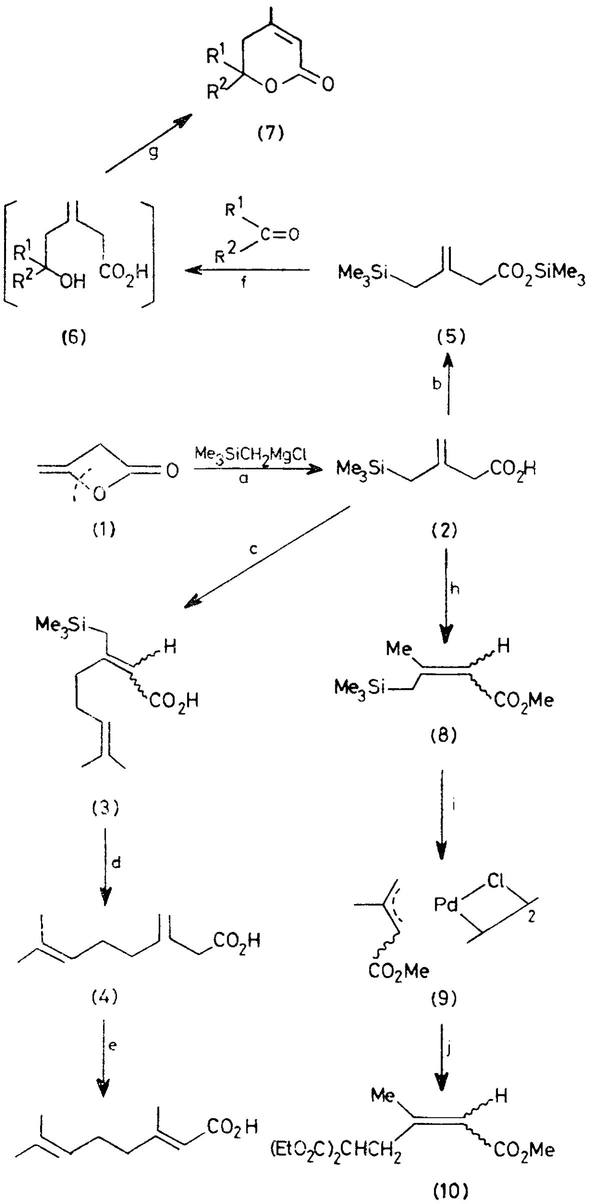
Diketen as a Butenoic Acid Synthon in Regioselective Olefin Syntheses

By KENJI ITOH,* MITSUYO FUKUI, and YASUO KURACHI
(*Department of Synthetic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho, Chikusa, Nagoya* 464, *Japan*)

Summary The adduct (**2**) between diketen (**1**) and Me_3SiCH_2MgCl is a versatile methylbutenoic (isoprenoid) acid synthon in allylation with prenyl bromide, in δ-lactone formation with several carbonyl compounds, and in palladium-mediated alkylation.



SCHEME. a, $NiCl_2$ (catalytic quantity) in THF (95% yield); b, $(Me_3Si)_2NH$ in refluxing Et_2O (78%); c, 1, $2LiNPr^i_2$; 2, CuI; **2**, $Me_2CC{=}HCH_2Br$ at −78 °C in n-hexane–THF (5:1 v/v) then 30 °C overnight: (**3**) (82%; E:Z = 75:25); d, 2MeONa in refluxing aq. MeOH (>95%); e, $LiN(SiMe_3)_2$ + $Me_2NCH_2CH_2NMe_2$ at room temp. (60%; E:Z = 91:9); f, $TiCl_4$ in CH_2Cl_2 at −78 °C then at room temp.; g, 3N HCl at 90 °C for 0·5–1 h: $R^1 = Pr^n$, R^2 = H (81%); $R^1 = Pr^i$, R^2 = H (79%); $R^1 = Bu^i$, R^2 = H (78%); $R^1 = R^2$ = Me (80%); $R^1, R^2 = -[CH_2]_4-$ (78%) h, 1, ref. 2; 2, CH_2N_2 in Et_2O at room temp. (**8**): (>95%; E:Z = 94:6); i, Na_2PdCl_4 in refluxing MeOH: (**9**) (85%); j, $NaCH(CO_2Et)_2$ in THF–Me_2SO (**10**): (83%; E:Z = 63:37).

DIKETEN (**1**) has been used as an acetyl keten or butane-1,3-dione equivalent in organic synthesis.[1] It could act as a but-3-enoic acid synthon, $CH_2{=}C^+{-}CH_2CO_2^-$, if it were cleaved at the vinyl–oxygen bond by a carbanionic nucleophile. We now report several regio- and stereo-selective olefin syntheses with the diketen adduct (**2**) which was obtained readily by nickel-catalysed alkylation of (**1**)[2] with Me_3SiCH_2MgCl. The double bond of (**2**) is the regioselective reaction site for the alkylations summarized in Scheme.

Treatment of (**2**) with excess of lithium di-isopropylamide followed by transmetallation with CuI[3] in tetrahydrofuran (THF)–n-hexane gave the dicopper dienolate of (**2**), which was treated with prenyl bromide. Hydrolytic work-up yielded (**3**), with no transposed product. Desilylation of (**3**) with sodium methoxide in aq. methanol gave (**4**), which rearranged to geranic acid with strong base.[4] An analogous reaction sequence of (**2**) with geranyl chloride yielded farnesoic acid in 35% overall yield.

Recently, allylsilanes were reported to be highly versatile in the allylation of carbonyl compounds under Lewis acid catalysis;[5] however, little information is available on functionalized allylsilane derivatives. The adduct (**2**) is an attractive reagent in this context, because it contains an isoprenoid skeleton. The acidic proton of (**2**) was protected readily by trimethylsilylation with hexamethyldisilazane to give (**5**), b.p. 67 °C at 1·5 Torr. Addition of various aldehydes or ketones to (**5**) in the presence of $TiCl_4$ (1 mol. equiv.) gave the hydroxy-acids (**6**) which, without isolation, were treated directly with 3N HCl at 90 °C. Cyclization of (**6**) and double bond migration occurred simultaneously to yield the corresponding conjugated δ-lactones (**7**) in fair yields.

The methyl ester (**8**) of the conjugated acid isomer of (**2**),[2] b.p. 46—48 °C at 1·0 Torr, was converted[6] into the η^3-allylpalladium complex (**9**) with fair retention of configuration [(**8**), E:Z 94:6 and 71:29, gave (**9**), *syn*:*anti* 84:16 and 63:37, respectively]. Complex (**9**) reacted with diethyl sodiomalonate[7] to give (**10**), E:Z 63:37.

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