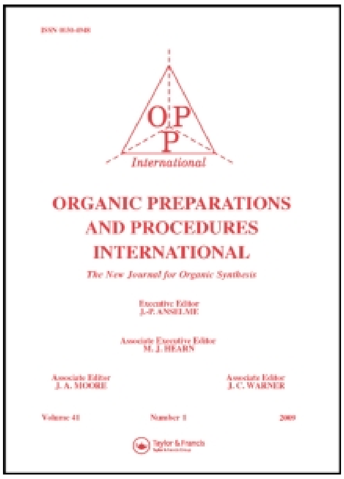
This article was downloaded by:
On: *27 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

ROBINSON ANNELATION WITH A β-HYDROXYKETAL IN THE PRESENCE OF AN ACID

P. A. Zoretic[a]; B. Branchaud[a]; T. Maestrone[a]
[a] Department of Chemistry, Southeastern Massachusetts University, North Dartmouth, Massachusetts

To cite this Article Zoretic, P. A. , Branchaud, B. and Maestrone, T.(1975) 'ROBINSON ANNELATION WITH A β-HYDROXYKETAL IN THE PRESENCE OF AN ACID', Organic Preparations and Procedures International, 7: 1, 51 — 54
To link to this Article: DOI: 10.1080/00304947509356816
URL: http://dx.doi.org/10.1080/00304947509356816

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

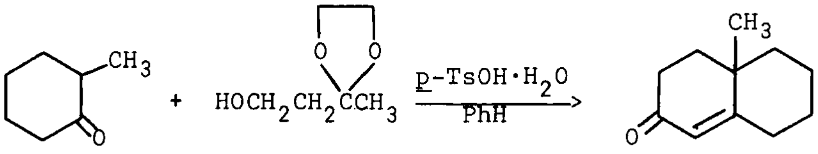
ORGANIC PREPARATIONS AND PROCEDURES INT. 7(1), 51-54 (1975)

ROBINSON ANNELATION WITH A β-HYDROXYKETAL IN THE PRESENCE OF AN ACID

P. A. Zoretic*, B. Branchaud[1] and T. Maestrone[1]

Department of Chemistry
Southeastern Massachusetts University
North Dartmouth, Massachusetts 02747

Recently we reported[2] that Robinson annelation reactions can be carried out directly with a β-chloroketone in the presence of an acid. We now report that a Robinson annelation can be achieved in moderate yields with a β-hydroxyketal in the presence of an acid. In this method the acid is presumably utilized as a catalyst for the *in situ* generation of methyl vinyl ketone[3] and in both the Michael and aldol steps of the reaction.



The results of the synthesis of 10-methyl-1(9)-octalone-2 (III) using different molar ratios of (I) and (II) in benzene in the presence of *p*-toluenesulfonic acid are summarized in Table I. The yields reflected in Table I are similar in magnitude to those obtained from the Robinson annelation under basic conditions utilizing methyl vinyl ketone or its equivalent in the synthesis of (III).[4]

Table 1

Acid	Molar Ratio I:II	% Yield, III Distilled
p-TsOH·H_2O	2:1	35
p-TsOH·H_2O	1:1.5	32
p-TsOH·H_2O	1:1	24

EXPERIMENTAL

4-Hydroxy-2-butanone ethylene ketal (II). – Lithium aluminum hydride (11.8 g, 0.31 mole) was added to 350 ml of anhydrous ether in a three neck one liter flask fitted with a reflux condenser, addition funnel, stopper and magnetic stirrer. The suspension was heated to reflux and ethyl acetoacetate ethylene ketal[5] (66 g, 0.38 mole) dissolved in 150 ml of anhydrous ether was added dropwise over a 45 minute period. The resulting mixture was refluxed for an additional 2.5 hrs and then cooled to 0° with an ice bath. A saturated solution of Na_2SO_4 was added dropwise to destroy excess lithium aluminum hydride and the resulting white solids were filtered with suction and washed with 150 ml of ether. The ethereal solution was dried over anhydrous $MgSO_4$, filtered and concentrated on a rotary evaporator, giving 50 g of an oil. Distillation of the oil afforded 39.4 g (78.5%) of 4-hydroxy-2-butanone ethylene ketal (II), bp 135-39° at 15 mm, lit.[6] 102-5° at 20 mm; ir 3450 cm^{-1} (OH); nmr (CCl_4) δ 1.35 (s, 3H), 1.9 (t, 2H), 3.7 (t, 2H), 4.0 (s, 4H), 3.58 (shoulder, 1H).

10-Methyl-1(9)-octalone-2 (III). – To a solution of 2-methylcyclohexanone (5.6 g, 0.05 mole) and 4-hydroxy-2-butanone ethylene ketal II (9.8 g, 0.75 mole) dissolved in 25 ml of benzene was added p-toluenesulfonic acid monohydrate (400 mg) and the resulting mixture was heated to reflux for 20 hrs. The reaction was cooled to room temperature, poured into a 3% $NaHCO_3$ solution (75 ml) and the resulting mixture was extracted with three 75 ml portions of ether. The ethereal extracts were combined and washed with 100 ml of H_2O, dried over anhydrous $MgSO_4$, filtered and concentrated on a rotary evaporator, giving 5.2 g of a crude residue.[7a,b] Analysis (glc) showed that the residue consisted mainly of two compounds. The major component was shown to have a retention time identical to that of authentic 10-methyl-1(9)-octalone-2. The minor component was presumably a α, β-double bond isomer or an aldol intermediate, since on treatment with base this compound was converted to 10-methyl-1(9)-octalone-2.

The crude residue was dissolved in an aqueous HCl/THF solution[7a] [10% HCl (12 ml) and THF (23 ml)] and stirred at room temperature for one hour. The reaction was poured into H_2O (100 ml) and extracted with 2 x 100 ml portions of ether. The ethereal solutions were combined and washed with a 5% $NaHCO_3$ solution (50 ml) and 100 ml of H_2O. Evaporation of the ether solution afforded an oil which was dissolved in a 4% NaOH/MeOH solution (25 ml) and refluxed under N_2 for 1.5 hrs. The reaction mixture was cooled to room temperature and poured into 100 ml of water; and extracted with 2 x 125 ml portions of ether. The ethereal extracts were combined, washed with 100 ml of H_2O and dried over anhydrous $MgSO_4$. Concentration of the ether solution and distillation of the resulting oil afforded 2.6 g (32%) of 10-methyl-1(9)-octalone-2 III, bp 79-81° at 0.2 mm, lit.[8] bp 70° at 0.3 mm; (III) was identical in all respects (ir, nmr, glc) to an authentic sample.[8]

ACKNOWLEDGEMENT. – We are grateful to the National Science Foundation - SMU Institutional Grant (GU-3445) for partial support of this work.

REFERENCES

1. Undergraduate research participants.
2. P. A. Zoretic, B. Branchaud and T. Maestrone, Tetrahedron Letters, 527, 1975.
3. For examples of acid-catalyzed Robinson annelations with vinyl ketones

see: C. H. Heathcock and J. E. Ellis, Chem. Comm., 1474, 1971; and b) C. H. Heathcock, J. E. Ellis, J. E. McMurry and A. Coppolino, Tetrahedron Letters, 4995, 1971.

4. E. C. duFew, F. J. McQuillin and R. Robinson, J. Chem. Soc., 53, 1937; J. H. Brewster and E. L. Eliel, Org. Reactions, 7, 99, 1953.

5. J. Boeseken and F. Tellegen, Rec. Trav. Chim., 57, 133, 1938; and E. J. Salmi,Ber., 71B, 1803, 1938.

6. S. Canonica, L. Gaudenzi, G. Jommi, and U. Valcavi, Gass. Chim. Ital., 91, 1400, 1961.

7. (a) Analysis (nmr) indicated that a small amount of a compound containing a ketal moiety was present in the crude residue. (b) Analysis (tlc) of the crude residue showed that the Rf of the major component was identical to that of authentic 10-methyl-1(9)-octalone-2.

8. J. A. Marshall and W. I. Fanta, J. Org. Chem., 29, 2501, 1964.

(Received December 23, 1974; in revised form March 18, 1975)