

## Diketen as a Butenoic Acid Synthone in Regioselective Olefin Syntheses

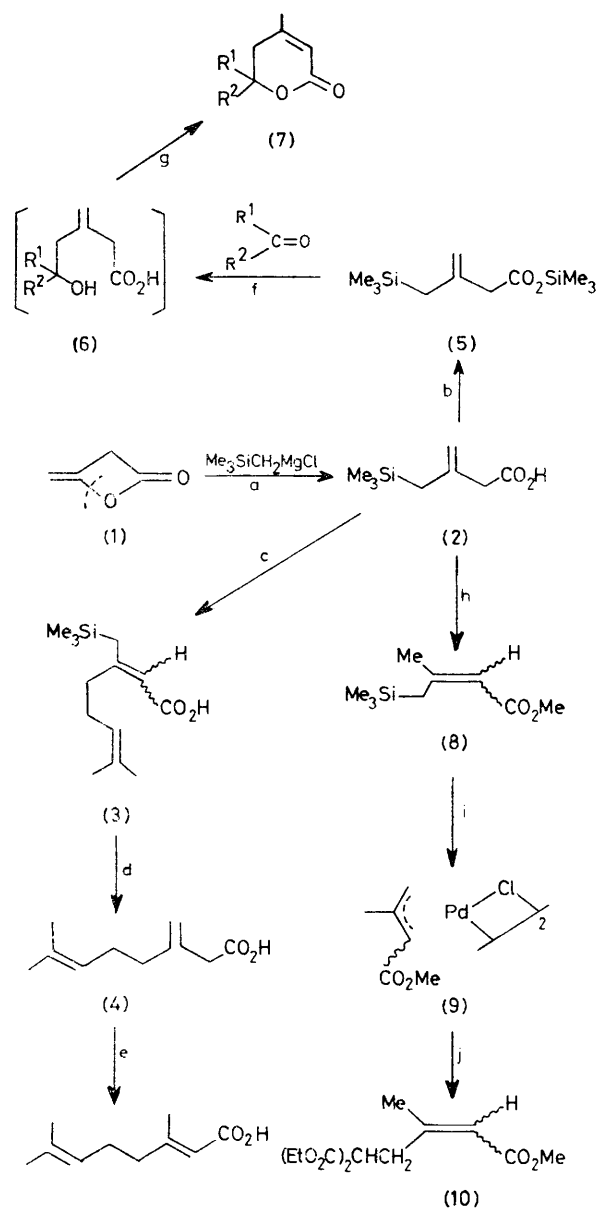
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**Summary** The adduct (**2**) between diketen (**1**) and  $\text{Me}_3\text{-SiCH}_2\text{MgCl}$  is a versatile methylbutenoic (isoprenoid) acid synthon in allylation with prenyl bromide, in  $\delta$ -lactone

formation with several carbonyl compounds, and in palladium-mediated alkylation.

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SCHEME. a,  $\text{NiCl}_2$  (catalytic quantity) in THF (95% yield); b,  $(\text{Me}_3\text{Si})_2\text{NH}$  in refluxing  $\text{Et}_2\text{O}$  (78%); c, 1,  $2\text{LiNPr}_2$ ; 2,  $\text{CuI}$ ; 2,  $\text{Me}_2\text{C}=\text{HCH}_2\text{Br}$  at  $-78^\circ\text{C}$  in n-hexane-THF (5:1 v/v) then  $30^\circ\text{C}$  overnight: (3) (82%;  $E:Z = 75:25$ ); d,  $2\text{MeONa}$  in refluxing aq.  $\text{MeOH}$  (>95%); e,  $\text{LiN}(\text{SiMe}_3)_2 + \text{Me}_2\text{NCH}_2\text{CH}_2\text{NMe}_2$  at room temp. (60%;  $E:Z = 91:9$ ); f,  $\text{TiCl}_4$  in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ\text{C}$  then at room temp.; g,  $3\text{N HCl}$  at  $90^\circ\text{C}$  for 0.5–1 h:  $\text{R}^1 = \text{Pr}^n$ ,  $\text{R}^2 = \text{H}$  (81%);  $\text{R}^1 = \text{Pr}^i$ ,  $\text{R}^2 = \text{H}$  (79%);  $\text{R}^1 = \text{Bu}^i$ ,  $\text{R}^2 = \text{H}$  (78%);  $\text{R}^1 = \text{R}^2 = \text{Me}$  (80%);  $\text{R}^1, \text{R}^2 = -[\text{CH}_2]_n-$  (78%) h, 1, ref. 2; 2,  $\text{CH}_2\text{N}_2$  in  $\text{Et}_2\text{O}$  at room temp. (8): (>95%;  $E:Z = 94:6$ ); i,  $\text{Na}_2\text{PdCl}_4$  in refluxing  $\text{MeOH}$ : (9) (85%); j,  $\text{NaCH}(\text{CO}_2\text{Et})_2$  in  $\text{THF}-\text{Me}_2\text{SO}$  (10): (83%;  $E:Z = 63:37$ ).

DIKETEN (1) has been used as an acetyl keten or butane-1,3-dione equivalent in organic synthesis.<sup>1</sup> It could act as a but-3-enoic acid synthon,  $\text{CH}_2=\text{C}^+-\text{CH}_2\text{CO}_2^-$ , 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)<sup>2</sup> with  $\text{Me}_3\text{SiCH}_2\text{MgCl}$ . 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 transmetalation with  $\text{CuI}$ <sup>3</sup> 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.<sup>4</sup> An analogous reaction sequence of (2) with geranyl chloride yielded farnesic acid in 35% overall yield.

Recently, allylsilanes were reported to be highly versatile in the alkylation of carbonyl compounds under Lewis acid catalysis;<sup>5</sup> 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.  $67^\circ\text{C}$  at 1.5 Torr. Addition of various aldehydes or ketones to (5) in the presence of  $\text{TiCl}_4$  (1 mol. equiv.) gave the hydroxy-acids (6) which, without isolation, were treated directly with  $3\text{N HCl}$  at  $90^\circ\text{C}$ . Cyclization of (6) and double bond migration occurred simultaneously to yield the corresponding conjugated  $\delta$ -lactones (7) in fair yields.

The methyl ester (8) of the conjugated acid isomer of (2),<sup>2</sup> b.p.  $46-48^\circ\text{C}$  at 1.0 Torr, was converted<sup>6</sup> into the  $\eta^3$ -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<sup>7</sup> to give (10),  $E:Z$  63:37.

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