

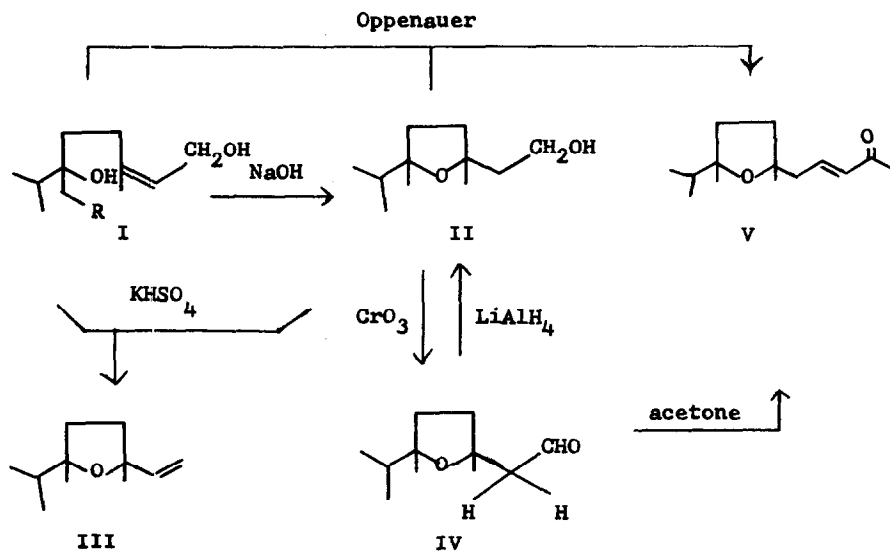
**A NEW SYNTHESIS OF IRONES IV (1)**  
**6-SUBSTITUTED GERANIOLS, 6-SUBSTITUTED IONONES AND**  
**TETRAHYDROFURAN ANALOGS**

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In their attempted synthesis of 6,9,10-trimethyl-9-hydroxy-undeca-3,5-dien-2-one, a precursor of  $\alpha$ -irone, Mousseron-Canet and coworkers (2) reported that 6-methyl-6-hydroxydihydrogeraniol I (R=H) failed to undergo the Oppenauer oxidation in acetonic medium. The hydroxydienone in question has been, however, successfully synthesized by us (1) by using a modified Grignard reaction involving the intermediate methylgrignard of 6-ketodihydrogeraniol VI and acetone. Also, contrary to the report of the French group we found that the Oppenauer oxidation of glycol I (R=H) afforded as the major reaction product (70%) 2,5-dimethyl-5-isopropyl-2-(4'oxopent-2'-en-1'-yl)-tetrahydrofuran V (b.p. 105-108° at 1 mm.,  $n_D^{20}$  1.4695, semicarbazidosemicarbazone m.p. 176-177° (EtOH), Calcd. for  $C_{16}H_{32}N_6O_3$ : C, 53.9; H, 9.65; N, 23.6. Found: C, 53.38; H, 9.37; N, 23.6; 2,4-dinitrophenylhydrazone, m.p. 100° (EtOH), Calcd. for  $C_{20}H_{28}N_4O_5$ : C, 59.40; H, 6.98; N, 13.85. Found: C, 59.12; H, 6.88; N, 14.-; 4-phenylsemicarbazone, m.p. 158-158.5° (EtOH), Calcd. for  $C_{21}H_{31}N_3O_2$ : C, 70.53; H, 8.74; N, 11.75. Found: C, 70.29; H, 8.97; N, 11.92).

The formation of the tetrahydrofuran ring system was also the predominant reaction when glycol I (R=H) was treated with strong bases or acids. Thus, when I (R=H) was distilled over a pellet of NaOH around 220° it afforded 2-(2,5-dimethyl-5-isopropyltetrahydrofuran)-ethanol II (b.p. 82-85° at 2 mm.,  $n_D^{20}$  1.4545, Calcd. for  $C_{11}H_{22}O_2$ : C, 70.93; H, 11.85. Found: C, 71.41; H, 11.77) as a mixture of two stereoisomers in nearly equal proportions.



Dehydration of either I (R=H) or II with  $KHSO_4$  around 140° afforded 2,5-dimethyl-5-isopropyl-2-vinyltetrahydrofuran III which appeared as a single peak in gas liquid chromatography but consisted probably of a mixture of two stereoisomers (b.p. 74-76° at 20 mm.,  $n_D^{20}$  1.4410, Calcd. for  $C_{11}H_{18}O$ : C, 78.51;

H, 11.98. Found: C, 78.9; H, 12.3).

Chromic oxidation of II afforded 2-(2,5-dimethyl-5-isopropyltetrahydrofuran)-acetaldehyde IV as a probable mixture of stereoisomers which appeared, however, as a single peak in the gas liquid chromatogram (b.p. 110-112° at 20 mm.,  $n_D^{20}$  1.4465, semicarbazone m.p. 115-115.5° (Benz. + Hexane). Calcd. for  $C_{12}H_{23}N_2O_3$ : C, 59.73; H, 9.60; N, 17.41. Found: C, 59.63; H, 9.49; N, 17.70). Reduction of IV with  $LiAlH_4$  afforded II as the original equimolar mixture of the two stereoisomeric alcohols. Acetone condensation of IV afforded V in good yields as a probable mixture of stereoisomers which showed, however, one single peak in a 20 M carbowax column chromatogram.

The structure of IV and its semicarbazone was determined by N.M.R.\* and was shown to favor the tetrahydrofuran system where two  $\alpha$  protons are present as against one  $\alpha$  proton in an alternate tetrahydropyran structure. Indeed the multiplet below  $\delta$  which may be assigned to these  $\alpha$  protons has an area about twice as great as that due to the aldehyde proton.

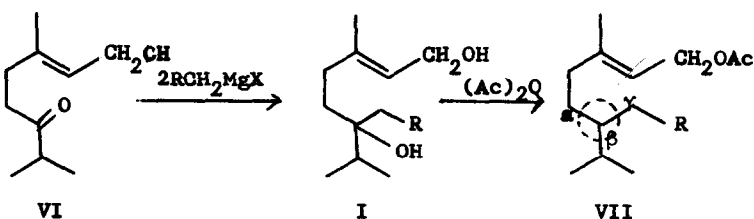
The possibility of the aldehyde being a 1:1 mixture of stereoisomers is to be considered in view of the presence of eight clearly resolved peaks in the methyl region where one

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\* We are grateful to Prof. Martin Saunders of Yale University for the NMR curves and the interpretation of the tetrahydrofuran structures of II, III and IV.

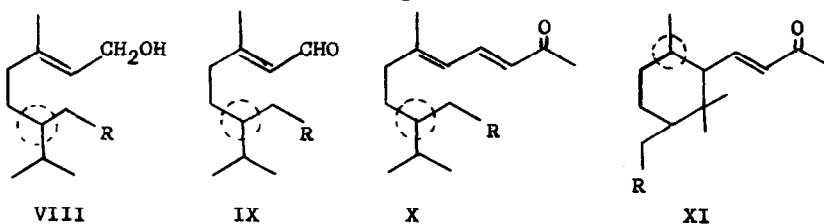
would expect four of an area 1.5 protons for the isopropyl group. Similar conclusions on the tetrahydrofuran system were derived from the N.M.R. studies of II and III.

Finally, the successful dehydration of a series of 6-alkyl homologs of I with the exclusion of cyclic derivatives was achieved by prolonged heating with acetic anhydride. Thus, two or three isomeric 6-alkyl substituted geranyl acetates (VII) were usually obtained in each series in which the newly formed alkene bonds were distributed alongside the three available ( $\alpha, \beta, \gamma$ ) positions around carbon atom 6



Treatment of I (R=H) with acetic anhydride yielded a 4:1 mixture of isomeric acetates (b.p. 95-97° at 1 mm., major  $\gamma$ -isomer of VII (R=H),  $n_D^{20}$  1.4619 with specific =  $CH_2$  infrared bands at 6.05 and 11.25  $\mu$  and minor  $\beta$ -isomer, 6-methylgeranyl acetate,  $n_D^{20}$  1.4690) which was saponified to a mixture of two corresponding  $\gamma, \beta$  isomeric alcohols consisting of 3,7-dimethyl-6-methylene-2-octenol VIII (R=H) (b.p. 96-98° at 2 mm.,  $n_D^{20}$  1.4754. Calcd. for  $C_{11}H_{20}O$ : C, 78.5; H, 11.98. Found: C, 79.1; H, 12.1) accompanied by a small amount (25% of the

6-methylgeraniol (3) ( $n_D^{20}$  1.4812). Both isomers were easily separated by gas liquid chromatography\*. The  $\gamma$ -isomer of VIII (R=H) had specific =CH<sub>2</sub> infrared bands at 6.1 and 11.30  $\mu$ . Chromic oxidation of the mixture of VIII (R=H) afforded a mixture of the two corresponding isomeric aldehydes with 3,7-dimethyl-6-methylene-2-octenal ( $\gamma$ -isomer) IX (R=H) (4) as the major product (b.p. 90-95° at 2 mm.,  $n_D^{20}$  1.4823, semicarbazone m.p. 189-190° (EtOH). Calcd. for C<sub>12</sub>H<sub>21</sub>N<sub>3</sub>O: N, 18.83. Found: N, 18.67) and 6-methylcitral ( $\beta$ -isomer) (3) ( $n_D^{20}$  1.4926) as the minor one\*.



The  $\gamma$ -isomer of IX (R=H) gave upon condensation with acetone 6,10-dimethyl-9-methyleneundeca-3-5-dien-2-one X (R=H) (4) (b.p. 120-130° at 1 mm.,  $n_D^{20}$  1.5230; 2,4-dinitrophenylhydrazone, m.p. 155-156° (EtOH) Calcd. for C<sub>20</sub>H<sub>26</sub>N<sub>4</sub>O<sub>4</sub>: C, 62.16; H, 6.78; N, 14.57. Found: C, 62.32; H, 7; N, 14.16; it melted at 135° when mixed with the dinitrophenylhydrazone, m.p. 152-153°, derived from an authentic sample of pseudo-

\* We are indebted to Mr. P. Porcaro for the separation of the isomers on a 20 M carbowax column in a Wilkins Aerograph Autoprep. Model A-700.

irone). X (R=H) was also obtained through the Oppenauer oxidation of VIII.

Treatment of X with 85% phosphoric acid afforded a mixture of  $\alpha$ -irones identical to that obtained from  $\Psi$ -irone. Likewise, acetic anhydride treatment of the higher homologs of I (R=CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub> and C<sub>3</sub>H<sub>7</sub>) afforded the 6-substituted geraniol derivatives described in Table I. Thus, the way to the 6-substituted ionones XI was made possible by using the 6-substituted geraniols VIII via the Oppenauer oxidation or through the intermediate 6-alkylcitral IX to the 9-alkylpseudoionones X. The 9-alkylpseudoionones X mixture obtained from the Oppenauer oxidation of the corresponding 6-alkylgeraniols consisted usually of a mixture of three main isomers and their cyclization with 85% phosphoric acid afforded a mixture of usually four main isomers of the corresponding 6-alkylionones XI possessing a very persistent iris note.

The resolution of the different 6-substituted isomers of VII through XI in Table I is being further investigated.

TABLE I

	I	VII	VIII	IX	X	XI
$R = CH_3$						
Bp. 1 Torr	125-130°	95-98°	96-100°	95-104°	125-135°	125-130°
$n_D^{20}$	-	1.4638	1.4790	1.4795	1.5210	1.4988
Isomer Ratio	-	3:4:3	3:4:3	3:4:3	3:4:3	4:8:5:3
M.P.	55-56°					
$R = C_2H_5$						
Bp. 1 Torr	130-135°	105-108°	107-117°	100-115°	130-140°	130-140°
$n_D^{20}$	-	1.4615	1.4780	1.4770	1.5175	1.4985
Isomer Ratio	-	5:3:2	5:3:2	5:3:2	4:4:2	1:15:5:2
M.P.	67-68°					
$R = C_3H_7$						
Bp. 1 Torr	135-140°	112-115°	117-120°	110-120°	145-150°	140-145°
$n_D^{20}$	1.4845	1.4620	1.4780	1.4765	1.5160	1.4980
Isomer Ratio	-	2:1:1	2:1:1	3:2:1	3:2:1	1:10:5:4

References

- (1) Part III E. H. Escuinasi and M. L. Cotter, Tetrahedron Letters 47, 3481 (1964).
- (2) M. Mousseron-Canet, M. Mousseron and Ch. Levallois, Bull.Soc.Chim. France (1964) 297.
- (3) Y. R. Naves and V. Grampoloff, Helv.Chim.Acta 30, 1599 (1947).
- (4) H. Grütter, R.Helg and H. Schinz, Helv.Chim.Acta, 35, 771 (1952). Stoll, Wilhelm, Helv.Chim.Acta, 35, 775 (1952); Y. R. Naves, P. Ardizio & C. Favre, Bull. Soc.Chim. Fr. 1954, 968, 975.