (95:5) allowed the separation of the pure compounds **8** and **9** as oils.

**1-Methyl-2-nonyl-5-(1-pyrrolidino)-3-oxocyclopentene (8a):** yield 59%; IR ($CCl_4$) $\nu_{max}$ 2970, 2940, 2865, 1700, 1650, 1380, 1350, 1290, 1125, 1075, 916 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 4.05 (m, 1 H), 2.40 (m, 4 H), 2.60–2.15 (br m, 4 H), 2.04 (s, 3 H), 1.33 (m, 17 H), 0.90 (m, 3 H); mass spectrum, *m/e* 291 ($M^+$). Anal. Calcd for $C_{19}H_{33}NO$: C, 78.29; H, 11.41; N, 4.81. Found: C, 78.15; H, 11.50; N, 4.97.

**1-Methyl-2-nonyl-4-(1-pyrrolidino)-3-oxocyclopentene (9a):** yield 32%; IR ($CCl_4$) $\nu_{max}$ 2990, 2950, 1700, 1645, 1460, 1384, 1243, 1135, 1075, 842 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 3.27 (m, 1 H), 2.50 (m, 4 H), 2.80–2.40 (br m, 4 H), 2.55 (m, 4 H), 1.94 (s, 3 H), 1.14 (m, 17 H), 0.77 (m, 3 H); mass spectrum, *m/e* 291 ($M^+$). Anal. Calcd for $C_{19}H_{33}NO$: C, 78.29; H, 11.41; N, 4.81. Found: C, 78.20; H, 11.35; N, 4.70.

**1-Methyl-2-nonyl-5-(1-piperidino)-3-oxocyclopentene (8b):** yield 33%; IR ($CCl_4$) $\nu_{max}$ 2980, 2870, 2710, 1700, 1650, 1422, 1383, 1338, 1286, 1242, 1112, 1088, 1042, 1001 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$ 3.82 (m, 1 H), 2.40–2.08 (br m, 8 H), 1.98 (s, 3 H), 1.28 (m, 17 H), 0.94 (m, 3 H); mass spectrum, *m/e* 305 ($M^+$). Anal. Calcd for $C_{20}H_{35}NO$: C, 78.63; H, 11.55; N, 4.58. Found: C, 78.50; H, 11.69; N, 4.70.

**1-Methyl-2-nonyl-4-(1-piperidino)-3-oxocyclopentene (9b):** yield 53%; IR ($CCl_4$) $\nu_{max}$ 2980, 2870, 1697, 1643, 1422, 1388, 1285, 1242, 1118, 1038, 989 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$ 3.10 (dd, 1 H, $J_1$ = 6 Hz, $J_2$ = 3 Hz), 2.72 (m, 2 H), 2.50 (m, 4 H), 2.09 (m, 2 H), 2.00 (s, 3 H), 1.29 (s, 17 H), 0.90 (m, 3 H); mass spectrum, *m/e* 305 ($M^+$). Anal. Calcd for $C_{20}H_{35}NO$: C, 78.63; H, 11.55; N, 4.58. Found: C, 78.77; H, 11.68; N, 4.45.

**1-Methyl-2-nonyl-5-(1-morpholino)-3-oxocyclopentene (8c):** yield 27%; IR ($CCl_4$) $\nu_{max}$ 2980, 2945, 2875, 1701, 1650, 1450, 1381, 1292, 1254, 1120, 1010 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$ 3.75 (m, 1 H), 3.60 (t, 4 H, $J$ = 4.5 Hz), 2.33 (m, 4 H), 2.60–2.20 (br m, 4 H), 1.99 (s, 3 H), 1.27 (s, 17 H), 0.90 (m, 3 H); mass spectrum, *m/e* 307 ($M^+$). Anal. Calcd for $C_{19}H_{33}NO_2$: C, 74.22; H, 10.82; N, 4.56. Found: C, 74.05; H, 11.00; N, 4.60.

**1-Methyl-2-nonyl-5-(1-morpholino)-3-oxocyclopentene (9c):** yield 63%; IR ($CCl_4$) $\nu_{max}$ 2980, 2942, 2874, 1701, 1646, 1454, 1387,

(5) In tetrahydrofuran and dioxane the initial Michael addition was very fast; the subsequent cyclization needed very prolonged reaction times, which caused remarkable decomposition of the materials.

1291, 1180, 1120, 1070 $cm^{-1}$; $^1H$ NMR ($CCl_4$) $\delta$ 3.59 (t, 4 H, $J$ = 4.5 Hz), 3.08 (m, 1 H), 2.78 (m, 2 H), 2.50 (m, 4 H), 2.10 (m, 2 H), 2.00 (s, 3 H), 1.28 (s, 17 H), 0.90 (m, 3 H); mass spectrum, $m/e$ 307 ($M^+$). Anal. Calcd for $C_{19}H_{33}NO_2$: C, 74.22; H, 10.82; N, 4.56. Found: C, 74.09; H, 10.96; N, 4.50.

**Registry No. 4d**, 74563-08-9; **8a**, 74563-09-0; **8b**, 74563-10-3; **8c**, 74563-11-4; **9a**, 74563-12-5; **9b**, 74563-13-6; **9c**, 74563-14-7; pyrrolidine, 123-75-1; piperidine, 110-89-4; morpholine, 110-91-8; 2-methyl-5-decylfuran, 74563-15-8.

## One-Pot Syntheses of Cyclopent-2-enones from Furan Derivatives

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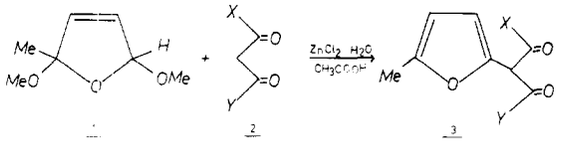
*Received March 11, 1980*

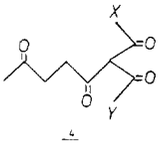
The most versatile method of synthesis of cyclopent-2-enones requires a two-step route: initial preparation of a suitable 1,4-diketone followed by base-catalyzed intramolecular condensation. Furans, which can be considered condensed forms of 1,4-diketones, are often used as starting materials for this sequence.[1]

In a previous paper[2] we reported an efficient synthesis of 2-(5-methyl-2-furyl) 1,3-dicarbonyl compounds **3**, obtained in high yield by intramolecular condensation of 2-methyl-2,5-dihydro-2,5-dimethoxyfuran (**1**) with active methylene compounds.



a: X = Me, Y = OEt
b: X = Ø, Y = OEt
c: X = Me, Y = Me
d: X = Ø, Y = Ø

We now describe a useful application of **3** as starting materials for the direct synthesis of cyclopent-2-enones. These furans are precursors of 1,4-diketones of type **4** and are capable of undergoing cyclization in the same acidic medium in which the opening of the furan ring occurs.



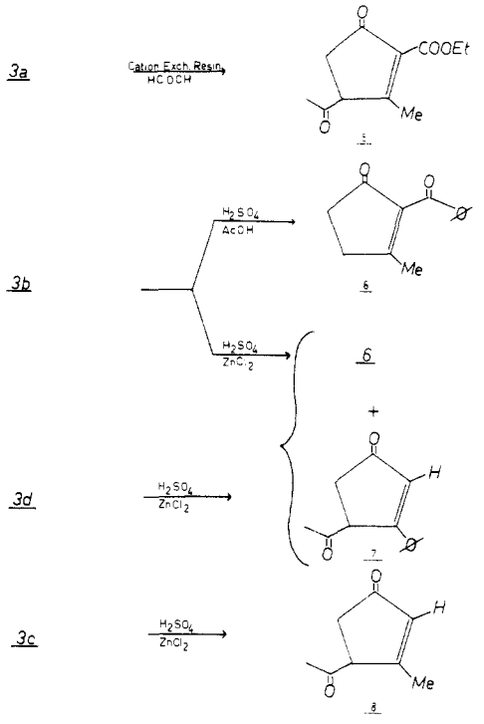
**3a–c** were prepared by a simplified modification of the previous procedure,[2] using **2** and **1** in a 1.5:1 mol ratio. **3d** was prepared under similar conditions, using **2d** and **1** in 1:1.5 mol ratio and dimethoxyethane as a solvent for **2d**.

Treatment of **3a–d** with acid and $ZnCl_2$ in acetone–water at 70 °C for several hours converted them to the cyclopentenones **5–8**, which had analytical and spectroscopic data in agreement with those reported for similar compounds[3] and consistent with the proposed structures.

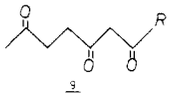
Table I. $^{13}C$ NMR Data[a]

| carbon | 6 | 7 | 8 |
|---|---|---|---|
| C-1 | 179.1 (s) | 171.5 (s) | 174.7 (s) |
| C-2 | 141.6 (s) | 131.7 (d) | 132.9 (d) |
| C-3 | 204.8 (s) | 206.3 (s)[b] | 206.8 (s)[b] |
| C-4 | 35.3 (t) | 39.0 (t) | 39.1 (t) |
| C-5 | 32.6 (t) | 54.9 (d) | 57.8 (t) |
| C-1-$CH_3$ | 18.6 (q) | | 18.2 (q) |
| C-2-CO | 193.5 (s) | | |
| C-5-CO | | 205.6 (s)[b] | 206.0 (s)[b] |
| $COCH_3$ | | 26.1 (q) | 28.1 (q) |

[a] Multiplicity in off resonance: s = singlet, d = doublet, t = triplet, q = quartet. [b] Signals within any vertical column may be reversed.



The reaction mechanism may involve the intermediate formation of 1,4-diketones of type **4** by acid fission of the furan ring.[4] The subsequent ring closure depends on the nature of the 1,3-dicarbonyl moiety of **3**; hydrogen bonding may be a factor that determines the reaction path. The strong electrostatic interaction in **3a**, which is completely enolized under the reaction conditions,[5] stabilizes the ester function and prevents acid-catalyzed hydrolysis. This stabilization does not occur in **3b**, which is only 50% enolized;[5] thus, in addition to ring opening this compound undergoes both ester hydrolysis and decarboxylation to a 1,4-diketone **9** (R = Ph). Treatment of **3b** with 1.5%



R = Me
R = Ø

(1) R. A. Ellison, *Synthesis*, 397 (1973).
(2) R. D'Ascoli, M. D'Auria, G. Piancatelli, A. Scettri, *Tetrahedron*, **35**, 2905 (1979).
(3) G. Piancatelli, A. Scettri, G. David, M. D'Auria, *Tetrahedron*, **34**, 2775 (1978), and references therein.
(4) The detection of these intermediates by TLC control was unsuccessful and the interruption of the reactions at various degrees of completion did not allow their isolation.
(5) The degrees of enolization were determined on the grounds of $^1H$ NMR spectra, recorded in $CD_3COCD_3$–$H_2O$ (4:1) solution. **3a**: 17.0 ppm (br, 1 H). **3b**: 14.0 ppm (br, 0.5 H), 5.50 (s, 0.5 H).

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