Tetrahedron Letters No.15, pp. 1899-1901, 1968. Pergamon Press. Printed in Great Britain.

A METHOD FOR THE STEREOSELECTIVE INTRODUCTION OF ANGULAR METHYL GROUPS

Daniel J. Dawson and Robert E. Ireland

Contribution No. 3635 from the Gates and Crellin Laboratories

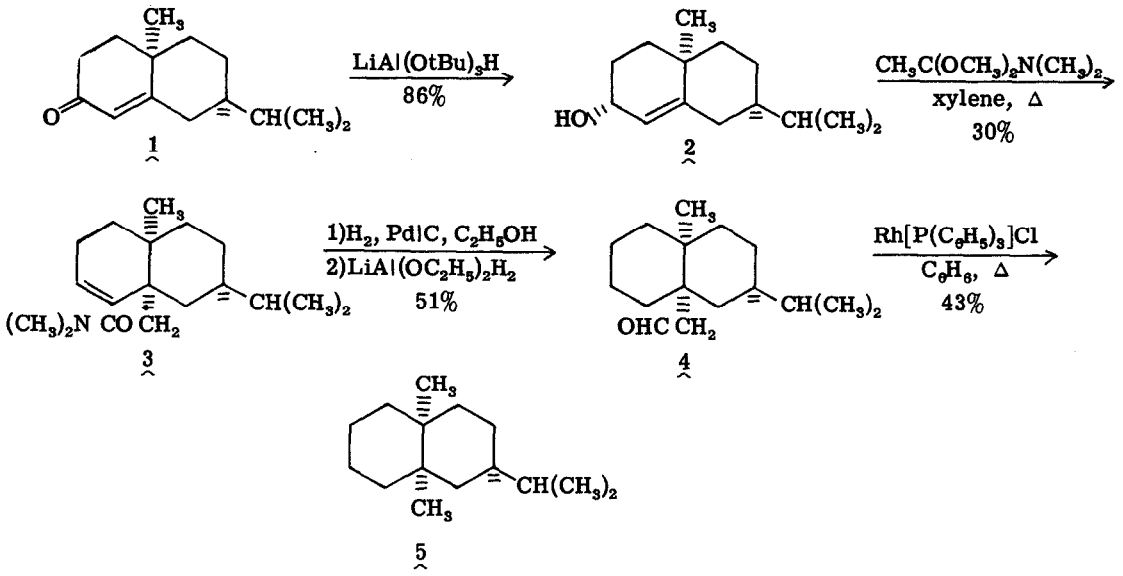
of Chemistry, California Institute of Technology, Pasadena, California 91109

(Received in USA 10 January 1968)

The synthesis of many naturally occurring substances requires the construction of polycyclic materials that bear a substituent at the ring fusion. In the case of steroids and terpenes this substituent is usually an angular methyl group, and often the success of a particular synthetic scheme turns on the ease with which this carbon is introduced. Indeed there is quite a body of literature (1) that pertains to the introduction of just such an angular methyl group. We report here our initial observations on yet another approach to the solution of this problem that has distinct stereochemical advantages and potentially general application.

The reaction sequence we devised takes advantage of the stereoselectivity (2) of the Claisen rearrangement and the recently reported decarbonylation of aldehydes (3) by tristriphenylphosphinechlororhodium (I) (4). Earlier work from these laboratories (5) and others (6) has demonstrated the value of the Claisen rearrangement of allyl vinyl ethers for the introduction of an angular acetaldehyde residue. The control of the stereochemical outcome of this sequence through the choice of allylic alcohol used is particularly attractive, and we have long sought an efficient method whereby one carbon could be removed from the acetaldehyde side chain. Such a method appeared at hand when it was reported that certain transition metal complexes that were soluble in organic solvents led to the decarbonylation (3) of both aliphatic and aryl aldehydes. To test this hypothesis we investigated the transformation of the enone 1 to the hydrocarbon 5.

Employing the procedures developed by Marshall and co-workers (7), we converted ℓ-carvone to the desired enone 1, and thence to the required allylic alcohol 2 in 86% yield by reduction with lithium aluminum tri-t-butoxy hydride. The crystalline alcohol 2 [m.p. 83-84°] (8) was homogeneous by thin layer and gas liquid chromatography and from both analogy (5) to similar reductions and analysis of the proton magnetic resonance spectrum was taken to be the quasi-equatorial epimer 2.



Rather than apply the more standard vinyl ether in the Claisen rearrangement (5), we chose to investigate the more recent amide acetal procedure (9). Application of this method to the alcohol 2 resulted in the generation of the amide 3 [m.p. ~ 35°] (8) in 30% yield together with hydrocarbon by-products which probably result from dehydration (10). The low yield at this stage of the sequence will undoubtedly be overcome with further experimentation. The corresponding saturated amide, anoil (8), was obtained in 95% yield after catalytic hydrogenation and was converted to the desired aldehyde 4 by reduction with lithium aluminum diethoxy hydride. The aldehyde 4 was isolated and purified through its semicarbazone derivative [m.p. 170-173°] (8).

After the aldehyde 4, freed from its semicarbazone by brief acid treatment, was heated in benzene solution under reflux with 1.15 equivalents of tristriphenylphosphinechlorohodium (I) (4) for 22 hours, there resulted a 43% yield of the hydrocarbon 5 [oil; evap. dist. at 130-150° (bath temp.)/10-12 mm] (8). The presence of a new angular methyl group in the hydrocarbon 5 was clearly evident from the infrared spectrum that indicated the loss of the aldehyde function and the proton magnetic resonance spectrum which showed additional three protons in the methyl region (9.12 τ and 9.16 τ).

This conversion of the enone 1 to the hydrocarbon 5 not only allows for the stereoselective introduction of an angular methyl group in such bicyclic substances, but through modification of the functionality at intermediate stages would be applicable to the synthesis of more complex

structures that bear an angular methyl group. We are currently investigating several such modifications and commend the method to the consideration of others.

REFERENCES

(1) H. O. House and B. M. Trost, J. Org. Chem. 30, 2502 (1965) and references cited therein; E. Wenkert and D. A. Berges, J. Am. Chem. Soc. 89, 2507 (1967).

(2) A. W. Burgstahler and I. C. Nordin, J. Am. Chem. Soc. 83, 198 (1961).

(3) J. Tsuji and K. Ohno, Tetrahedron Letters, 3969 (1965); J. A. Osborn, F. H. Jardine, J. F. Young and G. Wilkinson, J. Chem. Soc. (A), 1711 (1966).

(4) J. F. Young, J. A. Osborn, F. H. Jardine and G. Wilkinson, Chem. Comm. 131 (1965).

(5) R. F. Church, R. E. Ireland and J. A. Marshall, J. Org. Chem. 31, 2526 (1966); R. A. Bell, R. E. Ireland and R. A. Partyka, J. Org. Chem. 31, 2530 (1966).

(6) G. Büchi and J. D. White, J. Am. Chem. Soc. 86, 2884 (1964); K. Mori and M. Matsui, Tetrahedron Letters, 2347 (1965).

(7) J. A. Marshall, W. I. Fanta and H. Roebke, J. Org. Chem. 31, 1016 (1966).

(8) Satisfactory combustion analyses were obtained on all new substances.

(9) A. E. Wick, D. Felix, K. Steen and A. Eschenmoser, Helv. Chim. Acta, 47, 2425 (1964).

(10) H. Muxfeldt, R. S. Schneider and J. B. Mooberry, J. Am. Chem. Soc. 88, 3670 (1966).