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THE SYNTHESIS OF REGIOISOMERS OF DEHYDROACETIC ACIDS

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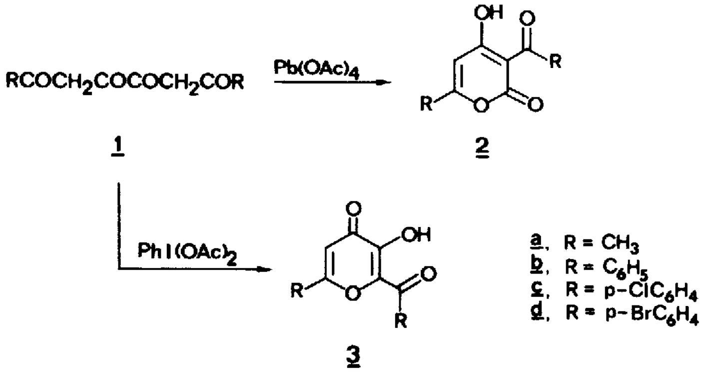
*Summary — The method for the synthesis of new 2-acyl-6-alkyl(aryl)-3-hydroxy-4*H*-pyran-4-ones (3), is described, involving the oxidation of 1,3,4,6-tetraketones 1 with iodosobenzene diacetate.*

The regiospecific dimerization of diketene to dehydroacetic acid (2a) was observed soon after the first announcement of the discovery of diketene[1]. In spite of the interest in the biogenetic-type syntheses of polyketides[2], it has not been possible so far to prepare the regioisomer 3a. The oxidative cyclization of oxalyldiacetone (1a) promised access to 3a, however, the reaction with lead tetraacetate proceeded with rearrangement to give only dehydroacetic acid (2a)[3,4].

A convenient solution to the problem was found when conducting the oxidation of tetraketones 1 with iodosobenzene diacetate, opening the way to the first synthesis of regioisomers 3 of dehydroacetic acids.



To a stirred suspension of tetraketone[5] (1, 0.05 mol) in acetic acid (50 ml), iodosobenzene diacetate[6] (0.1 mol) was gradually added and stirring was continued for 10-15 h (iodimetric test). After removal of the solvent the product was crystallized from ethanol. The structure was assigned on the basis of chemical and spectroscopical evidence, and results for individual compounds 3a-d are summarized in the Table. The straightforward structural assignment to the regioisomer 3a of dehydroacetic acid can be made from its ^{1}H NMR spectrum in deuteriochloroform: a broad signal at δ 9.78 (exchangeable with D_2O), the allylic AX_3 pattern (^4J 0.7) at δ 6.31 (q,=CH-) and 2.41 (d,CH_3), and a three-proton singlet at δ 2.60 (CH_3), were consistent with the 2-acetyl-3-hydroxy-6-methyl-4*H*-pyran-4-one structure.

Table. 2-Acyl-6-alkyl(aryl)-3-hydroxy-4*H*-pyran-4-ones

3[a]	Yield[b]	m.p.[c]	λ*max* (nm)[d]	ν*max* (KBr), cm^{-1}	M$^+$(m/e)[e]	δH(5)[f]
a	83%	147°	235,300	3225,1680,1632,1618	168	6.31q
b[g]	33%	177°	265,300,315	3200,1677,1626,1620	292	6.99s
c	61%	219°	272,310-320	3100,1660,1637,1620	360,362	6.07s
d	47%	199°	274,310-320	3090,1661,1638,1622	448,450,452	6.98s

a) Satisfactory analytical data (±0.4% for C,H,Br,Cl,and N) were obtained for all new compounds and their derivatives. *b)* Yields are based on recrystallized products (EtOH). *c)* M.ps. are uncorrected. *d)* Methanolic solution. *e)* Spectra of 3 displayed intense peaks due to M-CO, M-COR, $RC_3H_2O_2$, RCO, and R. An equivalent of diketene (RCOCH=C=O) was produced under electron impact by the retro-Diels-Alder reaction. *f)* $CDCl_3$. *g)* An unstable isomeric compound, $C_{18}H_{12}O_4$, m.p. 165°, was also obtained in a 30% yield. Its structure is under investigation. Derivatives of 3b: boron trifluoride-catalysed reaction of 3b with ethereal diazomethane afforded the corresponding 3-methoxy derivative, m.p. 144°(MeOH), MS,m/e 306(M$^+$); ν*max* (KBr) 1676,1638,1623/cm; λ*max* (MeOH) 265,290 nm; ^{1}H NMR ($CDCl_3$), δ 8.0-7.4(m,10H),6.93(s,1H),3.92(s,3H). Bromination of 3b in chloroform gave pale yellow needles of 5-bromo derivative in a 40% yield, m.p. 155°(EtOH), MS, m/e 370,372(M$^+$); ν*max* (KBr) 1651,1647,1566/cm; ^{1}H NMR ($CDCl_3$), δ 10.8(br,1H),8.1-7.4(m,10H). Mono-2,4-dinitrophenylhydrazone of 3b, red needles, m.p. 248-50°.

Although iodosobenzene diacetate and lead tetra-acetate are reagents with similar properties, tetraketones 1 were oxidized in a different manner. The question of which is the controlling factor of the two possible reaction paths remains unexplained. A possible explanation might be found in the analogy with the oxidative rearrangements of aurones[7]. It seems probable that oxidations of 1 may involve the same type of hydroxyfuranone intermediate[4,8], from which by migration of suitable bonds the products 2 or 3 may be derived. Studies directed toward the identification of such intermediates are currently in progress[9].

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