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A NEW SYNTHESIS OF 5-METHYLENE-2(5H)-FURANONE DERIVATIVES

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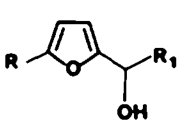
ABSTRACT: 5-methylene-2(5H)-furanone derivatives are easily obtained by treatment of tertiary 2-furylcarbinols with pyridinium dichromate in dimethylformamide solution. Through this procedure, a natural product, the thiophene lactone, isolated from **Chamaemelum Nobile L.**, has been synthesized.

2-Furylcarbinols 1 are useful starting materials for the synthesis of a remarkable variety of compounds[1,2,3] and some of them (4, 5) are characterized by very interesting biological properties[2,3]. In particular, compounds 5, which are also key-intermediates in the total synthesis of monosaccharides from furfuryl alcohols, show to be the final product of the treatment of 1 with several oxidizing systems[3,4], such as a) bromine in methanol, b) electrolytic methoxylation, c) organic peracids, d) pyridinium chlorochromate, etc.

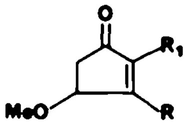
In the course of investigation that we have been carrying out for some years on the reactivity both of 2-furylcarbinols and some Cr(VI) derivatives*, we have found that, by action of a mild oxidizing agent, pyridinium dichromate (PDC) in dimethylformamide solution[7], tertiary furylcarbinols 6, suitably substituted, can be conveniently converted into 5-diarylmethylene-2(5H)-furanones 7** (table). This result is completely original and can be considered the first report on this type of conversion. Methylene-2(5H)-furanones 7 represent a class of very interesting compounds, including many natural substances of widespread biological activity, as antibiotic, herbicides, plant growth regulators, etc[9].



1

$R_1CH_2\overset{}{\underset{\displaystyle O}{\underset{\|}{C}}}CH_2CH_2COOCH_3$

2



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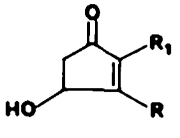

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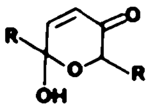

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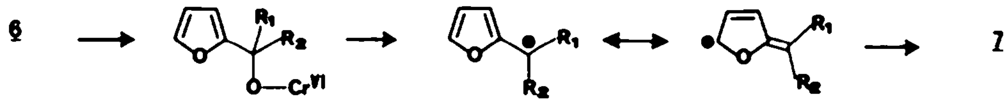
*Many of our results have been recently reviewed[5,6].

Compounds 7 have been named according **Chemical Abstracts nomenclature: see ref. 8)

Although furan derivatives have been widely used for the synthesis of butenolides, up to date there are a few data, concerning their exploitation for the preparation of the title compounds[10,11,16]. Two recent reviews summarize the present methodologies and illustrate the absence of a general synthetic route to this class of compounds; there are various particular methods, which require several steps and sometimes hard reaction conditions[8,17]. Our method, that involves easily available starting materials, represents a new route for the shortness and the simplicity of the procedure.

In every case, a good selectivity in 7 is obtained only when furylcarbinols 6 have two aromatic substituents, although a competitive process of C–C bond fission, leading to carbonyl compound 8, occurs in not negligible manner*. If this condition is not strictly observed, an additional side reaction causes the decrease of the yield of 7; it involves an oxidative ring enlargement of 6 to 2H-pyran-3,6-diones 9, that is the most favoured process when both R_1 and R_2 are alkyl groups (6e)**.

Therefore, it seems conceivable that the conversion of 6 to 7 requires necessarily the formation of a highly stabilized carbenium ion intermediate, probably deriving from the decomposition of an initial chromate ester, that, subsequently, undergoes the nucleophilic attack by the oxidant on 5 position of the furan ring. In fact, the trimethylsilyl derivative of carbinol 6a has been recovered completely unchanged after very prolonged reaction times. The above assumption has been confirmed by submitting the secondary furfuryl alcohols 6f–h to the same treatment. So, while in presence of one only phenyl group (6f) the expected oxidation product 10f is essentially obtained, the further stabilization due to the α-situated heteroatom, allows again the evolution to furanones 7g–h in fair yields***. It has to be noted that this new procedure, besides broadening the synthetic utility of 2-furylcarbinols, has been conveniently exploited for the preparation of the thiophene lactone 7h (Z-isomer), a natural substance isolated from **Chamaemelum Nobile** L.; furthermore, because of its mild and simple conditions, it can be considered a valid alternative to the routes hitherto employed[13,14]. Further studies are in progress for a full explanation of the reaction mechanism of Cr(VI) derivatives on 2-furylcarbinols.



EXPERIMENTAL: M.ps were determined on a Kofler block and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 spectrometer, in 1% CCl_4 solution (unless otherwise indicated) and are given in cm^{-1}. PMR spectra were recorded on a Varian EM-360 spectrometer, usually in CCl_4 solution (unless otherwise indicated), and shifts are reported in ppm (δ) relative to Me_4Si. Mass spectral data were obtained with an AEI-MS 12 spectrometer (70 eV). Carlo Erba precoated silica gel plates were used in TLC. Commercial Merck dry 40–63 μm silica gel was used for column flash chromatography. The starting materials 6 were prepared by reacting the appropriate carbonyl compound with a 20% excess of furyllithium according already reported procedures[15] and they were purified through flash chromatography by eluting with light petroleum/diethyl ether mixtures; their structures were confirmed through IR, PMR and Mass spectral data. Compounds 8 and 10 were identified by comparison with authentic samples.

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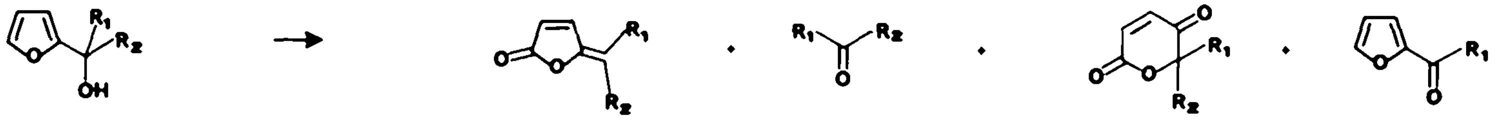
*Analogous formation of ketones, deriving from C-C cleavage, has been observed with the pyridinium chlorochromate oxidation of tertiary α-phenylallylic alcohols[12].

**The formation of the enlargement products could be rationalized through a mechanism, previously described, for the reaction of pyridinium chlorochromate with 2-furylcarbinols.

***The isolation of the only Z-isomer for 7g–h likely derives from the easy E ⟶ Z isomerization, already reported for this kind of compounds[13,14].

TABLE



6 Substrate	time/h	t°C	**7**	**8** Products (yields, %)**	**9**	**10**
a) $R_1 = R_2 = C_6H_5$	6	25	70%	20%	-	-
b) $R_1 = R_2 = p\text{-}C_6H_4OCH_3$	4	25	65%	35%	-	-
c) $R_1 = C_6H_5$; $R_2 = p\text{-}C_6H_4CH_3$	2	25	65% (E+Z)	35%	-	-
d) $R_1 = C_6H_5$; $R_2 = CH_3$	20	25	26% (E/Z 1/4)	35%	31%	-
e) $R_1 = R_2 = -(CH_2)_5-$	18	25	-	1%	99%	-
f) $R_1 = C_6H_5$; $R_2 = H$	24	25	-	25%	-	67% (100%)*
g) $R_1 =$ 2-furyl; $R_2 = H$	6	0	40%	-	-	10%
h) $R_1 =$ 2-(5-methyl)-thienyl; $R_2 = H$	2	-25	40%	-	-	-

*This result has been obtained at -25°C

**All yields refer to isolated chromatographically pure products.

General procedure: Carbinol 6 (5 mmol), dissolved in DMF (5 ml), is rapidly added to a solution of PDC (10 mmol) in DMF (10 ml). The mixture is stirred under the conditions given in table in N_2 atmosphere. Then the mixture is poured into water and extracted many times with diethyl ether. The neutral organic phase is dried over anhydrous Na_2SO_4. The removal of the solvent in vacuo yields a crude product that is purified through flash chromatography by eluting with light petroleum/diethyl ether mixtures.

5-Diphenylmethylene-2(5H)-furanone 7a: needles from hexane, mp 110-112°C (lit. 111°C)[16]. IR: 3050, 3020, 1774, 1750, 1660, 1100, 870, 860. PMR: 7.3-7.0 (m, 11H), 5.92 (d, 1H, J= 5.5 Hz). MS (m/e): 248 (M^+). Anal. calc. for $C_{17}H_{12}O_2$: C 82.24, H 4.87. Found: C 82.18, H 4.91%

5-Di(4-methoxyphenyl)methylene-2(5H)-furanone 7b: 7b is a syrup, whose crystallization failed in spite of several attempts. IR: 2920, 1770, 1738, 1640, 1600, 1100, 880. PMR: 7.5-6.6 (m, 9H), 5.97 (d, 1H, J= 5.5 Hz), 3.82 (s, 3H), 3.80 (s, 3H). MS (m/e): 308 (M^+). Anal. calc. for $C_{19}H_{16}O_4$: C 74.01, H 5.23. Found: C 74.11, H 5.17%.

5-(4-Methylphenyl)phenylmethylene-2(5H)-furanone 7c: 7c has been obtained as an unresolvable mixture of E/Z isomers. IR: 3060, 3025, 1785, 1775, 1749, 1605, 1102, 885. PMR: 7.5-6.9 (m, 10H), 5.92 (s, 1H, J= 5.5 Hz), 2.37 and 2.28 (two s, 3H). MS (m/e): 262 (M^+). Anal. calc. for $C_{18}H_{14}O_2$: C 82.14, H 5.38. Found: C 82.08, H 5.45%.

5-Methylphenylmethylene-2(5H)-furanone 7d: E/Z mixture have been separated through repeated crystallizations from CCl_4. The assignation of the configuration has been achieved through comparison with PMR data already reported for similar compounds[14]. 7d (Z-isomer), plates, mp 97-98°C. IR (ν_{max}, $CHCl_3$): 1770, 1744, 1635, 1110, 900, 885. PMR ($CDCl_3$, δ): 7.78 (d, 1H, J= 5.5 Hz), 7.7-7.3 (m, 5H), 6.17 (d, 1H, J= 5.5 Hz), 2.30 (s, 3H). MS (m/e): 186 (M^+). Anal. calc. for $C_{12}H_{10}O_2$: C 77.40, H 5.41. Found: C 77.33, H 5.43%. 7d (E-isomer), oil. IR 1772, 1744, 1595, 1115, 905, 880. PMR: 7.60 (d, 1H, J= 5.5 Hz), 7.4-7.1 (m, 5H), 5.92 (d, 1H, J= 5.5 Hz), 2.22 (s, 3H). MS (m/e): 186 (M^+). Anal. calc. for $C_{12}H_{10}O_2$: C 77.40, H 5.41. Found: C 77.41, H 5.35%.

Z-5-(2-Furyl)methylene-2(5H)-furanone 7g: needles from CCl_4, mp 77-79°C. IR: 3100, 3040, 1785, 1782, 1632,1098, 882, 877. PMR ($CDCl_3$, δ): 7.34 (m, 1H), 7.23 (d, 1H, J= 5.5 Hz), 6.89 (d, 1H, J= 4 Hz), 6.39 (dd, 1H, J_1= 4 Hz, J_2= 1 Hz), 6.04 (d, 1H, J= 5.5 Hz), 5.94 (s, 1H). MS (m/e): 162 (M^+). Anal. calc. for $C_9H_6O_3$: C 66.67, H 3.73. Found: C 66.77, H 3.71%.

Z-5-(5-Methyl-2-thienyl)methylene-2(5H)-furanone 7h: plates from hexane, mp 114-116°C (lit. 117°C)[13]. IR: 1784, 1752, 1640, 1100, 878. PMR: 7.42 (d, 1H, J= 5.5 Hz), 7.12 (d, 1H, J= 4 Hz), 6.7 (m, 1H), 6.20 (s, 1H), 6.12 (d, 1H, J= 5.5 Hz), 2.62 (s, 3H). MS (m/e): 192.26 (M^+), in agreement with the formula $C_{10}H_8O_2S$).

2-Methyl-phenyl-2H-pyran-3,6-dione 9d: plates from hexane, mp 87-88°C. IR (ν_{max}, $CHCl_3$): 1725, 1697, 1616, 1290, 1085, 850. PMR ($CDCl_3$, δ): 7.32 (s, 5H), 6.78 (d, 1H, J= 10 Hz), 6.60 (d, 1H, J= 10 Hz), 1.87 (s, 3H). MS (m/e): 202 (M^+). Anal. calc. for $C_{12}H_{10}O_3$: C 71.28, H 4.98. Found: C 71.18, H 5.03%.

2,2-Pentamethylene-2H-pyran-3,6-dione 9e: plates from CCl_4, mp 82-84°C. IR: 2930, 2850, 1732, 1690, 1618, 1300, 1105, 1000. PMR: 6.80 (d, 1H, J= 10 Hz), 2.2 (m, 4H), 1.7 (m, 6H). MS (m/e): 180 (M^+). Anal. calc. for $C_{10}H_{12}O_3$: C 66.65, H 6.71. Found: C 66.67, H 6.62%.

REFERENCES

1) K.G. Lewis, J. **Chem. Soc.**, 531 (1957)
2) G. Piancatelli, A. Scettri, S. Barbadoro, **Tetrahedron Lett.**, 3555 (1976)
3) N.L. Holder, **Chem. Rev.**, 82, 287 (1982)
4) G. Piancatelli, A. Scettri, M. D'Auria, **Tetrahedron Lett.**, 2199 (1977)
5) G. Piancatelli, **Heterocycles**, 19, 1735 (1982)
6) G. Piancatelli, A. Scettri, M. D'Auria, **Synthesis**, 245 (1982)
7) E.J. Corey, G. Schmidt, **Tetrahedron Lett.**, 399 (1979)
8) Y.S. Rao, **Chem. Rev.**, 76, 625 (1976)
9) A.A. Avetisyan, M.T. Dangyan, **Russ. Chem. Rev.**, 46, 643 (1977)
10) M. D'Auria, G. Piancatelli, A. Scettri, **Tetrahedron**, 36, 3071 (1980)
11) G.A. Kraus, H. Sugimoto, J. **Chem. Soc.**, **Chem. Comm.**, 30 (1978)
12) W.G. Dauben, D.M. Michno, J. **Org. Chem.**, 42, 682 (1977)
13) F. Bohlmann, C. Zdero, **Chem. Ber.**, 99, 1226 (1966)
14) K. Yamada, Y. Togawa, T. Kato, Y. Hirata, **Tetrahedron**, 27, 5445 (1971)
15) V. Ramanathan, R. Levine, J. **Org. Chem.**, 27, 1216 (1962)
16) H. Gilman, R.A. Franz, A.P. Hewlett, G.F. Wright, J. **Am. Chem. Soc.**, 31, 3 (1950)
17) S. Kano, S. Shibuya, T. Ebata, **Heterocycles**, 14, 661 (1980)