be noted that the methyl migration and concomitant bond fissions (e or e′) are completely analogous to those (b or b′) encountered[5] in the octalone I and that the same radical (i or ii in ref 5) is produced in each case The postulated intermediate ion d formally corresponds to the molecular ion of 1-furfurylidene-8-methylhydrindane (VI). We have synthesized its benzylidene analog VII by treatment of benzylmagnesium chloride with 8-methylhydrindan-1-one followed by dehydration, and found in its mass spectrum an *m/e* 131 peak (f, furfuryl replaced by phenyl) of virtually the same relative intensity as encountered in 2-benzylidene-9-methyl-1-decalone,[9] thus offering support (though not proof[10]) for the intermediacy of an ion such as d.

Further work on the scope and other mechanistic implications of this and related[5] methyl migrations is under way in our laboratory.

(9) W. S. Johnson, *J. Am. Chem. Soc.*, **65**, 1317 (1943).
(10) *Cf.* W. H. Pirkle, *ibid.*, 87, 3023 (1965).
(11) National Institutes of Health Postdoctoral Fellow, 1964–1965.

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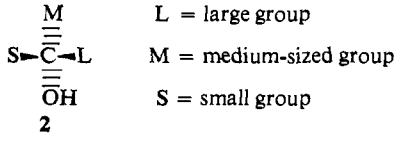
## Configurational Correlation of Alcohols by Asymmetric Synthesis of Sulfinate Esters[1]

*Sir:*

The asymmetric synthesis of menthyl sulfinates by the reaction of *l*-menthol with sulfinyl chlorides has been developed as a general method for use in the assignment of absolute configurations to sulfinate esters and derived sulfoxides.[2] It has now been established that, conversely, the asymmetric synthesis of alkyl *p*-toluenesulfinates provides a rapid, convenient, and highly stereoselective general method for the configurational correlation of alcohols.

Reaction of *p*-toluenesulfinyl chloride with a variety of optically active secondary alcohols at −78° in the presence of pyridine gives a mixture of diastereomers which can be directly converted to optically active methyl *p*-tolyl sulfoxide (**1**) in 80–90% yields by reaction with methylmagnesium iodide. We find that the sign of the predominant enantiomer of **1** is uniquely related to the absolute configuration of the inducing alcohol: alcohols corresponding to stereoformula **2** yield an excess of the (−)-(*S*) enantiomer of **1**.[3]




**2**

L = large group
M = medium-sized group
S = small group

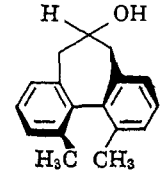
(1) This work was supported by the National Science Foundation under Grant No. GP-3375.
(2) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, 87, 1958 (1965).
(3) Alcohols of configuration **2** induce formation of an excess of the (−)-(*R*) enantiomer of atrolactic acid by the method of Prelog,[4] and of the (+)-(*S*) enantiomer of α-phenylbutyric acid by the method of Horeau.[5]
(4) V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953); V. Prelog and H. L. Meier, *ibid.*, **36**, 320 (1953).
(5) A. Horeau, *Tetrahedron Letters*, **No. 15**, 506 (1961); **No. 21**, 965 (1962); A. Horeau and H. B. Kagan, *Tetrahedron*, **20**, 2431 (1964).

**Table I.** Asymmetric Synthesis of Methyl *p*-Tolyl Sulfoxide (**1**)

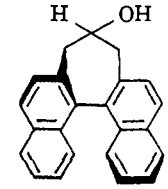
| Inducing Alcohol | Produced Sulfoxide **1** Obsd $[\alpha]^{25}D$ (ethanol), degrees | Calcd optical yield, %[c] |
|---|---|---|
| (−)-Methanol | −39 | 25.0 |
| (−)-Isoborneol[a] | −60 | 50.2 |
| (−)-Borneol[b] | −22 | 22.7 |
| (+)-2-Butanol | +16 | 10.0 |
| (+)-3-Methyl-2-butanol | +28 | 18.0 |
| (+)-3,3-Dimethyl-2-butanol | +29 | 18.6 |

[a] A mixture of 84% (−)-isoborneol and 16% (+)-borneol. [b] A mixture of 88% (−)-borneol and 12% (+)-isoborneol. [c] Calculated on the basis of $[\alpha]^{25}D$ +156° (ethanol) for optically pure **1** (*cf.* K. Mislow, M. Axelrod, D. R. Rayner, H. Gotthardt, L. M. Coyne, and G. S. Hammond, *J. Am. Chem. Soc.*, **87**, 4958 (1965), ref 13). The optical yields calculated for (−)-isoborneol[a] and (−)-borneol[b] have been corrected and refer to the pure stereoisomers (*i.e.*, the major components in the respective mixtures).

Representative results are collected in Table I. The three levorotatory terpene derivatives have the (*R*) configuration at the asymmetric carbinol carbon,[4] fit stereoformula **2**, and preferentially induce the formation of (−)-(*S*)-**1**. Dextrorotatory methylethyl-, methylisopropyl-, and methyl-*t*-butylcarbinols have the (*S*) configuration at the asymmetric carbinol carbon,[6] fit the enantiomer of stereoformula **2**, and preferentially induce the formation of (+)-(*R*)-**1**. Since the ratio of enantiomeric sulfoxides produced in the Grignard reaction equals the ratio of diastereomeric precursor sulfinates,[2] it follows that the optical yield is an accurate measure of the stereoselectivity of the esterification reaction. The high optical purities of the sulfoxides produced in the Grignard reactions (Table I) therefore reflect the high stereoselectivity of the asymmetric esterifications. High stereoselectivity is also demonstrated by the finding that (+)-(*S*)-2-propanol-1-$d_3$ (**3**)[6] functions as an inducing alcohol to give (−)-(*S*)-**1** of 0.26% optical purity. The sign of rotation indicates that **3** fits stereoformula **2** and that, accordingly, $CH_3$ exceeds $CD_3$ in effective steric bulk. This result is consistent with previous conclusions to the same effect.[7] Finally, use of (+)-(*S*)-4′,1″-dimethyl-1,2,3,4-dibenz-1,3-cyclohepta-diene-6-ol (**4**)[6,8] as the inducing alcohol affords (+)-(*R*)-**1**, 6% optically pure. The sign of rotation of **1** indicates that **4** corresponds to the enantiomer of stereoformula **2**, a result which is consistent with the finding[9] that (*R*)-binaphthyl **5** gives a preponderance of (−)-(*R*)-atrolactic acid and thus corresponds to stereoformula **2**.[3]




**4**




**5**

(6) K. Mislow, R. E. O'Brien, and H. Schaefer, *J. Am. Chem. Soc.*, **84**, 1940 (1962), and references cited therein.
(7) K. Mislow, R. Graeve, A. J. Gordon, and G. H. Wahl, Jr., *ibid.*, **86**, 1733 (1964); A. Horeau, A. Nouaille, and K. Mislow, *ibid.*, 87, 4957 (1965).
(8) K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, and C. Djerassi, *ibid.*, **82**, 1455 (1962).
(9) K. Mislow, V. Prelog, and H. Scherrer, *Helv. Chim. Acta*, **41**, 1410 (1958).

Our work in this area is continuing.[10]

(10) We should like to thank Professor A. Horeau for kindly informing us that our method has been independently applied in his laboratory.

(11) National Institutes of Health Predoctoral Fellow, 1964–1965.
(12) National Aeronautics and Space Administration Fellow, 1964–1966.

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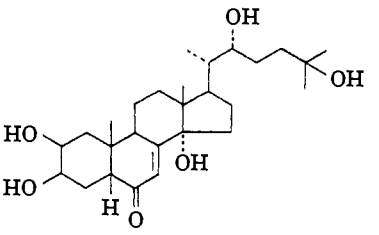
*Received January 3, 1966*

## Steroids. CCXCII.[1] Synthetic Studies on Insect Hormones. II. The Synthesis of Ecdysone

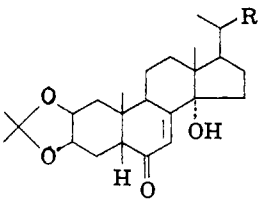
*Sir:*

We wish to report the completion of the synthesis of the insect moulting hormone ecdysone (Ia),[2] from readily available starting materials, by further transformations of the previously reported[1] methyl 14$\alpha$-hydroxy-2$\beta$,3$\beta$-isopropylidenedioxy-6-oxo-22,23-bis-nor-5$\beta$-chol-7-enoate (IIa).

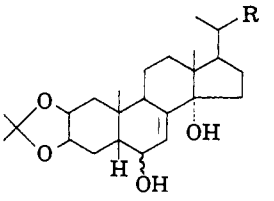
Reduction of IIa with tri-*t*-butoxylithium aluminum hydride afforded a mixture of the corresponding 6$\alpha$- and 6$\beta$-carbinols[3] IIIa which, on alkylation[4] at C-24 with a tetrahydrofuran solution of the lithium salt of 2-methyl-4-sulfoxyphenylbutan-2-ol tetrahydropyranyl ether,[5] furnished 6,14$\alpha$-dihydroxy-2$\beta$,3$\beta$-isopropylidenedioxy-25-tetrahydropyranyloxy-23-sulfoxyphenyl-5$\beta$-cholest-7-en-22-one [IIIb, $\lambda_{max}^{CHCl_3}$ 5.86 $\mu$; $\nu^{CDCl_3}$ 73 (26- and 27-H) and 454 (phenyl H) cps][7] as a mixture of C-6 and side-chain epimers.[3] The crude product was separated from excess alkylating agent by thin layer chromatography on Merck HF silica gel and the phenylsulfinyl group hydrogenolyzed with aluminum amalgam[4] to give IIIc [$\lambda_{max}^{CHCl_3}$ 5.87 $\mu$]. Reduction of this 22-ketone with lithium aluminum hydride to yield the epimeric 22-carbinols IIId followed by manganese dioxide[8] oxidation of the allylic 6-hydroxyl group afforded the epimeric enones IIb [$\lambda_{max}^{MeOH}$ 240 m$\mu$; $\lambda_{max}^{CHCl_3}$ 5.99 $\mu$; $\nu^{CDCl_3}$ 59.5 (19-H), 75 (26- and 27-H), and 350 (7-H) cps]. Hydrolysis of IIb with 0.1 *N* hydrochloric acid in 10% aqueous tetrahydrofuran to remove the acetonide and tetrahydropyranyl ether protecting groups afforded fractions A [15% from IIIa, $R_f$ 0.06; $\lambda_{max}^{THF\ film}$ 6.10 $\mu$; $\nu$ 47.5 (18-H), 63.5 (19-H), and 84.5 (26- and 27-H) cps], B [12%, $R_f$ 0.10; $\nu$ 44 (18-H), 64 (19-H), and 82 (26- and 27-H) cps], C [6%, $R_f$ 0.14; $\lambda_{max}^{CHCl_3}$ 6.01 $\mu$; $\nu$ 48 (18-H), 63.5 (19-H), and 75 (26- and 27-H) cps], D [6%, $R_f$ 0.21; $\lambda_{max}^{CHCl_3}$ 5.86 and 5.98 $\mu$; $\nu$ 42.5 (18-H), 62 (19-H), and 129 cps], and E [5%, $R_f$ 0.28; $\lambda_{max}^{THF\ film}$ 6.07 $\mu$; $\nu$ 43.5 (18-H), 64.5 (19-H), and 74.5 (26- and 27-H) cps] which were separated on 0.25-mm plates using Merck GF silica gel with 10% methanol in chloroform as the developing system.



Ia
b, 20$\xi$,22$\xi$



IIa, R = COOMe (20$\alpha_F$)
b, R = CHOHCH$_2$CH$_2$C(CH$_3$)$_2$OTHP



IIIa, R = COOMe (20$\alpha_F$)
b, R = COCH(SOC$_6$H$_5$)CH$_2$C(CH$_3$)$_2$OTHP
c, R = COCH$_2$CH$_2$C(CH$_3$)$_2$OTHP
d, R = CHOHCH$_2$CH$_2$C(CH$_3$)$_2$OTHP

Fraction D did not show the 26- and 27-H resonances required for the cholestane side chain.[9] Fractions A, C, and E are most probably the three possible C-20 and -22 isomers[10] Ib of ecdysone. Further characterization of these compounds will be the subject of future reports. Fraction B was crystallized from tetrahydrofuran and then water to yield ecdysone [Ia, phase change 165–167°; mp 237–239.5°; [$\alpha$]D 58° (*c* 0.1, EtOH); $\lambda_{max}^{EtOH}$ 241 m$\mu$ ($\epsilon$ 12,300); $\lambda_{max}^{KBr}$ 2.92 and 6.04 $\mu$; $\nu_{max}$ 73 (18-H), 107 (19-H), 124 and 131 (21-H), and 138 (26- and 27-H) cps];[11] identical in all physical properties with those reported by Karlson, *et al.*,[2] for the natural product.[12]

The synthetic material was tested for biological activity by Professor Carroll M. Williams of Harvard University.[13] For this purpose a sample of the

(1) For part I see Steroids. CCXCI: J. B. Siddall, J. P. Marshall, A. Bowers, A. D. Cross, J. A. Edwards, and J. H. Fried, *J. Am. Chem. Soc.*, 88, 379 (1966).

(2) P. Karlson, H. Hoffmeister, W. Hoppe, and R. Huber, *Ann.*, 662, 1 (1963); W. Hoppe and R. Huber, *Chem. Ber.*, 98, 2353 (1965); H. Hoffmeister, C. Rufer, H. H. Keller, H. Schairer, and P. Karlson, *ibid.*, 98, 2361 (1965); C. Rufer, H. Hoffmeister, H. Schairer, and, M. Traut, *ibid.*, 98, 2383 (1965); R. Huber and W. Hoppe, *ibid.*, 98, 2403 (1965).

(3) Separation of the epimers was not deemed necessary since the asymmetry was to be removed in subsequent steps.

(4) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, 87, 1345 (1965).

(5) Prepared from the corresponding carbinol[6] and dihydropyran in the presence of *p*-toluenesulfonic acid.

(6) I. Montanari, R. Danieli, H. Hogeveen, and G. Maccagnani, *Tetrahedron Letters*, 2685 (1964).

(7) Nmr spectra were recorded on a Varian A-60 spectrometer using deuteriopyridine as solvent unless indicated otherwise. We wish to thank Dr. L. Throop, J. Murphy, Dr. T. Toube, and their associates for the determination of physical properties.

(8) Obtained from Beacon Chemical Industries, Inc., Cambridge 40, Mass.

(9) The spectral data suggest a methyl ketone, probably 2$\beta$,3$\beta$,14$\alpha$-trihydroxy-24-nor-20$\xi$-chol-7-ene-6,22-dione.

(10) The formation of all four possible ecdysone side-chain stereoisomers suggests epimerization at C-20 of the methyl ester or the derived 22-ketone. The maintenance of the 19-H resonance at *ca.* 63 cps excludes[1] isomerization at C-5.

(11) This spectrum was recorded on a Varian HA-100 spectrometer using deuteriopyridine as the solvent. We wish to thank Dr. N. Bhacca of Varian Associates for carrying out this determination. The mass spectrum of ecdysone was determined on an Atlas CH-4 spectrometer at a source temperature appreciably below 150° and was in satisfactory agreement with the fragmentation pattern reported by Karlson, *et al.*[2]

(12) The completion of the synthesis of ecdysone from readily available starting materials also completes the formal total synthesis of this natural product.

(13) We are deeply indebted to Professor C. M. Williams for this evaluation.