# Michael Addition to *trans*-Enediones: A Facile Route to 2,3,4,5-Tetrasubstituted Furans

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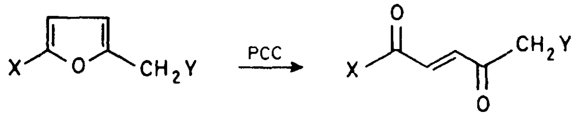
The enediones (2) are useful starting materials for a two-step synthesis of tetrasubstituted furans, which are not otherwise easily available. Michael addition of active methylene compounds to the enediones (2) led to the two regioisomeric adducts (8) and (9), which then cyclized to furans under very mild conditions.

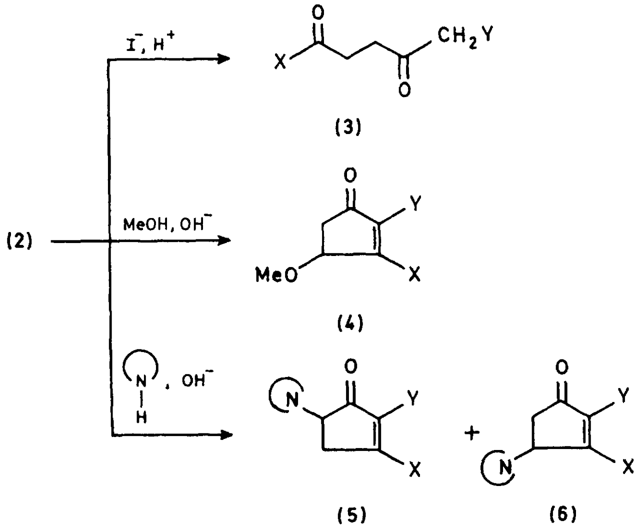
THE addition of nucleophilic reagents to the activated carbon–carbon double bond of enediones has been little investigated, probably because the preparation of these substrates is difficult.

Recently we reported a useful synthesis of *trans*-enediones (2) by the oxidative ring opening of 2,5-dialkylfurans (1) with pyridinium chlorochromate (PCC) (yields >90%).[1]



(1) (2)

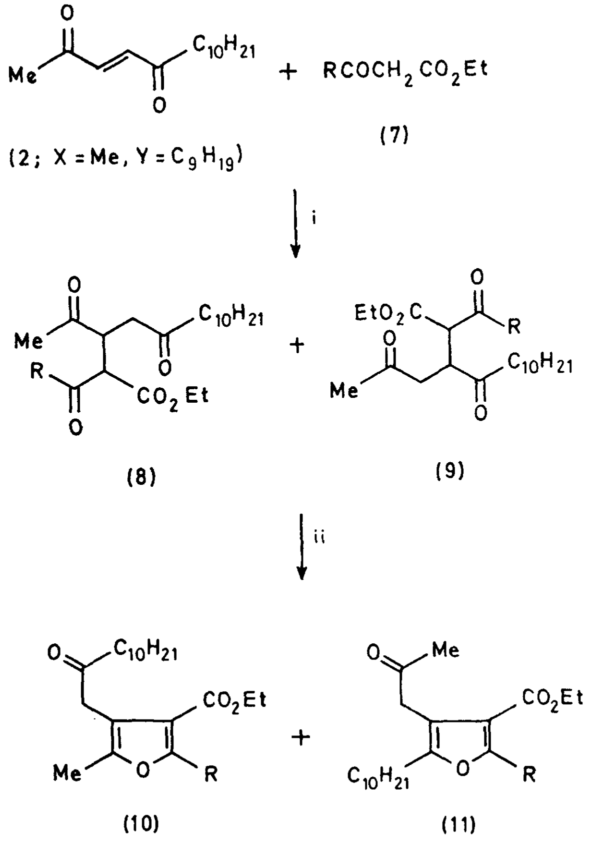
Compounds (2) were synthetically useful as Michael acceptors,[1-3] the first step in their reactions being the addition of a nucleophile to the olefinic double bond with either acid or base catalysis (Scheme 1).



SCHEME 1

We now report a new application of the Michael addition of some active methylene compounds to (2) achieved under mild and simple conditions of phase-transfer catalysis, that allows the easy synthesis of 2,3,4,5-tetrasubstituted furans, a class of compound which is not easily available.

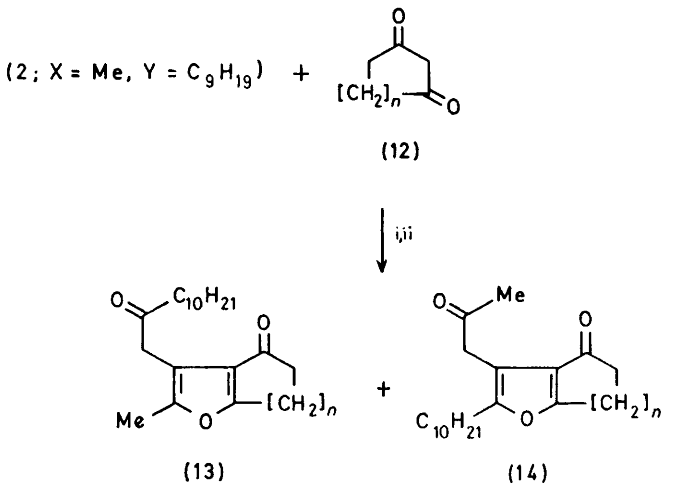
Since the normal procedure for generation of carbanions from active methylene compounds [50% sodium hydroxide in the presence of triethylbenzylammonium chloride (TEBAC)] led to substantial decomposition, the reaction was generally carried out by using equimolar quantities of the starting compound (2; X = Me, Y = $C_9H_{19}$), an active methylene compound, and anhydrous sodium carbonate in benzene at 75—80 °C in the presence of catalytic amounts of TEBAC (Schemes 2 and 3).



a; R = Me
b; R = Ph

SCHEME 2 *Reagents:* i, $Na_2CO_3$, TEBAC ii, HCl, $Et_2O$

The formation of the Michael adducts, monitored by t.l.c., proceeded satisfactorily with both β-ketoesters (7) and the cyclic 1,3-diones (12), but they could not be isolated because of their reactivity during purification.



a; $n = 2$
b; $n = 1$

SCHEME 3 *Reagents:* i, $Na_2CO_3$, TEBAC; ii, HCl, $Et_2O$

Only for (7b) was it possible to isolate the addition product, an inseparable mixture of the two regioisomeric adducts (8) and (9) in nearly 1 : 1 ratio as shown by $^1H$ n.m.r. spectroscopy.*

In spite of their lability, all the Michael adducts were of synthetic value; treatment, without purification, with hydrogen chloride-saturated diethyl ether caused their conversion into the corresponding more stable 2,3,4,5-tetrasubstituted furans (10), (11), (13), and (14) in good yields (Table).

TABLE

Preparation and characterization of (10), (11), (13), and (14)

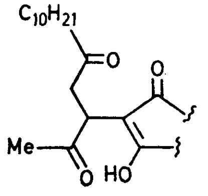
| Product | Reaction time/h | M.p. ($t$/°C) | % Yield [a] |
|---|---|---|---|
| (10a) | 0.5 | 31—32 | 34 |
| (11a) | | 44—45 | 32 |
| (10b) | 1.0 | 28—30 | 27 |
| (11b) | | [b] | 45 |
| (13a) | 12.0 | Syrup | 35 |
| (14a) | | 48—50 | 23 |
| (13b) | 0.5 | 32—34 | 17 |
| (14b) | | 46—48 | 18 |

[a] All the yields refer to isolated chromatographically pure compounds. [b] Compound (11b) decomposed extensively during attempted crystallization.

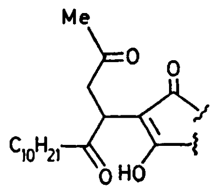
Normal routes to furans from 1,4-diones require much more drastic conditions; in fact, the saturated analogue of (2; X = Me, Y = $C_9H_{19}$) was unaffected by the foregoing treatment. However, the Michael addition allowed the preparation of 1,4-diones particularly activated by the presence of an easily enolizable group.

The mildly acidic conditions clearly promoted conversion into the enolic forms (15) and (16), which then cyclized to furans by the usual path.

We conclude by pointing out that, even though enediones have been known for a long time, this is the first example of the successful Michael addition of active methylene compounds to (2). Furthermore, the easy conversion of the Michael adducts, in spite of their reactivity, into furan derivatives is of significance synthetically since alternative routes for the preparation of complex furans are not at present available.



(15)



(16)

## EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. $^1H$ N.m.r. spectra were recorded with a Perkin-Elmer R 32 spectrometer for $CCl_4$ solutions with $Me_4Si$ as an internal standard. I.r. spectra were recorded with a Perkin-Elmer 257 Infracord spectrometer for 1% solutions in $CCl_4$. Commercial Merck silica gel was used for column chromatography. Merck pre-coated silica gel plates were used in t.l.c. and preparative t.l.c. The chromatograms were visualized by spraying with 5 N-$H_2SO_4$ and heating at 110 °C for 10 min. Mass spectra were obtained with an AEI MS-12 spectrometer at 70 eV, by using direct insertion at a source temperature of 150 °C.

2,3,4,5-*Tetrasubstituted Furans: General Procedure.*—A mixture of pentadec-3-ene-2,5-dione (2; X = Me, Y = $C_9H_{19}$) (200 mg, 8.4 mmol), the appropriate active methylene compound (8.4 mmol), dry $Na_2CO_3$ (98 mg, 8.4 mmol), and TEBAC (20 mg) in benzene (20 ml) was stirred at 75—80 °C for 24 h (7a and b) or 48 h (12a and b), and then diluted with $Et_2O$ and the organic phase washed with brine. The organic phase was dried ($Na_2SO_4$) and the solvent removed *in vacuo* to give the crude Michael adducts, which were immediately treated with hydrogen chloride-saturated $Et_2O$ (20 ml). When t.l.c. showed the reaction was complete [benzene–$Et_2O$ (4 : 1) as eluant for (7a and b) and benzene–ethyl acetate (1 : 1) for (12a and b)], the solution was diluted with $Et_2O$, washed several times with brine, and dried ($Na_2SO_4$). Removal of solvent under reduced pressure and purification by column or preparative thin-layer chromatography gave the furans (10), (11), (13), and (14).

*Ethyl* 2,5-*dimethyl*-4-(2-*oxododecyl*)-3-*furoate* (10a) *and ethyl* 5-n-*decyl*-2-*methyl*-(2-*oxopropyl*)-3-*furoate* (11a). The isomeric *esters* (10a) and (11a) were purified by preparative t.l.c. with benzene–diethyl ether (9 : 1) as eluant; (10a) gave needles from MeOH–$H_2O$ (Found: C, 72.1; H, 9.9. $C_{21}H_{34}O_4$ requires C, 72.0; H, 9.8%); $^1H$ n.m.r., $\delta$ 4.17 (2 H, q, $J$ 7 Hz, $OCH_2Me$), 3.44 (2 H, s, 4-$CH_2$), 2.46 (3 H, s,

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* Determined from the relative intensity of the methyl resonances: $\delta$ 2.08 (s, 1.5 H) and 1.98 (s, 1.5 H) for (8b) and (9b), respectively.

2-Me), 2.34 (2 H, t, *J* 7 Hz, COCH$_2$), 2.11 (3 H, s, 5-Me), 1.30 (3 H, partially obscured t, *J* 7 Hz, OCH$_2$*Me*), 1.27 (16 H, m, 8 × CH$_2$), and 0.80 (3 H, m, [CH$_2$]$_9$*Me*); i.r. $\nu_{max.}$ 1 720br. cm$^{-1}$; *m/e*: 350 (*M*$^+$); (11a) gave plates from MeOH–H$_2$O (Found: C, 72.1; H, 9.6%); $^1$H n.m.r., δ 4.19 (2 H, q, *J* 7 Hz, OC*H*$_2$Me), 3.47 (2 H, s, 4-CH$_2$), 2.47 (3 H, s, 2-Me), 2.34 (2 H, t, *J* 6 Hz, 5-CH$_2$), 2.04 (3 H, s, COMe), 1.27 (19 H, m, 8 × CH$_2$ and OCH$_2$*Me*), and 0.88 (3 H, m, [CH$_2$]$_9$*Me*); i.r. $\nu_{max.}$ 1 740 and 1 720 cm$^{-1}$; *m/e*: 350 (*M*$^+$).

*Ethyl* 5-*methyl*-4-(2-*oxododecyl*)-2-*phenyl*-3-*furoate* (10b) *and ethyl* 5-*n-decyl*-4-(2-*oxopropyl*)-2-*phenyl*-3-*furoate* (11b). The isomeric *esters* (10b) and (11b) were purified by preparative t.l.c. with benzene–diethyl ether (8 : 2) as eluant; (10b) gave needles from MeOH–H$_2$O (Found: C, 75.5; H, 8.7. $C_{26}H_{36}O_4$ requires C, 75.7; H, 8.8%); $^1$H n.m.r., δ 7.69 (2 H, m, ArH), 7.38 (3 H, m, ArH), 4.17 (2 H, q, *J* 7 Hz, OC*H*$_2$Me), 3.53 (2 H, s, 4-CH$_2$), 2.40 (2 H, t, *J* 7 Hz, COCH$_2$), 2.26 (3 H, s, 5-Me), 1.40—1.21 (19 H, m, 8 × CH$_2$ and OCH$_2$*Me*), and 0.89 (3 H, m, [CH$_2$]$_9$*Me*); i.r., $\nu_{max.}$ 1 730—1 710br cm$^{-1}$; *m/e*: 412 (*M*$^+$); (11b) (Found: C, 75.5; H, 9.0%); $^1$H n.m.r., δ 7.69 (2 H, m, ArH), 7.27 (3 H, m, ArH), 4.17 (2 H, q, *J* 7 Hz, OC*H*$_2$Me), 3.53 (2 H, s, 4-CH$_2$), 2.56 (2 H, t, *J* 7 Hz, 5-CH$_2$), 2.10 (3 H, s, COMe), 1.27 (16 H, m, 8 × CH$_2$), 1.22 (3 H, partially obscured t, *J* 7 Hz, OCH$_2$*Me*), and 0.90 (3 H, m, [CH$_2$]$_9$*Me*); i.r., $\nu_{max.}$ 1 740—1 710br cm$^{-1}$; *m/e* 412 (*M*$^+$).

6,7-*Dihydro*-2-*methyl*-3-(2-*oxododecyl*)*benzofuran*-4(5H)-*one* (13a) *and* 2-*n-decyl*-6,7-*dihydro*-3-(2-*oxopropyl*)*benzofuran*-4(5H)-*one* (14a). The *benzofurans* (13a) and (14a) were purified by preparative t.l.c. with benzene–diethyl ether (9 : 1) as eluant; (13a) was a syrup (Found: C, 75.6; H, 9.65. $C_{21}H_{32}O_3$ requires C, 75.9; H, 9.7%); $^1$H n.m.r. δ 3.52 (2 H, s, 3-CH$_2$), 2.68 (2 H, t, *J* 6 Hz, 7-H$_2$), 2.50—2.00br (4 H, m, COCH$_2$ and 5-H$_2$), 2.17 (3 H, s, 2-Me), 1.60 (2 H, m, 6-H$_2$), 1.28 (16 H, m, 8 × CH$_2$), and 0.89 (3 H, m, [CH$_2$]$_9$*Me*); i.r., $\nu_{max.}$ 1 720br. and 1 675 cm$^{-1}$; *m/e*: 332 (*M*$^+$); (14a) gave prisms from MeOH–H$_2$O (Found: C, 76.0; H, 9.55); $^1$H n.m.r., δ 3.52 (2 H, s, 3-CH$_2$), 2.80 (2 H, m, 7-H$_2$), 2.60—2.00br (4 H, m, 2-CH$_2$ and 5-H$_2$), 2.10 (3 H, s, COMe), 1.60 (2 H, m, 6-H$_2$), 1.20 (16 H, m, 8 × CH$_2$), and 0.89 (3 H, m, [CH$_2$]$_9$*Me*); i.r., $\nu_{max.}$ 1 730, 1 715, and 1 675 cm$^{-1}$; *m/e*: 332 (*M*$^+$).

5,6-*Dihydro*-2-*methyl*-3-(2-*oxododecyl*)*cyclopenta*[b]*furan*-4-*one* (13b) *and* 2-*n-decyl*-5,6-*dihydro*-3-(2-*oxopropyl*)*cyclopenta*[b]*furan*-4-*one* (14b). The *cyclopentafurans* (13b) and (14b) were purified by column chromatography on silica gel with benzene–acetonitrile–water (68.5 : 23.3 : 8.2) as eluant; (13b) gave plates from MeOH–H$_2$O (Found: C, 75.2; H, 9.7. $C_{20}H_{30}O_3$ requires C, 75.4; H, 9.5%); $^1$H n.m.r., δ 3.96 (2 H, s, 3-CH$_2$), 2.65 (2 H, m, 6-H$_2$), 2.40—2.20br (4 H, m, COCH$_2$ and 5-H$_2$), 2.15 (3 H, s, 2-Me), 1.22 (16 H, m, 8 × CH$_2$), and 0.90 (3 H, m, [CH$_2$]$_9$*Me*); i.r., $\nu_{max.}$ 1 720 and 1 698 cm$^{-1}$; *m/e*: 318 (*M*$^+$); (14b) gave plates from MeOH–H$_2$O (Found: C, 75.6; H, 9.6%); $^1$H n.m.r. δ 3.96 (2 H, s, 3-CH$_2$), 2.75 (2 H, m, 6-H$_2$), 2.40—2.20br (4 H, m, 5-H$_2$ and 2-CH$_2$), 2.04 (3 H, s, COMe), 1.26 (16 H, m, 8 × CH$_2$), and 0.80 (3 H, m, [CH$_2$]$_9$*Me*); i.r., $\nu_{max.}$ 1 720 cm$^{-1}$; *m/e*: 318 (*M*$^+$).

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## REFERENCES

[1] G. Piancatelli, A. Scettri, and M. D'Auria, *Tetrahedron*, 1981, **36**, 661.

[2] M. D'Auria, G. Piancatelli, and A. Scettri, *Synthesis*, 1980, 245.

[3] R. D'Ascoli, M. D'Auria, A. De Mico, G. Piancatelli, and A. Scettri, *J. Org. Chem.*, 1980, **45**, 4500.