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# OXIDATIVE RING OPENING OF FURAN DERIVATIVES TO $\alpha,\beta$-UNSATURATED $\gamma$-DICARBONYL COMPOUNDS, USEFUL INTERMEDIATES FOR 3-OXOCYCLOPENTENES SYNTHESIS†

G. PIANCATELLI*, A. SCETTRI and M. D'AURIA
Centro di Studio per la Chimica delle Sostanze Organiche Naturali del CNR c/o Istituto di Chimica Organica dell'Università di Roma, Italia

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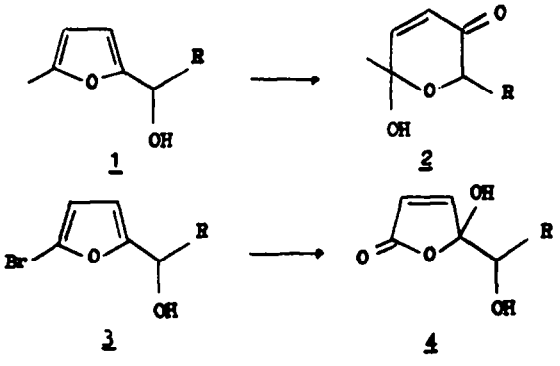
**Abstract**—$\alpha,\beta$-unsaturated $\gamma$-dicarbonyl compounds, easily obtained by reaction of pyridinium chlorochromate with alkylfurans, are interesting starting materials for the rapid synthesis of 3-oxo-cyclopentenes.

In previous papers we described some original applications of pyridinium chlorochromate (PCC), whose action on furan derivatives allowed several interesting products to be prepared: in fact, the oxidative ring enlargement of 5-methyl-2-furylcarbinols **1** led directly to 2,6-dialkyl-6-hydroxy-2H-pyran-3(6H)-ones **2**,[1] while 5-bromo-2-furylcarbinols **3** were converted into $\gamma$-hydroxy butenolides **4**.[2]



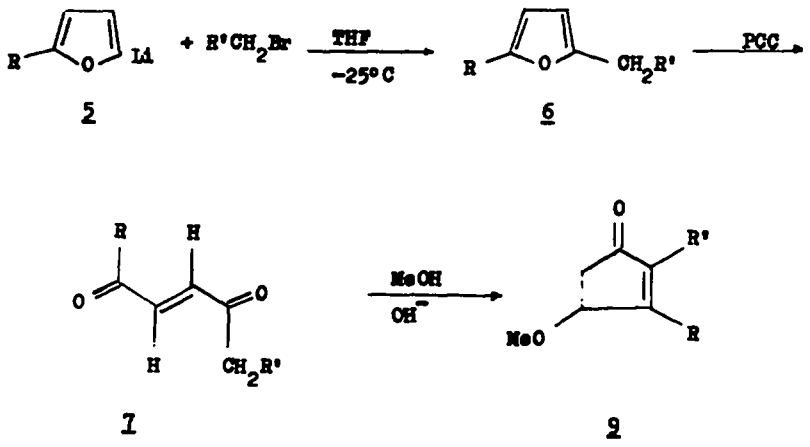
†Dedicated to Professor Luigi Panizzi on the occasion of his 70th birthday.

In this paper we wish to report a novel synthetic application of PCC, demonstrating its particular reactivity towards the alkylfurans. Metalation of furan (or 2-methyl-furan) with n-BuLi in THF solution yields 2-furyllithium (or 5-methyl-2-furyllithium) **5**, which, by condensation with alkyl bromides, gives the starting materials **6**. Alkylfurans **6**, by action of PCC in $CH_2Cl_2$ solution (Scheme 1), undergo an oxidative ring fission to $\alpha,\beta$-unsaturated $\gamma$-dicarbonyl compounds **7** in high yields (Table 1).

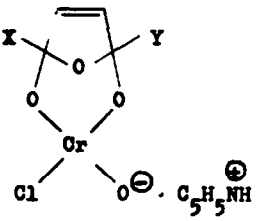
Invariably, products **7** are obtained in *trans* stereoisomeric configuration, e.g. **7c**: $^1$H-NMR ($d_6$-acetone, $\delta$): 9.83 (d, 1 H, J = 7 Hz), 7.08 (d, 1 H, J = 16 Hz), 6.80 (dd, 1 H, $J_1$ = 16 Hz, $J_2$ = 7 Hz), 2.77 (t, 2 H, J = 7 Hz). IR ($CCl_4$, $\nu_{max}$ cm$^{-1}$): 2720, 1690, 1620, 980.

As reported for similar processes of oxidative fission, compounds of type **7** are first obtained in *cis* configuration, and, then, *cis-trans* isomerisation,[4] catalysed by acid or heating, occurs (PCC is already known to effect this conversion because of its mildly acidic character[5]).

A general mechanism of action of PCC on furan derivatives can be proposed: in fact the experimental data are in agreement with the preliminary formation of an addition compound **8** by 1,4-electrophilic attack of chlorochromate anion upon the furan ring.



Scheme 1.



8

X = $-CH_3$ ; Y = $-\underset{\underset{OH}{|}}{CH}-R$

X = $-Br$ ; Y = $-\underset{\underset{OH}{|}}{CH}-R$

X = $-H$, $-CH_3$ ; Y = $-CH_2R'$

Subsequently, the decomposition pattern of the unstable key-intermediate **8** (leading to final products **2**,**4**, and **7** by heterolytic cleavage of Cr-O bond) depends strictly on the nature of the X and Y substituents; furthermore, the conversion **1**→**2** indicates a nucleophilic participation of the side alcoholic function in the heterolysis of **8**.

Since the routes at present employed are characterised by drastic conditions and poor yields of *cis-trans* mixtures,[4] the process described is considered especially effective in view of the following synthetic uses. α,β-Unsaturated γ-diketones **7**, are promising and versatile intermediates in a new and widely applicable methodology for the preparation of 3-oxocyclopentene derivatives.

Compounds **7** do not undergo the ring closure leading to products of type **9**, while we have achieved this conversion through a mild and selective procedure. In fact, base catalysed cyclisation, occurring through the initial nucleophilic addition of methanol to the activated double bond and subsequent intramolecular condensation, affords 5-methoxy-3-oxocyclopentenes **9** in high yields (Table 1); e.g. **9c**: $^1$H-NMR ($CCl_4$, δ) 7.30 (m, 1 H), 4.38 (m, 1 H), 3.32 (s, 3 H), 2.54 (dd, 1 H, $J_1$ = 18 Hz, $J_2$ = 6 Hz), 2.14 (dd, 1 H, $J_1$ = 18 Hz, $J_2$ = 2 Hz), 2.15 (m, 2 H). IR ($CCl_4$, $\nu_{max}$ cm$^{-1}$): 1712, 1645, 1100.

## EXPERIMENTAL

M.ps were determined on a Kofler block and are uncorrected. $^1$H-NMR spectra were taken with a Perkin–Elmer R 32 spectrometer, using usually $CDCl_3$ or $CCl_4$ solns with TMS as an internal standard. IR spectra were taken with a Perkin–Elmer 257 Infracord spectrometer. Commercial Merck silica gel and Woelm alumina were used for column chromatography. Merck precoated silica gel plates were used in tlc. The chromatograms were detected by spraying with 5 N $H_2SO_4$ and heating at 110° for 10 min. Mass spectra were obtained with an AEI MS-12 spectrometer at 70 eV, by using direct insertion at source temperature of 150°.

*2-n-Dodecyl-5-methyl-furan* **6a**. 1.32 N n-BuLi (26.5 ml) was added to 3 g of 2-methyl-furan, diluted with 20 ml of anhyd THF, at −25° under $N_2$. The mixture was stirred for 4 hr at −15°, then, again at −25°, 7.6 ml of $C_{12}H_{25}Br$, dissolved in 15 ml of anhyd THF, was added, and the mixture stirred at −15° for 1.5 hr, then at room temperature for 16 hr. Then, 50 ml of a cold soln, satd with $NH_4Cl$ was added and vigorous stirring maintained for 1 hr. The organic layer was separated and the aqueous phase was extracted 3 times with $Et_2O$. The neutral extracts were dried over $Na_2SO_4$ and the removal of the solvent yielded a crude product which was chromatographed on $SiO_2$. Elution with hexane gave 8 g (89%) of pure **6a**. (Found: C, 81.29; H, 11.90. Calc. for $C_{17}H_{32}O$: C, 81.54; H, 12.07%) $n_D^{25}$ = 1.4613. IR (film, $\nu_{max}$ cm$^{-1}$): 1570. $^1$H-NMR ($CCl_4$, δ): 5.70 (m, 2 H), 2.52 (t, 2 H), 2.20 (s, 3 H), 1.25 (m, 20 H), 0.88 (t, 3 H). MS (*m/e*): 250 ($M^+$).

*2-n-Octyl-5-methyl-furan* **6b**. 1.32 N n-BuLi (25 ml) was added to 2.7 g of 2-methyl-furan, diluted with 20 ml of anhyd THF, at −25° under $N_2$. The mixture was stirred for 4 hr at −15°, then, again at −25°, 5.8 ml of $C_8H_{17}Br$, dissolved in 15 ml anhyd THF, was added, and the mixture stirred at −15° for 1.5 hr, then at room temp. for 16 hr. Then 50 ml of a cold soln, satd with $NH_4Cl$ was added and vigorous stirring maintained for 1 hr. The usual isolation procedure yielded the crude product which was chromatographed on $SiO_2$. Elution with hexane gave 5.4 g (85%) of pure **6b**. (Found: C, 80.50; H, 11.30. Calc. for $C_{13}H_{22}O$: C, 80.35; H, 11.41%) $n_D^{25}$ = 1.4583. IR (film, $\nu_{max}$ cm$^{-1}$): 1570. $^1$H-NMR ($CCl_4$, δ): 5.70 (m, 2 H), 2.50 (t, 2 H), 2.20 (s, 3 H), 1.27 (m, 12 H), 0.90 (t, 3 H). MS (*m/e*): 194 ($M^+$).

*2-n-Dodecyl-furan* **6c**. 1.32 N n-BuLi (26 ml) was added to 2.24 g of furan, diluted with 20 ml of anhyd THF, at −25° under $N_2$. The mixture was stirred for 4 hr at −15°, then, again at −25°, 7.2 ml of $C_{12}H_{25}Br$ dissolved in 15 ml of anhyd THF, was added, and the mixture was stirred at −15° for 1.5 hr, then at room temp. for 16 hr. Then 50 ml of a cold soln, satd with $NH_4Cl$, was added and vigorous stirring maintained for 1 hr, The usual isolation procedure yielded the crude product which was chromatographed on $SiO_2$. Elution with hexane gave 7.0 g (90%) of pure **6c**. (Found: C, 81.43; H, 11.75. Calc. for $C_{16}H_{28}O$: C, 81.29; H, 11.94%) $n_D^{25}$ = 1.4604. IR (film, $\nu_{max}$ cm$^{-1}$): 1595. $^1$H-NMR ($CCl_4$, δ): 7.20 (m, 1 H), 6.18 (m, 1 H), 5.9 (m, 1 H), 2.53 (t, 2 H), 1.25 (m, 20 H), 0.9 (t, 3 H). MS (*m/e*): 236 ($M^+$).

trans-3-*Heptadecen-2,5-dione* **7a**. PCC (2.6 g) was added to 600 mg of **6a**, dissolved in 50 ml of dry $CH_2Cl_2$. The mixture was stirred at room temp. for 24 hr then it was refluxed for 9 hr. The usual isolation procedure[5] gave a crude product which was chromatographed on $SiO_2$. Elution with $C_6H_6$-$Et_2O$ 9:1 gave

Table 1.

| Compound | Yield %* | R | R' | Compound | Yield %* |
|---|---|---|---|---|---|
| 7a | 90 | $CH_3$ | $C_{11}H_{23}$ | 9a | 80 |
| 7b | 90 | $CH_3$ | $C_7H_{15}$ | 9b | 75 |
| 7c | 60 | H | $C_{11}H_{23}$ | 9c | 50**. |

*All yields refer to isolated chromatographically pure products.

**Generally, α,β-unsaturated aldehydes do not give satisfactory yields of Michael adducts.[3]

574 mg (90%) of pure **7a**, plates from hexane, m.p. 75–76°. (Found: C, 76.43; H, 11.50. Calc. for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35%) IR (1%, $CHCl_3$, $\nu_{max}$ $cm^{-1}$): 1683, 1620, 980. $^1$H-NMR ($CDCl_3$, $\delta$): 6.84 (s, 2 H), 2.65 (t, 2 H), 2.35 (s, 3 H). MS (*m/e*): 266 ($M^+$).

trans-3-*Tridecen*-2,5-*dione* **7b**. PCC (2.1 g) was added to 383 mg of **6b**, dissolved in 50 ml of dry $CH_2Cl_2$. The mixture was stirred at room temp. for 24 hr, then it is refluxed for 9 hr. The usual isolation procedure[5] gave a crude product which was chromatographed on $SiO_2$. Elution with $C_6H_6$–$Et_2O$ 9:1 gave 373 mg (90%) of pure **7b**, plates from hexane, m.p. 59–61°. (Found: C, 74.43; H, 10.58. Calc. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54%) IR (1%, $CCl_4$, $\nu_{max}$ $cm^{-1}$): 1680, 1620, 980. $^1$H-NMR ($CCl_4$, $\delta$): 6.72 (s, 2 H), 2.57 (t, 2 H), 2.28 (s, 3 H). MS (*m/e*: 210 ($M^+$).

trans-2-*Hexadecen*-1-*al*-4-*one* **7c**. PCC (2.14 g) was added to 472 mg of **6c**, dissolved in 50 ml of dry $CH_2Cl_2$. The mixture was stirred at room temp. for 24 hr, then it is refluxed for 9 hr. The usual isolation procedure gave a crude product which was chromatographed on $SiO_2$. Elution with $C_6H_6$–$Et_2O$ 9:1 gave 302 mg (60%) of pure **7c**, prisms from hexane, m.p. 58–59°. (Found: C, 76.25; H, 11.30. Calc. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18%) IR (1%, $CHCl_3$, $\nu_{max}$ $cm^{-1}$): 2720, 1690, 1620, 980. $^1$H-NMR ($CDCl_3$, $\delta$): 9.80 (dd, 1 H, $J_1 \simeq 7$ Hz, $J_2 = 2$ Hz), 6.82 (m, 2 H), 2.68 (t, 2 H). MS (*m/e*): 252 ($M^+$).

1-*Methyl*-2-*n*-*undecyl*-3-*oxocyclopentene*-5-*methoxy* **9a**. 0.1 N NaOH (3.8 ml) was added to 270 mg of **7a**, dissolved in 30 ml of MeOH. The mixture was stirred at room temp. for 48 hr. Then the mixture was poured into dilute acid and extracted with $Et_2O$. The neutral extracts were dried over $Na_2SO_4$ and the removal of the solvent yielded a crude product which was chromatographed on neutral $Al_2O_3$ B III. Elution with $C_6H_6$–$Et_2O$ 9:1 gave 228 mg (80%) of pure **9a**, prisms from hexane, m.p. 37–39°. (Found: C, 77.03; H, 11.39. Calc. for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50%) IR (1%, $CCl_4$, $\nu_{max}$ $cm^{-1}$): 1710, 1655, 1100. $^1$H-NMR ($CCl_4$, $\delta$): 4.20 (m, 1 H), 3.32 (s, 3 H), 2.47 (dd, 1 H, $J_1 = 18$ Hz, $J_2 = 6$ Hz), 2.10 (dd, 1 H, $J_1 = 18$ Hz, $J_2 = 2$ Hz), 2.13 (m, 1 H), 1.98 (s, 3 H). MS (*m/e*): 280 ($M^+$).

1-*Methyl*-2-*n*-*heptyl*-3-*oxocyclopentent*-5-*methoxy* **9b**. 0.1 N NaOH (3.8 ml) was added to 210 mg of **7b**, dissolved in 30 ml of MeOH. The mixture was stirred at room temp. for 48 hr. Then, the mixture was poured into dilute acid and extracted with $Et_2O$. The neutral extracts were dried over $Na_2SO_4$ and the removal of the solvent yielded a crude product which was chromatographed on neutral $Al_2O_3$ B III. Elution with $C_6H_6$–$Et_2O$ 9:1 gave 168 mg (75%) of pure **9b**, as very dense oil. (Found: C, 75.05; H, 10.65. Calc. for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78%) IR (1%, $CCl_4$, $\nu_{max}$ $cm^{-1}$): 1710, 1657, 1100. $^1$H-NMR ($CCl_4$, $\delta$): 4.23 (m, 1 H), 3.34 (s, 3 H), 2.50 (dd, 1 H, $J_1 = 18$ Hz, $J_2 = 6$ Hz), 2.12 (dd, 1 H, $J_1 = 18$ Hz, $J_2 \simeq 2$ Hz), 2.13 (m, 2 H), 2.00 (s, 3 H). MS (*m/e*): 224 ($M^+$).

2-*n*-*Undecyl*-3-*oxocyclopentene*-5-*methoxy* **9c**. 0.1 N NaOH (3.8 ml) was added to 252 mg of **7c**, dissolved in 30 ml of MeOH. The mixture was stirred at room temp. for 48 hr. Then, the mixture was poured into dilute acid and extracted with $Et_2O$. The neutral extracts were dried over $Na_2SO_4$ and the removal of the solvent yielded a crude product which was chromatographed on neutral $Al_2O_3$ B III. Elution with $C_6H_6$–$Et_2O$ 9:1 gave 133 mg (50%) of pure **9c**, as very dense oil. (Found: C, 76.75; H, 11.20. Calc. for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35%) MS (*m/e*): 266 ($M^+$). For IR and $^1$H-NMR data, see the initial section.

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