excess oxalyl chloride to give crude acid halide: ir (film) 1750 (acyl C=O), 1625 (C=C), 992 and 965 (conjugated triene, *trans* C=C conjugated to C=O, *i.e.*, 965 is a composite).

The acid halide was added to an ice-cold solution of 117 mg of isobutylamine and 161 mg of triethylamine in anhydrous ether. The product was obtained as described for the aziridide to give, upon crystallization from petroleum ether (bp 30–60°), 299 mg (77.6%) of nearly white powder: mp 61–63° (lit.[1] mp 69° for echinacein); ir (CCl_4) 3450, 3290, 3070 (N–H) 1670 (amide I) 1630 (C=C), 1542 (amide II), 990 and 965 cm^{-1} (conjugated triene and *trans* C=C conjugated to C=O). The adduct with maleic anhydride was prepared by heating in N_2 atmosphere in toluene under reflux overnight: mp 100–102°, after recrystallization from ether–petroleum ether (lit.[1] mp 99–100°); ir (Nujol mull) 3340, 3125, 3030, 1846, 1766, 1666, 1542, 976, sh 966 cm^{-1} w. This last named band represents unconjugated *trans* olefin, which confirms the contamination in this adduct by the adduct of the all-*trans* isomer.

Anal. Calcd for $C_{20}H_{27}NO_4$: C, 69.54; H, 7.88; N, 4.06. Found: C, 69.30; H, 7.96; N, 4.04.

Isobutylamide of *trans,trans,trans,trans*-2,6,8,10-Dodecatetraenoic Acid (2).—Amide 1 (108 mg) was dissolved in 25 ml of hexane (containing a few milliliters of ether to aid solution), a trace of I_2 was added, and the solution was kept under N_2 for 10 min. The mixture was chilled and filtered to give, after recrystallization from hexane, 74 mg (72%) of white needles: mp 100–111°; ir (CCl_4) 3450, 3300, 3115 (NH), 1680 (amide I), 1638 (C=C), 992 and sh 970 (conjugated triene and C=C conjugated to C=O; the latter band is again composite). The maleic anhydride adduct was prepared as before: mp 160.5–163°, after recrystallization from THF–hexane (lit.[1] mp 149–150°); ir (Nujol mull) 3335, 3030, 1845, 1766, 1666, 1544, 976 and 963. The last two bands named represent the expected conjugated and unconjugated *trans* C=C absorptions.

Anal. Calcd for $C_{20}H_{27}NO_4$: C, 69.54; H, 7.88; N, 4.06. Found: C, 69.36; H, 7.84; N, 3.99.

Registry No.—1, 504-97-2; 1 (maleic anhydride adduct) 18744-22-4; 2, 10076-00-3; 2 (maleic anhydride adduct), 18744-23-5; 3, 18744-19-9; 4, 18744-20-2; 5, 18744-21-3.

Acknowledgment.—The author is indepted to M. Jacobson of this division for his comments in the preparation of this manuscript and to J. H. Fales of this division for conducting the insecticidal tests.

Bicyclic Ketones. II. Abnormal Reduction of Umbellulone[1]

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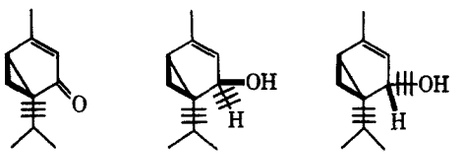
Stereoselective metal hydride reducing agents have become an important asset to the synthetic organic chemist.[2] Although abnormal reduction with these reagents is well established,[3] the metal hydride reduction of umbellulone[4] (1) affords a spectrum of abnormal reductions with reagents that are otherwise either stereoselective or often stereospecific.

As a synthetic entrance into certain tricyclic ketones, we wished to prepare umbellulols 2 and 3. It was anticipated that the least selective reducing agent for this purpose would be lithium aluminum hydride. That expectation was fulfilled, the products of the reaction being a 7:3 mixture of unsaturated alcohols 2 and 3. The assignment of configuration of these alcohols will be deferred until later.



1 2 3

Attempted reduction of umbellulone to 2 and 3 with more stereoselective reducing agents led to the results in Table I.

That these anomalous results are due, in large degree, to the presence of the bicyclic system can be seen by a comparison with the results in Table II. These results are analogous reductions of the α,β-unsaturated ketones, piperitone (6) and pulegone (7).

An inspection of a Drieding model of umbellulone leads to the conclusion that the α side of the molecule (steroid nomenclature) produces considerably less steric interaction to an incoming nucleophile than the β side (isopropyl group *vs.* cyclopropyl). If the incoming nucleophile is large, however, both sides are sterically hindered. The smaller lithium aluminum hydride has little trouble effecting a normal reduction of the carbonyl group without affecting the double bond that is conjugated to it. No 1,4 reduction is observed with this reagent unless a large excess of reducing agent is used. The much bulkier lithium aluminum tri-*t*-butoxyhydride is not able to approach the carbonyl group and is restricted to a 1,4 addition to the conjugated system leading to dihydroumbellulone (5) as the major product. In view of the unanticipated reduction of umbellulone to dihydroumbellulols 4 by sodium borohydride in methanol, one must conclude that this reducing agent is highly solvated preventing normal addition to the carbonyl group. That this reduction is indeed a 1,4 addition followed by further reduction to 4 is confirmed by the nonreducibility of umbellulols 2 and 3 under the same reaction conditions. Lithium borohydride, while not so useful as lithium aluminum hydride, leads predominantly to umbellulols 2 and 3.

(1) (a) Abstracted from the M.S. Thesis of R. H. Chung, Howard University, 1968. (b) Bicyclic Ketones. I: J. W. Wheeler, R. H. Chung, Y. N. Vaishnav, and C. C. Shroff, *J. Org. Chem.*, **34**, 545 (1969).

(2) H. O. House, "Modern Synthetic Reactions," Benjamin Publishing Co., New York, N. Y., 1965, Chapter 2; "Steroid Reactions, An Outline for Organic Chemists," C. Djerassi, Ed., Holden-Day Inc., San Francisco, Calif., 1963, Chapter 2.

(3) The most frequent exception to the rule that carbon–carbon double bonds are inert to reduction are β-aryl-α,β-unsaturated carbonyl compounds. See, for example, R. F. Nystrom and W. G. Brown, *J. Amer. Chem. Soc.*, **70**, 3738 (1948); F. A. Hochstein and W. G. Brown, *ibid.*, **70**, 3483 (1948); M. J. Jorgenson, *Tetrahedron Lett.*, No. 13, 559 (1962). For other examples, see H. Shechter, D. E. Ley, and E. B. Roberson, Jr., *J. Amer. Chem. Soc.*, **78**, 4984 (1956); C. Djerassi and W. Rittel, *ibid.*, **79**, 3528 (1957); E. Schenker, *Angew. Chem.*, **73**, 81 (1961); W. J. Bailey and M. E. Hermes, *J. Org. Chem.*, **29**, 1254 (1964); J. A. Marshall and R. D. Carroll, *ibid.*, **30**, 2748 (1965).

(4) The absolute configuration of umbellulone has been established by T. Norin [*Acta Chem. Scand.*, **16**, 640 (1962)], and by H. Smith and A. Gordon [*J. Amer. Chem. Soc.*, **84**, 2840 (1962)].

TABLE I

Reducing agent	Mol of reducing agent/ mol of ketone	Products, % 1	2 and 3	4	5
$LiAiH_4$	1/4	53	47		
	1/3	14	86		
	1/2	0	96	4	
$LiAl(O\text{-}t\text{-}Bu)_3H$	1	16	4		80
$LiBH_4$	1/3	1	62	33	3
$NaBH_4$	1/2	16	5	78	
	1/3	99+			

TABLE II

Reducing agent	Mol ratio	Products, % 6	8	9	10
$LiAlH_4$	1/3		100		
$LiAl(O\text{-}t\text{-}Bu)_3H$	1	29	24		47
$LiBH_4$	1/3	23	48.5	28.5	
$NaBH_4$	1/3	60	22.5	18.5	
	3/4	31	26	43	

		7	11	12	9	10
$LiAlH_4$	1/3	49	51			
$LiAl(O\text{-}t\text{-}Bu)_3H$	1	39	43			18
$LiBH_4$	1/3	7	93			
$NaBH_4$	1/3	18	36	46		

The assignment of configuration of the umbellulols is based upon (1) the steric hindrance to attack by a nucleophile and (2) their order of elution from an alumina column. Umbellulol has been prepared previously by the allylic oxidation of α-thujene (**13**)[5] but the stereochemistry of the product was not assigned.

13

Column chromatography (alumina) of the lithium aluminum hydride reduction product yielded unreacted umbellulone plus two fractions. The first fraction (A, 67%) was a liquid and later fractions (B, 33%) solidified, mp 52–52.5°. That the two compounds are epimeric is established by their elemental analysis and their oxidation to the original ketone. The infrared spectra indicated that both compounds were unsaturated alcohols containing a cyclopropyl ring. The nuclear magnetic resonance spectra of the two isomers were strikingly different. Fraction A is tentatively assigned structure **2** on the basis of less steric interaction by the isopropyl group in the reduction and its early elution from the column (cyclopropyl and hydroxyl group *cis*). The nmr spectrum showed a broad singlet at δ 5.0 (one proton assigned to the vinyl proton), broad singlet at 4.25 (CHOH), septet centered at 2.44 [1 H, $-CH(CH_3)_2$], singlet at 1.74 (3 H, $CH_3C=$), multiplet centered at 1.46 (1 H, cyclopropyl), multiplet centered at 0.85 (2 H, cyclopropyl) and most important two doublets centered at 1.05 and 0.66 (6 H, J = 7 cps for each). The position of the OH proton was a function of the concentration of the solution. The solid isomer B is tentatively assigned structure **3**. The nmr spectrum leaves no doubt that the compounds are different. It exhibited a broad singlet at 4.79 (2 H, assigned to the vinyl and the CHOH protons), singlet at 1.70 (3 H, $CH_3C=$), multiplet at 1.35 (1 H), multiplet at 0.55 (2 H, cyclopropyl) and two doublets near 0.95 [7 H, $(CH_3)_2CH$]. The position of the OH proton was again a function of concentration.

Since the methyls of the isopropyl group in umbellulone are attached to an asymmetric carbon atom, they are inherently nonequivalent[6] and might be expected to exhibit different chemical shifts. However, the large different in chemical shift of the isopropyl methyl groups in **2** and **3** which differ in configuration only at C-2 is surprising.[7] This difference appears to be due to the introduction of a new asymmetric

(5) E. Klein and W. Rojahn, *Chem. Ber.*, **98**, 3045 (1965).

(6) D. W. Mathieson, Ed., "Nuclear Magnetic Resonance for Organic Chemists," Academic Press, New York, N.Y., 1967, p 39.

center at C-2 as no change was observed in the nmr spectrum of either compound at elevated temperatures. In dimethyl sulfoxide-d_6 a chemical transformation occurred at elevated temperatures. This reaction is currently under investigation.

Experimental Section

Melting points were taken on a Thomas–Hoover melting point apparatus in open capillaries and are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 137B Infracord with sodium chloride optics using polystyrene as a calibration. Nuclear magnetic resonance spectra were taken on a Varian A-60 spectrometer in carbon tetrachloride or deuteriochloroform (unless indicated otherwise) with tetramethylsilane as an internal reference. Gas chromatography was done on an Aerograph Model 661 flame ionization instrument using $^1/_8$-in. stainless steel columns. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Umbellulone 1 (1-Isopropyl-4-methylbicyclo[3.1.0]hex-3-en-2-one).—Umbellulone was extracted from oil of mountain laurel (Fritszche) by the method of Wienhaus and Todenhöfer[8] and had bp 90–92° (10 mm) [lit.[9] 80° (5 mm)]; infrared 5.89 (C=O), 9.74 μ (cyclopropane); nmr δ 5.18 (1 H, C=CH, broad singlet), 2.09 (3 H, CH_3C=, doublet), 2.00 [1 H, -C**H**$(CH_3)_2$, septet], complex absorption 0.8–1.4 (9 H).

Umbellulol 2 and 3 (1-Isopropyl-4-methylbicyclo[3.1.0]hex-3-en-2-ol).—A suspension of lithium aluminum hydride (2.50 g, 0.066 mol) in 250 ml of anhydrous ether was stirred at room temperature for 40 min. To this ether solution, cooled in an ice bath, a solution of umbellulone (20 g, 0.133 mol) in 30 ml of anhydrous ether was added over a 35-min period. The ice bath was removed and the solution stirred for 24 hr. Saturated ammonium chloride was added until the solid dissolved, the ether layer decanted, and the aqueous layer extracted with ether. The combined ether extracts were washed three times with water, and dried (anhydrous sodium sulfate); the ether was removed on a rotatory evaporator. The crude product (19.8 g) was separated by column chromatography (Alumina, Fisher A-540 plus 3% by weight of water) with pentane–ether–methanol mixtures. The ratio of umbellulone, liquid unsaturated alcohol, and solid unsaturated alcohol was 4:56:31 eluted with pentane–ether (7:3), pentane–ether (1:1) and ether–methanol (8:2), respectively.

The liquid unsaturated alcohol (fraction A, **2**) exhibited the following spectra: infrared 2.99 (hydroxyl group), 6.09 (double bond), 9.69 and 9.94 μ (cyclopropane); nmr broad singlet at δ 5.0 (1 H, >C=CH–), broad singlet at 4.25 (1 H, –CHOH–), septet centered at 2.44 [1 H, C**H**$(CH_3)_2$], singlet at 1.74 (3 H, CH_3C=), multiplet centered at 0.85 (2 H, cyclopropyl), multiplet centered at 1.46 (1 H, cyclopropyl) and two doublets centered at 1.05 and 0.66 [6 H, J = 7 cps, $(CH_3)_2CH$]. The OH absorption was a function of the concentration of the solution, bp 80–82° (8 mm).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.76; H, 10.73.

The solid unsaturated alcohol (fraction B, **3**) was recrystallized from 95% alcohol giving material of mp 52.0–52.5° and exhibited the following spectra: infrared 3.05 (hydroxyl group), 6.07 (double bond), 9.65, 9.75 and 9.92 μ (cyclopropane ring?); nmr singlet at δ 4.79 (2 H, >C=CH– and CHOH), singlet at 1.70 (3 H, CH_3C=), multiplet at 1.35 (1 H, cyclopropane?), multiplet at 0.55 (2 H, cyclopropane) and a pair of doublets around 0.95 [7 H, J = 7 cps, $(CH_3)_2CH$]. The position of the OH absorption shifted with concentration. Both alcohols were reoxidized to the starting material (umbellulone) with chromium trioxide–pyridine in good yields.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.85; H, 10.58.

Reduction of Umbellulone with Sodium Borohydride.—A solution of sodium borohydride (0.494 g, 0.013 mol) and sodium hydroxide (0.19 g, 0.0025 mol) in 50 ml of water was dropped slowly into a stirred solution of umbellulone (2.0 g, 0.013 mol) in methanol (50 ml). The reaction mixture was stirred at room temperature for 24 hr. A saturated solution of ammonium chloride was added until all the solids dissolved. The product was extracted with ether, dried over sodium sulfate and the ether removed on a rotatory evaporator. The crude product (1.89 g) was analyzed by gas chromatography (15% Carbowax 1000 on Chromosorb W, 5 ft × $^1/_8$ in., 100°, nitrogen flow rate 40 ml/min). Using known mixtures, the ratio of saturated alcohol, unsaturated alcohol, umbellulone, and dihydroumbellulone was 68.6:14:7.9:5.7. Their retention times increased in the order dihydroumbellulone, saturated alcohol, unsaturated alcohol, umbellulone.

Reduction of Umbellulone with Lithium Borohydride.—Following the same method as with lithium aluminum hydride, umbellulone (2.54 g, 0.0169 mol) was reduced by lithium borohydride (0.15 g, 0.0069 mol) in ether. The crude product (2.32 g) was analyzed by gas chromatography and indicated unsaturated alcohol (62.8%), saturated alcohol (33.3%), saturated ketone (2.9%), and umbellulone (1%).

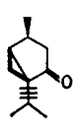
Reduction of Umbellulone with Lithium Aluminum Tri-*t*-butoxyhydride.—The lithium aluminum hydride procedure was followed. Umbellulone (5.0 g, 0.033 mol) was reduced with lithium tri-*t*-butoxyhydride (8.5 g, 0.033 mol) in ether giving 4.7 g of crude material. Analysis by gas chromatography indicated dihydroumbellulone (79.6%), umbellulone (16.6%), and saturated plus unsaturated alcohols (3.8%).

Reduction of Piperitone.[10]—The same methods were used as with umbellulone. Analysis was by gas chromatography (15% Carbowax 1000 on Chromosorb W, 5 ft × $^1/_8$ in., 108°).

Reduction of Pulegone.[10]—The same methods were used as with umbellulone. Analysis was by gas chromatography (15% Carbowax 1000 on Chromosorb W, 5 ft × $^1/_8$ in., 108°).

Registry No.—**1**, 546-78-1; **2**, 18750-22-6; **3**, 18750-23-7.

(7) Professor R. H. Eastman has pointed out that the same nonequivalence of methyl groups has been observed in the hydride reduction of dihydroumbellulone (i); J. N. Lowe, *Dissertation*, Stanford University, 1963. The assignment of configuration of the reduction products was made on the basis of steric arguments but the difference in chemical shift of the isopropyl groups is just the opposite of ours (*i.e.*, the major reduction product has nearly equivalent methyl groups while the minor one exhibits a large difference). While the assignment of configuration in dihydroumbellulone (i) rests on firm grounds, the difference in chemical shifts in the reduction products may be related to the difference in planarity of the five-membered ring in the umbellulols and dihydroumbellulols.



i

(8) H. Wienhaus and K. T. Todenhöfer, *Schimmel's Berichte*, 285 (1929).

(9) J. W. Wheeler, Jr., and R. H. Eastman, *J. Amer. Chem. Soc.*, **81**, 236 (1959).

(10) J. T. Baker Chemical Co.

The Synthesis of an A-Furano Steroid

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Numerous modifications of the steroid nucleus have been prepared in the search for an endocrine agent with a novel spectrum of biological activity. The substitution of a heteroatom such as nitrogen or oxygen for carbon seems an especially intriguing modification, for transport and metabolism may be altered without doing violence to the shape of the molecule. Thus a host of aza steroids are now known.[1]

(1) See, for example, S. Rakhit and M. Gut, *J. Org. Chem.*, **30**, 639 (1965); N. J. Dorrenbos and R. E. Havranek, *ibid.*, **30**, 2474 (1965).