

A P P E N D I X - II

159. Studies in the Synthesis of Sesquiterpenes Attempted Synthesis of Ethyl-4-(4' Methoxyphenyl)-3-Oxobutyrate.

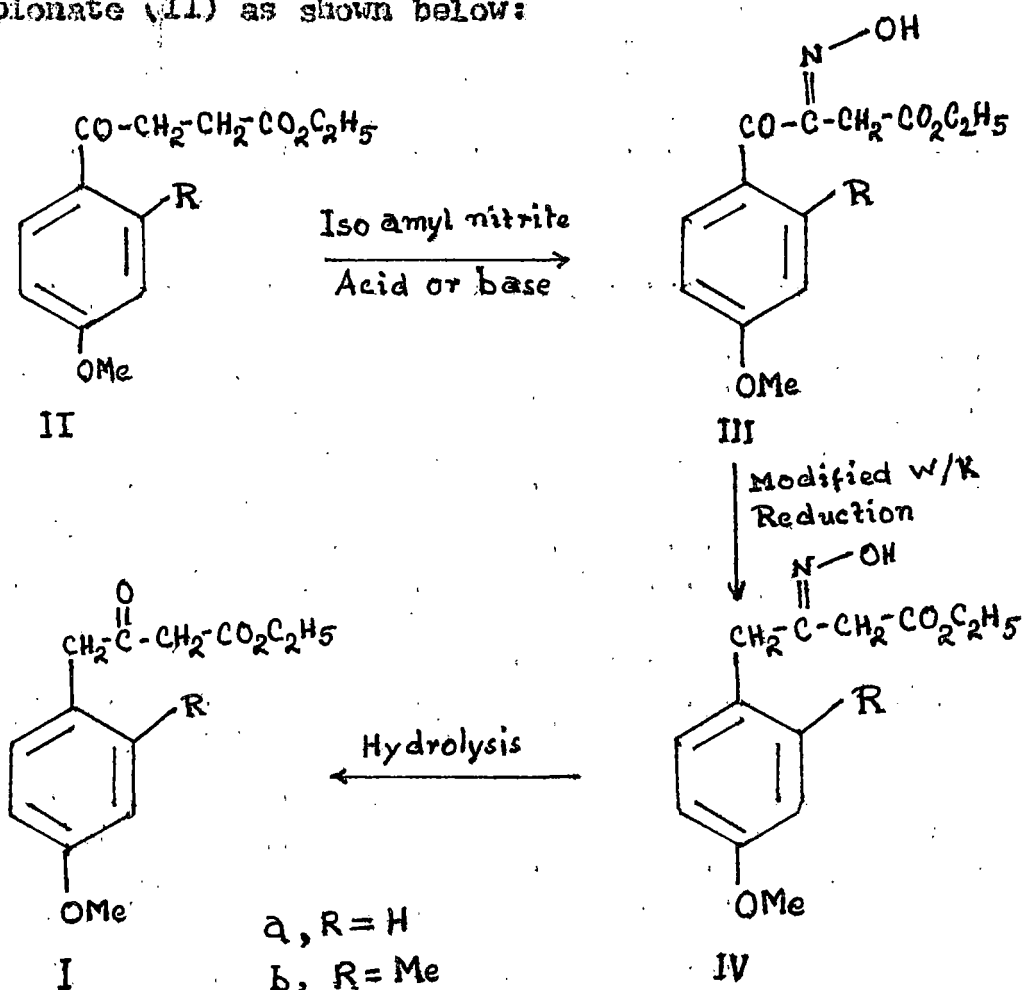
G. S. S. MURTHI, R. N. MUKHERJEE and A. MAJUMDER, Darjeeling

Nitrosation of ethyl-4-(4'-methoxyphenyl)-4-oxobutyrate with isoamyl-nitrite in presence of sodium ethoxide, potassium *tert* butoxide, hydrogen chloride was studied. Only with sodium ethoxide as the catalyst ethyl-4-(4'-methoxyphenyl)-4-oxo-3-oximino butyrate could be obtained. With other catalysts only anisic acid could be isolated from the reaction mixture. The oximino compound was found to be extremely labile and decomposed on standing to anisic acid.

STUDIES IN THE SYNTHESIS OF SESQUITERPENES
 ATTEMPTED SYNTHESIS OF ETHYL-4-(4'-METHOXYPHENYL)-3-OXOBUTYRATE

G. S. S. Murthi, R. H. Mukherjee and A. Majumdar

In connection with our studies in the synthesis of some sesquiterpenes ethyl-4-(4'-methoxy-2'-methylphenyl)-3-Oxobutyrates (I) was needed. This compound has not been described in literature. We planned to synthesize this compound from the easily accessible arylpropionate (II) as shown below:



Acid or base catalysed nitrosation ⁽¹⁻⁴⁾ of the propionate (II) was expected to give the oximino keto ester (III). Modified Wolff-Kishner reduction ⁽⁵⁻⁶⁾ followed by the acid hydrolysis ⁽⁶⁾ of the resulting oximino ester would then give the desired 3-oxobutyrates (I). It was felt that a detailed study of the nitrosation and Wolff-Kishner reduction of similar systems would prove rewarding. We therefore, decided to synthesize ethyl-4-(4'-methoxyphenyl)-3-oxobutyrates (Ia).

Succinoylation of anisole ⁽⁷⁻¹⁰⁾ followed by the esterification of the resulting 3-anisoyl propionic acid gave ethyl-4-(4'-methoxyphenyl)4-oxobutyrates (IIa) as a solid m.p. 45°. Treatment of this ester with iso-amyl nitrite using sodium ethoxide as a catalyst ⁽¹⁾ gave the oximino-ester (IIIa) as a white solid m.p. 132°-133° (decom) in about 30% yield. Using other catalysts like potassium tertiary butoxide ⁽²⁻³⁾ or hydrogen chloride ⁽⁴⁾ no oximino-ketoester (IIIa) could be isolated. Only anisic acid could be isolated from the reaction mixture.

The oximino ketone (IIIa) was found to be extremely sensitive to moisture and was found to decompose rapidly to anisic acid. It was therefore, not possible to attempt the Wolff - Kishner reduction of this compound.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded on Beckman 20 IR spectrophotometer. All new compounds gave

satisfactory elemental analyses. Solvents were dried in the usual way.

Ethyl 4-(4'-methoxyphenyl)-4-oxo butyrate (IIa)

4-(4'-methoxyphenyl)-4-oxo-butyric acid was prepared from anisole and succinic anhydride according to the method described in literature⁽⁸⁾. M.P. 146° (lit⁽⁸⁾ 146°). Esterification of this acid using alcohol and sulphuric acid gave the ethyl ester (IIa) as a white crystalline solid from petroleum ether m.p. 45° IR 1720, 1670 cm⁻¹.

Ethyl-4 (4'-methoxyphenyl)-4-oxo-3-oximino-butyrate (IIIa)

A solution of the ketoester (IIa) (11 g; 0.0466 mole) and freshly distilled iso-acylnitrite⁽¹¹⁾ (5.2 g; 0.0444 mole) in 50 ml of anhydrous alcohol was added drop-wise with constant stirring and at room temperature in an atmosphere of nitrogen to a solution of sodium ethoxide prepared from 3 g (0.1304 mole) of sodium and 250 ml of anhydrous alcohol. After the addition was complete the reaction mixture was stirred for another two hours and left overnight at room temperature. Filtration of the precipitated solid followed by the treatment of the aqueous solution of the same with hydrochloric acid afforded the oximino keto ester (IIIa) as a solid (3.6 g; 30% yield) m.p. (crude) 132 - 33° i.r. (crude) (nujol) : 3390 - 3340 cm⁻¹ (broad), 2740 - 2600 cm⁻¹, 1700 cm⁻¹, 1665 cm⁻¹ and 1630 cm⁻¹. Evaporation of the alcoholic solution afforded the unreacted starting material (6.3 g).

The experiment was repeated with 8 g of the ester (IIa) 5 ml of iso-amylnitrite but potassium tert butoxide instead of sodium ethoxide (5 g Potassium and 125 ml of dry tert butanol. No oximino ketone could be isolated after the usual work-up 6.9 g of anisic acid m.p. 179 - 80° (no depression on admixture with an authentic sample) was obtained.

Nitrosation of the keto ester (IIa) according to the method of Hartung and Crossley⁴ afforded only anisic acid.

Acknowledgements : The authors wish to express their gratitude to the UGC, New Delhi for the award of a fellowship under the FIP programme to one of them (RMD) and Junior Research Fellowship to another (AM).

R E F E R E N C E S.

1. Elad, D., and Ginsberg, D., : J. Chem. Soc. 2664 (1953).
2. Huneck, S., : Chem. Ber 93, 2288 (1965).
3. Barry, R. H., and Hartung, W. H., : J. Org. Chem. 12, 460 (1947).
4. Hartung H. and Crossley : Organic Syntheses Coll. Vol. II 263.
5. Huang-Minlon : J. Am. Chem. Soc., 68, 2487 (1946); see also Todd in Adams, Organic Reactions, Vol. IV, p. 385, John Wiley and Sons, New York, 1948.
6. Elad, D., and Ginsberg, D., : J. Chem. Soc. 3052 (1964).
7. Rodd, E. H., : "Chemistry of Carbon Compounds" Vol. IIIB p. 940.
8. Thomas, G. D. and Nathan, A.M. : J. Am. Chem. Soc. 70, 331 (1948).
9. Rao and Dev., S. : J. Ind. Chem. Soc. 34, 255, (1957).
10. Howel and Taylor., : J. Chem. Soc. 1248 (1958).
11. Vogel, A.I., : A Text book of Practical Organic Chemistry (Longmans, London) 306, 1975.