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SYNTHESIS OF A SPIROVETIVANE INTERMEDIATE: A PROBLEM IN CARBONYL TRANSPOSITION

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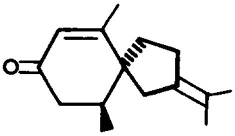
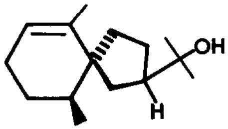
The spiro[4.5]decane ring system, which is found in sesquiterpenes of the spirovetivane class has been the target of many syntheses. Over the past eight years at least eight total syntheses of β-vetivone (1) and more than five of hinesol (2) have been recorded[1].

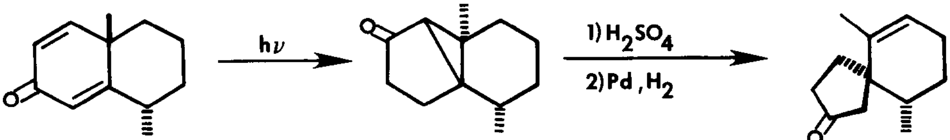


1



2

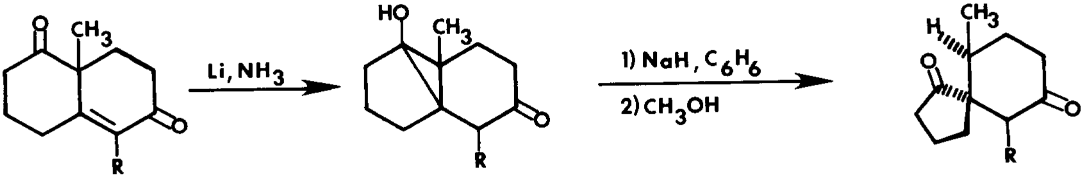
Marshall's landmark synthesis of β-vetivone[1a] proceeded via enone 4, prepared in three step (36% overall yield) from dienone 3. Other preparations of 4 have been published[2,3], but they do not match the original in either convenience or yield.



3

4

We recently showed that cyclopropanol 7 can be rearranged to spirodiketone 9 in good yield[4]. An equivalent rearrangement of the methyl homolog 8 serves to generate 10[7], a potentially useful intermediate in spirovetivane synthesis. We now report the conversion of 10 into 4, a transformation that establishes the structure and configuration of the former.



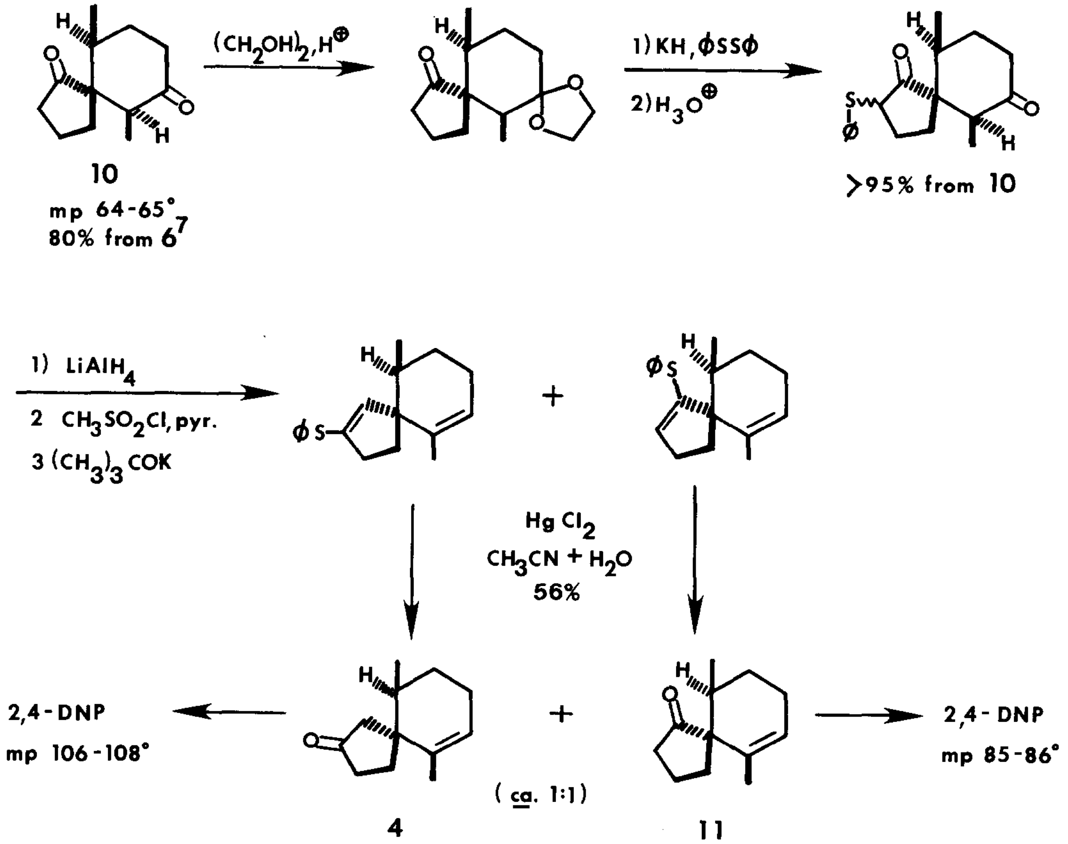
5 R=H
6 R=CH_3

7 R=H
8 R=CH_3

9 R=H
10 R=CH_3

The critical change that must be effected in the transformation of 10 to 4 is a 1,2-transposition of the carbonyl function in the five-membered ring. This was first attempted by the procedure developed by Trost et. al.[5]; however, this approach (Scheme I) proved disappointing. Apparently sulfide rearrangement, presumably via an episulfonium intermediate, leads to a mixture of transposed and unchanged ketones (4 and 11 respectively). In retrospect this failure is not surprising, because there is ample precedent for such neighboring group participation by sulfur[6].

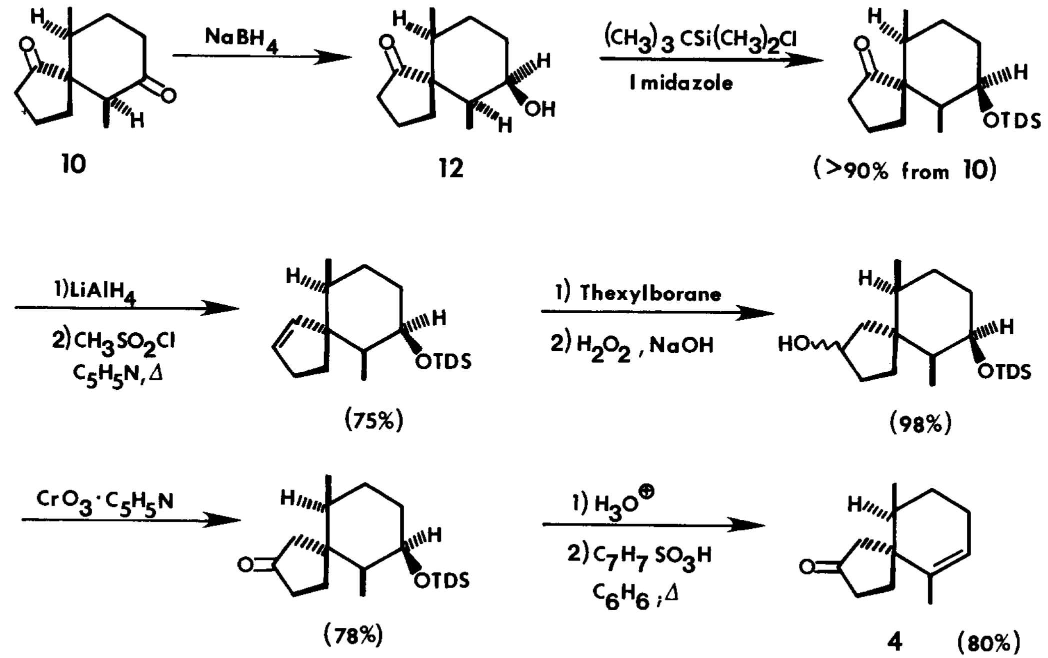
Scheme I



The mixture of unsaturated ketones 4 and 11 produced by this carbonyl transposition approach could not be separated by glpc (QF-1 column); however, its pmr spectrum agreed with our assignment. Identification of the components was effected by chromatographic separation of the corresponding 2,4-DNP derivatives. Pure samples of 4 and 11, prepared independently, gave 2,4-DNP derivatives which were identical with those isolated from this mixture. The unsaturated sulfide precursor to the ketone mixture displayed a pmr spectrum that indicated it was also a mixture (e.g., overlapping doublets at δ0.8 to 1.0 are observed for the secondary methyl group).

An alternative synthesis of 4 from spirodiketone 10 is described in Scheme II. The ketol 12 formed by borohydride reduction of 10 is predominantly the axial epimer (10:1), and this on acid-catalyzed dehydration gives enone 11. If cyclopropanol 8 is reduced (borohydride) before acid induced cleavage of the three-membered ring, the equatorial epimer of 12 is the major product (4:1). Since the axial epimer (12) undergoes acid-catalyzed dehydration with greater facility and regioselectivity than the equatorial epimer, it was used in this synthesis. The use of thexylborane in the hydroboration step may not be necessary, since Büchi et. al.[1h] report good regioselectivity in a similar reaction with diborane.

Scheme II



(TDS= $(CH_3)_3CSi(CH_3)_2$-)

The properties of 4 prepared in this manner agree very well with those reported by Marshall[1a] and Wenkert[3]. The overall yield of 4 from 10 is in the 40-50% range, making this synthesis competitive with the Marshall preparation.

References

1. β-vetivone syntheses:
   - a) J.A. Marshall and P. Johnson, J. Org. Chem., **35**, 192 (1970).
   - b) G. Stork, R. Danheiser and B. Ganem, J. Am. Chem. Soc., **95**, 3414 (1973).
   - c) P.M. McCurry and R. Singh, Tetrahedron Letters, 3325 (1973).
   - d) K. Yamaka, H. Nagase, Y. Hayakawa, K. Aoki and Y. Hirata, ibid., 4963 (1973).
   - e) G. Bozzato, J-P. Bachmann and M. Pesaro, J.C.S. Chem. Comm., 1005 (1974).
   - f) M. Deighton, C. Houghes and R. Ramage, ibid., 662 (1975).
   - g) W. Dauben and D. Hart, J. Am. Chem. Soc., **97**, 1623 (1975).
   - h) G. Büchi, D. Berthet, R. Decorzant, A. Grieder & A. Hauser, J. Org. Chem., **41**, 3208 (1976)

   hinesol syntheses:

   - i) J.A. Marshall and S.F. Brady, J. Org. Chem., **35**, 4068 (1970).
   - j) J. Mongrain, J. Lafontaine, A. Belanger & P. Deslongchamps, Can. J. Chem. **48**, 3273 (1970).
   - k) D. Chass, D. Buddhasukh and P.D. Magnus, J. Org. Chem., **43**, 1750 (1978).
     Also d), g) and h) from above.
2. P.M. McCurry, Tetrahedron Letters, 1845 (1971).
3. E. Wenkert, B. Buckwalter, A. Craveiro, E. Sanchez and S. Sathe, J. Am. Chem. Soc., **100**, 1267 (1978).
4. a) W. Reusch, K. Grimm, J. Karoglan, J. Martin, K.P. Subrahamanian, Y-C. Toong, P.S. Venkataramani, J. Yordy and P. Zoutendam, J. Am. Chem. Soc., **99**, 1953 (1977).
   - b) W. Reusch, K. Grimm, J. Karoglan, J. Martin, K.P. Subrahamanian, P.S. Venkataramani and J. Yordy, ibid., **99**, 1958 (1977).
5. B.M. Trost, K. Hiroi and S. Kurozumi, J. Am. Chem. Soc., **97**, 438 (1975).
6. a) A. Streitwieser, Solvolytic Displacement Reactions, McGraw-Hill, New York, 1962.
   - b) K.D. Gundermann, Ang. Chem Intl. Ed., **2**, 674 (1963).
7. K. Grimm, PhD. Thesis, Michigan State University, 1971.

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