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A METHOD FOR THE SYNTHESIS OF β-ALKYLIDENEBUTYROLACTONES, 3-SUBSTITUTED BUTENOLIDES, AND 3-SUBSTITUTED FURANS

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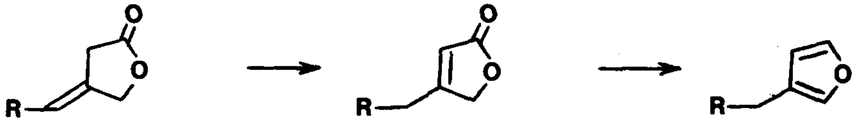
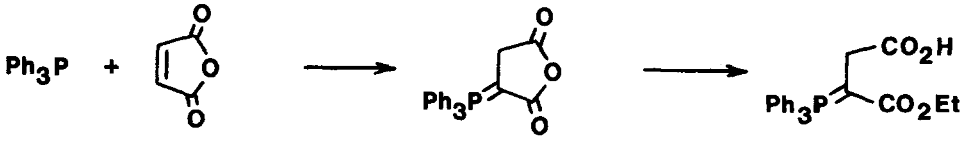
A synthetic project currently underway in our laboratory required that we devise a general synthesis of β-alkylidenebutyrolactones (1). Although we have found examples of this class of compound in the literature,[1] general methods of syntheses do not appear to exist. Such compounds would seem valuable, not only for our own immediate purposes, but also because they should be readily convertible into 3-substituted butenolides,[2] and thence by reduction, into 3-substituted furans.[3]



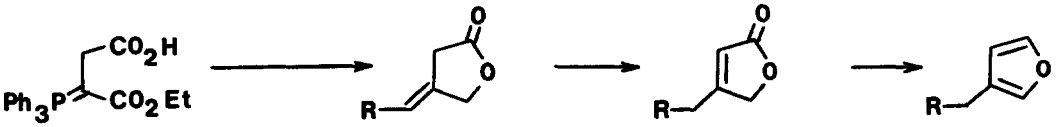
1 2 3

It has been known for some years[4] that the reaction of triphenylphosphine with maleic anhydride produces the succinylidene phosphorane, 4, which will undergo ethanolysis to yield the half ester acid 5. The structure of this remarkable carboxy phosphorane has been established by Ramage[5] who further showed,[6] in his elegant synthesis of lysergic acid, that dialkylsuccinylidenephosphoranes prepared from 5 will undergo Wittig reactions.



4 5

We reasoned that, if 5 itself would take part in Wittig reactions, the products might undergo selective reduction at the ester grouping to yield, after lactonization, compounds of the desired type. This has proved to be the case. Although 5 is somewhat thermally sensitive, we have found that when pure, it will react with aldehydes in benzene slurry (room temp;40 hr) to produce good yields of the olefins. Reduction of the product ester can be effected with a two-fold excess of $NaAlEt_2H_2$ in ether (0°; 2 hr) and, after a short reflux of the resultant hydroxy acid in benzene with a trace of p-toluenesulfonic acid, β-alkylidenebutyrolactones are produced. As expected, these lactones are isomerized to their conjugated isomers on slow silica gel chromatography or on standing overnight at room temperature with neutral Al_2O_3 in benzene. Reduction[7] with diisobutylaluminum hydride at -40° then furnishes the furans. Some of our results are presented in the Table.



RCHO	% Alkylidenelactone	% Butenolide	% Furan
C_6H_5CHO	65	70	85
n-$C_6H_{13}CHO$	78	80	95
$(CH_3)_2CCHCH_2CHO$	60	70	85

TABLE: Preparation of Butenolides and Furans from Aldehydes
(All compounds were fully characterized by their special properties. The yields given refer to isolated products.)

As can be seen from the examples in the table, products from both alkyl and aryl substituted aldehydes are obtained in good yields at all stages in the sequence. The third example is particularly interesting because the ultimate product is perillene,[8] a naturally occurring furan isolated from a species of fire ant, Lasius (Dendrolasius) fulginosus Latr.[9] Although the yield in the Wittig reaction is moderate in this case, undoubtedly due to the sensitivity of the starting 4-methyl-3-pentenal[10] towards conjugation, the fact that the reaction occurs at all attests to the mildness and generality of the scheme. We therefore feel that this new method for the preparation of 3-substituted butenolides and 3-substituted furans should be of value in organic synthesis.[11]

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10. 4-methyl-3-pentenal was prepared by oxidation of the corresponding alcohol (pyridinium chlorochromate; excess NaOAc buffer; CH_2Cl_2; -15° for 8 hr). The product consisted of an approximately 3:1 mixture of the desired unconjugated aldehyde plus conjugated isomer. This 3:1 mixture was carried through the sequence, and purification of the product was effected at the β,γ unsaturated lactone stage. The yields quoted in the table are corrected to take this factor into account.

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