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SYNTHESIS OF γ-METHYLENE BUTYROLACTONES (4-PENTEN-4-OLIDES)

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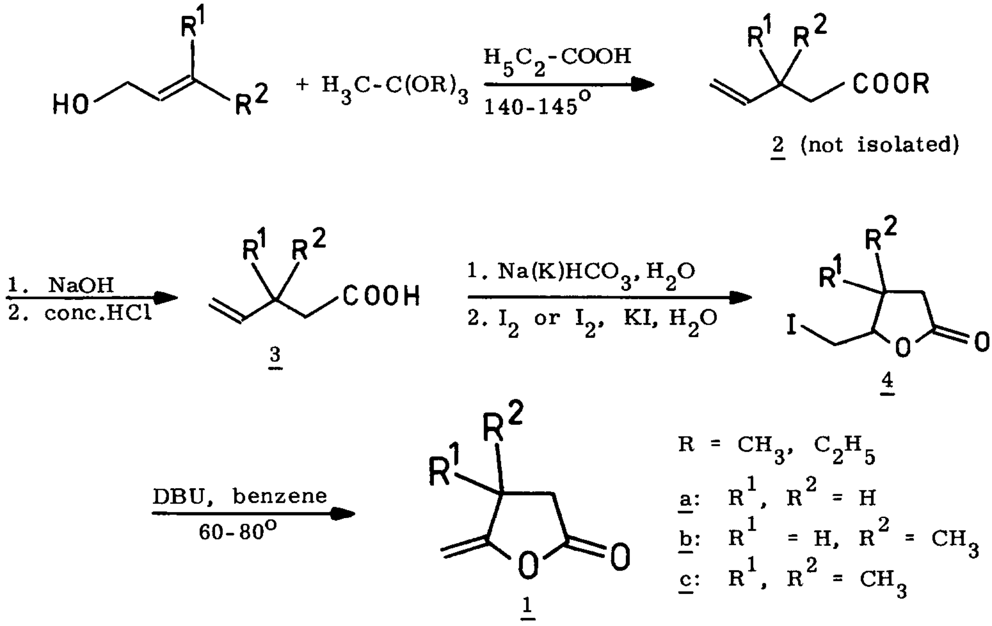
The synthesis of γ-alkylidene butyrolactones (4-alken-4-olides) hitherto has received scarce attention [1,2], contrary to the case with other unsaturated butyrolactones [3]. This is the more surprising, as 4- and 6-membered counterparts are common and useful synthetic intermediates [4]. The following note describes a general route to 5-unsubstituted members of this class 1.

The reaction sequence starts with allylic alcohols that are converted into 4-pentenoic acids by orthoester Claisen rearrangement/hydrolysis, and is followed by iodolactonization and dehydroiodination steps. Overall yields of the sequence detailed below range from 48 to 56%.



R = CH_3, C_2H_5

a: R^1, R^2 = H

b: R^1 = H, R^2 = CH_3

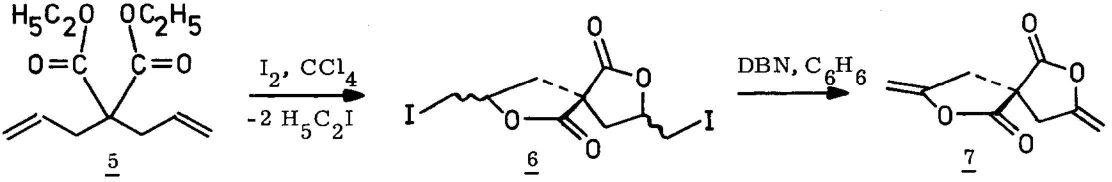
c: R^1, R^2 = CH_3

For the preparation of 4-pentenoic acids the original procedure [5a] (7 equiv. of orthoacetate; distillative work-up) was modified in view of the low molecular weight rearrangement products formed [6]. For example, a mixture of allyl alcohol with one equiv. of trimethyl orthoacetate and 0.06 equiv. of propionic acid was gradually heated to 130° (1 equiv. of methanol collected), then kept at 140-145° for 3 hrs. until distillation of methanol had ceased. 4-Pentenoic acid 3a was isolated after washing (water; dil. $NaHCO_3$), alkaline hydrolysis (2 equiv. of 15 n NaOH, 1 hr reflux), acidification (conc. HCl, 0°), ether extraction and distillation (70.5% yield; 2 mole scale). 3b and 3c were obtained similarly (60.5 and 69.5%, resp.); in the latter case 2 equiv. of triethyl orthoacetate were used and heating was effected for 4 days with daily addition of 5 drops of catalyst [5b] (0.1 mole scale).

4-Pentenoic acids 3 were iodolactonized in almost quantitative yield by modifications of the procedures [7] recorded previously. The reactions were performed at room temperature, one equiv. of iodine dissolved in KI solution or neat (more economical, identical yield) - was added to an aqueous mixture of 3 with sodium or potassium bicarbonate within ~1 hr. After another hour of stirring, a slight excess of iodine was added to ensure completion of the reaction (colour). After work-up (removal of excess iodine with some drops of $Na_2S_2O_4$ solution, $CHCl_3$ extraction, removal of solvent in vacuo) crude iodolactones 4 remained as colourless to pale-yellow oils (98-99% yield) [8, 9].

Hydrogen iodide elimination from 4a critically depends on the reaction conditions; optimum results (66-70% yield) have been found with diazabicycloundecene (or -nonene) in benzene at 60° for 2 hrs. (5-50 mmole scale). Removal of salts, washing with dil. HCl, drying, evaporation (at ~50 mm Hg) and Kugelrohr distillation finally affords 1a [10]. The synthesis of 1b, and 1c, is less critical; the latter, f.e., is obtained as above by base treatment at 80° for 5 hrs. (for yields and data see table 1).

We have developed an alternative procedure to effect iodolactionization under non-aqueous conditions which uses alkyl 4-pentenoates. Esters 2a (R = C_2H_5) and 5 diethyl diallylmalonate) on treatment with equivalent amounts of iodine in CCl_4 smoothly cyclize [12-14] (2a: reflux, 24 hrs., 80% of 4a; 5: 4 days, 40°, 75% of 6). Twofold dehydroiodination from 6 under carefully optimized conditions (2.015 equiv. DBN, 20 min. at 60°) furnishes the spiro-bislactone 7 (87.5%) [9].



Thus 4-penten-4-olides, substituted at positions 2 or 3, are readily accessible from cheap starting materials. A further point to be stressed is, that the elimination conditions elaborated permit to isolate γ-methylene butyrolactones virtually free from their endocyclic double bond isomers, a problem which has hampered the success of previous attempts[1a,2b].

Table 1, γ-Methylene Butyrolactones

Compound	yield[a] [%]	b.p. [°C/mm]	IR[b] [cm^{-1}]		^1H NMR[c], δ [ppm]		^{13}C NMR[d], δ [ppm]		
			C=O	C=C	H_{syn}	H_{anti}	C-1	C-4	C-5
1a	66-70	~80/17	1815	1667	4.7	4.25	174.8	155.8	89.0
1b	77-83	~40/0.015	1815	1668	4.65	4.25	173.6	161.9	87.5
1c	83	50-60/0.35	1805	1669	4.55	4.2	172.3	166.0	85.7
7	87.5	92 (m.p.)	1795	1677	4.95	4.45	171.1	151.7	90.8

a) purity of 1a-1c ≥98% (GLC rel. peak area).
b) 5-10% sol. in CCl_4 for 1a, 1b; neat for 1c; 7 in KI.
c) in CCl_4, TMS internal standard; 7 in $CDCl_3$.
d) CFT-20, $CDCl_3$; δ_{TMS} = 0 ppm.

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References and Notes

1. a) J.P.Wineburg, C.Abrams, and D.Swern, J.Heterocycl.Chem. 12, 749 (1975); b) H.Hart and E.-M.Shih, J.Org.Chem. 41, 3377 (1976); c) J.Haslouin and F. Rouessac, Tetrahedron Letters, 4651 (1976).
2. For 5-substituted examples see a) W.Parker and R.Ramage, J.Org.Chem. 28, 1722 (1963); b) Ger.Pat. 1276029 (1968), BASF (N.v. Kutepow, F.Meier, and D. Neubauer); C.A. 70, 37229 (1969); S.Afric.Pat. 670135 (1968), ICI (P.Hayden); C.A. 70, 114637 (1969); c) J.Auerbach and S.M.Weinreb, J.Org.Chem. 40, 3311 (1975); d) D.S.C.Black et al., J.Chem.Soc. Perkin Trans.I, 1944 (1976).
3. Y.S.Rao, Chem.Reviews 76, 625 (1976); H.Kröper in Houben-Weyl, Bd. VI/2, Kap. Lactone, p. 561-852 (834 ff.), G.Thieme Verlag, Stuttgart 1963; G.Ohloff, Fortschr.Chem.Forsch. 12, 186 (1969); P.A.Grieco, Synthesis, 67 (1975).
4. See f.e. J.Weill-Raynal, Synthesis, 49 (1969); J.Ficini, Tetrahedron 32, 1449, partic. 1458 f. (1976).
5. a) W.S.Johnson et al., J.Amer.Chem.Soc. 92, 741 (1970); b) alkylation to a quarternary carbon atom; for similar examples c.p. J.H.Babler, Tetrahedron Letters, 2045 (1976); J.Ficini and J.d'Angelo, Tetrahedron Letters, 2441 (1976).
6. A large excess of trialkyl orthoacetate [5a] is not necessary nor advisable in the cases described here: a) the allylic alcohols used are easily available, cheap material; b) orthoacetate and the products formed have similar m.w.; distillative as well as hydrolytic work-up is complicated with a large excess of orthoacetate present.
7. a) J.Bougault, Ann.Chim.phys. 14, 145 (1908); 15, 296 (1908); b) E.E.Van Tamelen and M.Shamma, J.Amer.Chem.Soc. 76, 2315 (1954); c) M.de Moura Campos and L.do Amaral, Arch.Pharm. 298, 92 (1956).
8. a) Pure according to ^{1}H NMR; the crude products 4 give correct elemental analysis; b) contrary to literature reports [7], 4a may be distilled unchanged (Kugelrohr, ~150°/15 Torr) leaving almost no residue. Compounds 4 are stable for months when kept at 0° in the dark; c) previously reported yields range from 40 [7b] to 88.5% [7c].
9. Compounds 1, 3-7 have been fully characterized by correct elemental analyses, IR, ^{1}H and ^{13}C NMR spectra.
10. 1a has been synthesized recently [1c,11]; the other 4-penten-4-olides 1b, 1c, and 7 are, to the best of our knowledge, new compounds.
11. Prepared from dehydronorcampher in three steps (last step thermolytic retro-Diels-Alder reaction); overall yield 43%.
12. Cp. B.Giese, Chem.Ber. 108, 2978, 2998 (1975).
13. For related bromolactonizations see R.Fittig and H.Hjelt, Liebigs Ann.Chem. 216, 52 (1883); R.T.Arnold, M.de Moura Campos, and K.L.Lindsay, J.Amer. Chem.Soc. 75, 1044 (1953).
14. Cp. O-alkyl cleavage of esters, ethers with trimethylsilyl iodide: T.L.Ho and G.A.Olah, Angew.Chem. 88, 847 (1976); Angew.Chem.Int.Edit.Engl. 15, 744 (1976); M.E.Jung and M.A.Lyster, J.Amer.Chem.Soc. 99, 968 (1977) and lit.cited.