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THE PREPARATION OF A NOVEL 3-OXO-CYCLOPENTEN-2-PHOSPHONATE DERIVATIVE, USEFUL INTERMEDIATE FOR 2-ALKYL-SUBSTITUTED CYCLOPENTENONES SYNTHESIS.

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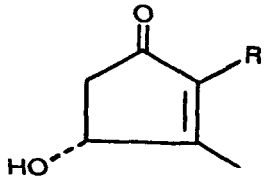
Summary: Starting from a phosphonyl-furylcarbinol derivative, diethyl(1-methyl--3-oxo-cyclopenten-2-yl)phosphonate, first example of oxocyclopentenyl-phosphonate and useful intermediate for the synthesis of 2-alkylsubstituted cyclopentenones, has been prepared.

There is continuing interest in the quest for new synthetic organophosphonates since many phosphonate-containing molecules have been observed to exhibit a variety of interesting biologically properties including antibiotic, antiviral, as well as insecticidal and herbicidal activity[1]. On the other hand, cyclopentenone molecule is present in numerous natural products as major structural feature and some of them, rethrolones 1 in particular, are of great interest for the insecticides industy.

In connection with a program directed toward the synthesis of physiologically active phosphonates[2], we considered the preparation of a molecule such as 2, bearing a phosphonyl group on a cyclopentenone skeleton closely related to rethrolone framework, to be of interest. Such a molecule could well be also a key intermediate for the synthesis of several biologically active natural products, like prostaglandins and pyrethrins themselves.

In this letter we wish to descibe an effective preparation of the novel 3-oxo-cyclopenten-2-phosphonate 3 starting from readily available carbinol 4 and its useful application for the synthesis of 2-alkyl-substituted cyclopentenone derivatives.

Compounds like 3 , combining the phosphonyl and the oxo-cyclopentenyl groups in the same structure, were hitherto unknown; considering the increasing



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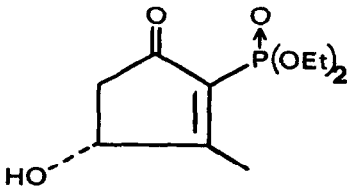

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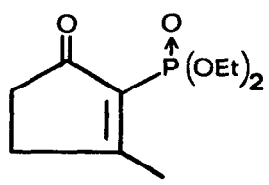

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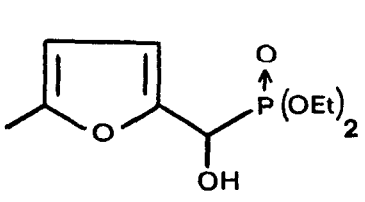
industrial importance assumed during recent years by both ketophosphonates and 2-substituted cyclopentenones[3], the preparation of compounds described in this letter results exceedingly interesting for a large group of researchers.

The starting diethyl-2(5-methyl)furyl-hydroxymethylphosphonate 4 [δ:6.38 (m, 1H), 5.90 (m, 1H), 4.92 (d, 1H, >C<u>H</u>-P, J = 13 Hz), 4.20 (m, 4H, 2-OC<u>H</u>$_2$CH$_3$), 2.32 (s, 3H, -CH$_3$), 1.30 (m, 6H, 2 -OCH$_2$C<u>H</u>$_3$); ν_{max}: 3580, 3360, 1060, 1025] [4], was prepared in quantitative yield[5] by a base-catalyzed addition of 5-methyl-2--furaldehyde to diethyl-hydrogenphosphite[6]. When 4 was treated with 1.25 N HCl in acetone at 58° for 8 hr, diethyl(hex-3-en-2,5-dione-1-yl)phosphonate 6 [CD_3COCD_3, δ: 7.00, 6.90 (each d, 1H, J = 16.5 Hz), 4.20 (quintet, 4H, 2-OC<u>H</u>$_2$--CH$_3$, J = 7 Hz), 3.45 (d, 2H, -CH$_2$-P, J = 23 Hz), 2.35 (s, 3H, -COCH$_3$), 1.30



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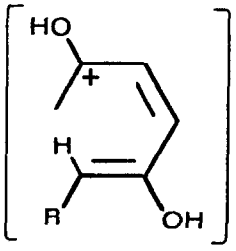

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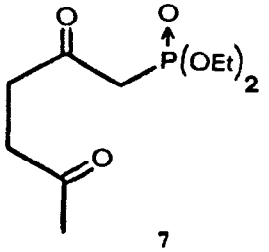

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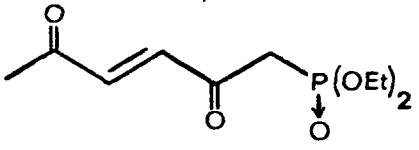

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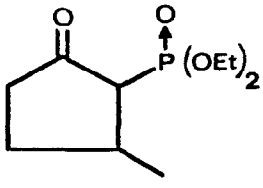

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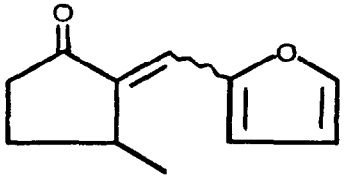

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(t, 6H, 2-$OCH_2\underline{CH}_3$, J = 7 Hz); ν_{max}: 1690, 1580, 1260, 1050, 985] was obtained (86%) in trans stereoisomeric configuration.

Since α,β-unsaturated-γ-dicarbonyl compounds have never been isolated before in acid-catalyzed rearrangements of 2-furyl-carbinols, this finding bears an effective contribution in clarifying the mechanism of these rearrangements that, as known, efford cyclopentenones directly[7]. In fact, the protolytic cleavage of 4 pointed out the key role of the intermediate 5 (R = $-PO(OEt)_2$) which was not stable enough to undergo an electrocyclic reaction because of the strongly electron-withdrawing effect of diethylphosphonyl group. Therefore 5 efforded 6 after eliminating a proton. As reported for similar processes, 6 was first obtained in cis configuration and then, cis-trans isomerisation, catalysed by acid and heating, occurred[8]. On the other hand, this facile preparation of 6 makes such procedure effectually employable for preparing in high yields β-keto-hexyl-phosphonates, greatly useful in the synthesis of prostaglandins.

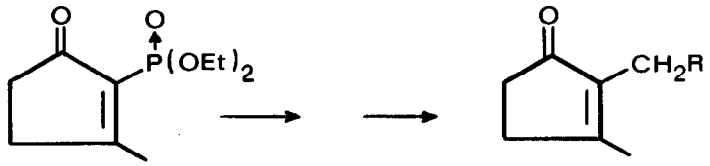
Dione 6 was transformed into its saturated analog, diethyl(hex-2,5-dione-1-yl)phosphonate 7 [δ: 4.20 (quintet, 4H, 2-$OC\underline{H}_2CH_3$, J = 7 Hz), 3.15 (d, 2H, $-CH_2$-P, J = 24 Hz), 3.05-2.60 (m, 4H, $-CH_2CH_2-$), 2.18 (s, 3H, $-COCH_3$), 1.30 (t, 6H, 2-$OCH_2C\underline{H}_3$, J = 7 Hz); ν_{max}: 1715, 1020, 975] by treatment with sodium iodide and 2 N hydrochloric acid in acetone for 20 min[9]. When a benzenic solution of 7 was stirred overnight at 35° with basic alumina[10], diethyl(3-oxo-1-methyl-cyclopenten-2-yl)phosphonate 3 [δ: 4.15 (quintet, 4H, 2-$OC\underline{H}_2CH_3$, J = 7 Hz), 2.71 (m, 2H), 2.53 (d, 3H, $-CH_3$, J = 2 Hz), 2.45 (m, 2H), 1.35 (t, 6H, 2-$OCH_2-C\underline{H}_3$, J = 7 Hz); ν_{max}: 1700, 1600, 1275, 1030, 970] was obtained in 82% yield.

The hitherto unknown phosphonate 3 presents a real usefulness as it allows a rapid preparation of several interesting products using a simple procedure. In fact, its dihydroderivative, diethyl[(3-methyl)-oxocyclopent-2-yl]phosphonate 8 [δ: 4.15 (br quintet, 4H, 2-$OC\underline{H}_2CH_3$, J = 7 Hz), 2.95-2.10 (complex m, 6H), 1.35 (t, 6H, 2-$OCH_2C\underline{H}_3$, J = 7 Hz), 1.25 (d, 3H, $-CH_3$, J = 6.5 Hz); ν_{max}: 1745, 1025, 980] (obtained in almost quantitative yield by catalytic hydrogenation of 3 with Pd on active carbon in ethyl acetate), underwent a base-catalysed Emmons-Horner reaction (Et_3N at 55° for 12 hr) when 2-furyl-carbaldehyde was added, affording smootly 2-(2-furyl)methylen-3-methyl-oxocyclopentane 9 in high yield (88%)[δ: 7.50, 6.65, 6.52 (each m, 1H, protons on furan), 7.10 (bs, 1H) 3.58 (m, 1H, $>C\underline{H}CH_3$), 2.55-1.70 (complex m, 4H, 2-CH_2-), 1.22 (d, 3H, $-CH_3$, J = 7 Hz); ν_{max}:1700, 1615, 1550, 890].

9 can be easily transformed into the isomer 10 by treatment with MgO[11] or iodine in toluene[12].

The easy preparation of 3, the mild and effective conditions used to prepare 9, the possible isomerization of 9 into the endo-cyclic olefin 10 by means of simple procedures, the high yields, are the features that make this method

a new and improved procedure to convert 3-oxo-cyclopenten-2-yl-phosphonates into 2-alkyl-substituted cyclopentenones (see Scheme I).



3 10

Scheme I

Further synthetic applications of the intermediates 3, 6 and 8 are under investigation.

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