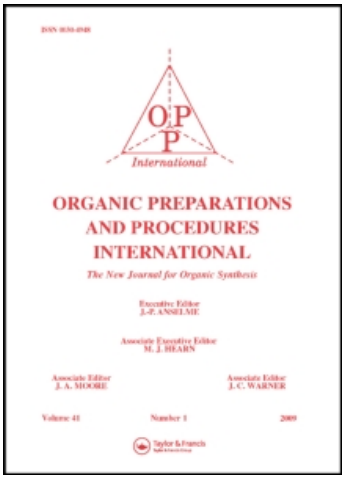

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A NEW SYNTHETIC ROUTE TO 2-CARBOMETHOXYCYCLOPENT-2-ENONE *via* RHODIUM(II)-MEDIATED DECOMPOSITION OF DIAZOESTERS

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A NEW SYNTHETIC ROUTE TO 2-CARBOMETHOXYCYCLOPENT-2-ENONE *via* RHODIUM(II)-MEDIATED DECOMPOSITION OF DIAZOESTERS

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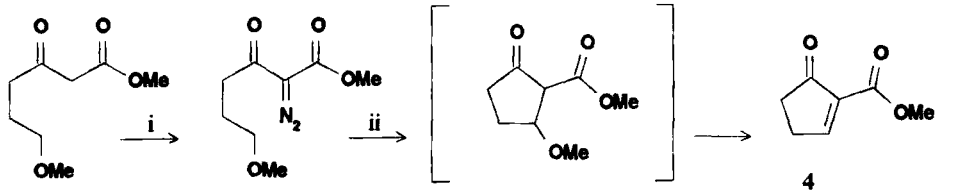
Wide interest in biologically active natural cyclopentenones has led to recent developments in organic synthetic methodology.[1] In this context, the structurally simple 2-carbomethoxycyclopent-2-enone (**4**), a synthon for prostaglandins and other natural products, had been selected as synthetic target.[2] The reported procedures for **4** were achieved through organoselenium chemistry. The present communication describes a new convenient route for the preparation of compound **4**.

The synthetic strategy was based on the assumption that diazo compound **2**, with dirhodium tetraacetate catalysis, would undergo intramolecular carbon-hydrogen insertion to cyclopentanone **3**, precursor of **4**. Insertion of the carbenoid into γ-carbon-hydrogen bond[6] is facilitated by the presence of an oxygenated function at the cyclization site.[7] Alkylation of the dianion of methyl acetoacetate with 2-bromoethyl methyl ether in THF[4] furnished the methyl 6-methoxy-3-oxohexanoate (**1**) in 68% yield. Exposure of ether **1** to tosyl azide in presence of Al_2O_3-KF[5] afforded the expected diazo compound **2** in 76% yield. Surprisingly, treatment of **2** with dirhodium tetraacetate led directly to 2-carbomethoxycyclopent-2-enone (**4**) in 72% yield; presumably, cyclopentenone **4** is formed through a β-elimination process of intermediate methoxyester **3**. The over-all yield of **4** from **1** was 46%.



1 **2** **3**

(i) $ATosN_3$, Al_2O_3 - KF, THF, rt; (ii) $Rh_2(OAc)_4$, rt.

EXPERIMENTAL SECTION

Infrared spectra of chloroform solutions were obtained on a Perkin-Elmer 1320 spectrophotometer. ^1H and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded on a Bruker AC 200 spectrometer operating at 200.1 and 50.3 MHz, respectively, in the Fourier transform mode. The carbon shifts are in parts per million downfield from Me_4Si; (Me_4Si) = ($CDCl_3$) + 76.9 ppm. Column chromatography was executed on 70-230 mesh Merck silica gel. All reactions were carried out under nitrogen, and all extracts were dried over Na_2SO_4.

Methyl 6-methoxy-3-oxohexanoate (1).- To a solution of diisopropylamine (9 g, 85 mmol) in 50 mL of tetrahydrofuran, cooled at -78°, was added a hexane solution of *n*-butyllithium (2.5 M in hexane, 32 mL, 80 mmol). The temperature was brought to -10° for 15 min, and then cooled back to -78°. A solution of methyl acetoacetate (4 g, 34.5 mmol) in 20 mL of tetrahydrofuran was added dropwise *via* a syringe over 10 min. The cooling bath was removed, the reaction mixture was stirred for 45 min and then 2-bromoethyl methyl ether (12,6 g, 90 mmol) was added. Stirring was continued for 30 min, and then the mixture was quenched with 10% aqueous hydrochloric acid and extracted with ether. The combined organic extracts were concentrated *in vacuo* and the residual oil chromatographed on silica gel with 49:1 hexane-ethyl acetate gave 4.4 g (76%) of liquid ester **1**. ^{1}H NMR: δ 1.87 (m, 2, C-5 Hs), 2.64 (t, 2, J = 7 Hz, C-4 Hs), 3.31 (s, 3, OMe), 3.37 (t, 2, J = 6 Hz, C-6 Hs), 3.48 (s, 2,C-2 Hs), 3.73 (s, 3, CO_2Me); ^{13}C NMR: δ 23.3 (C-5), 39.2 (C-4), 48.6 (C-2), 51.8 (CO_2-Me), 58.2 (OMe), 71.1 (C-6), 167.3 (C-1), 202.0 (C-3).

Anal Calcd. for $C_8H_{14}O_4$: C, 55.17; H, 8.10. Found: C, 55.09; H, 8.14

Methyl 2-diazo-6-methoxy-3-oxohexanoate (2).- A mixture of β-ketoester **1** (3.4 g, 19.5 mmol) and tosylazide (3.9 g, 195 mmol) in 35 mL of tetrahydrofuran with 7.4 g of potassim fluoride on alumina[5] was stirred at room temperature for 24 hrs. After filtration, the solid was washed with tetrahydrofuran. Ether was added and the organic solution washed with 3% aqueous solution of potassium hydroxide. The organic phase was evaporated *in vacuo*. Chromatography of the residue on neutral alumina (activity III) and elution with 24:1 hexane-ethyl acetate gave 3.1 g (84%) of the diazoketone 2 as a yellow amorphous solid. [IR: C=N_2 2118 (s), C=O 1715 and 1645 (s) cm^{-1}] ^{1}H NMR: δ 1.92 (m, 2, C-5 Hs), 2.93 (t, 2, J = 7 Hz, C-4 Hs), 3.32 (s, 3, OMe), 3.43 (t, 2, J = 6 Hz, C-6 Hs), 3.84 (s, 3, Co_2Me).

2-Carbomethoxycyclopent-2-enone (4).- A solution of diazoketone 2 (2 g, 10 mmol) in 100 mL of methylene chloride was added dropwise over a 3 hrs period to a suspension of 0.08 mmol dirhodium tetraacetate in 50 mL of methylene chloride. The mixture was evaporated under vacuum and the residue was filtered through a short chromatrographic column, using 24:1 hexane-ethyl acetate as eluent to afford 1.1 g (72%) of pure liquid 4. ^{1}H NMR was identical with reported data.[2a] ^{13}C NMR δ 26.5 (C-4), 35.4 (C-S), 51.6 (OMe), 136.6 (C-2), 162.1($\underline{C}O_2$Me),172.8(C-3),202.8(C-1).

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