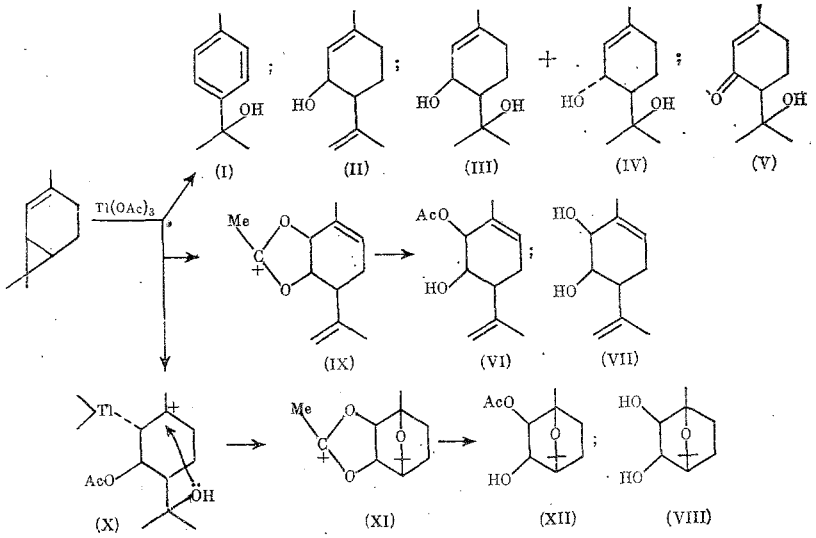
OXIDATION OF CARENE BY THALLIUM(III) ACETATE

V. V. Ratner, Z. G. Isaeva, I. P. Povodyreva,
N. F. Goryachkina, Yu. Ya. Efremov, and B. A. Arbuzov

UDC 542.943.7:547.597

According to the data cited in [1], thallium(III) acetate adds across both of the unsaturated fragments of the 3-carene molecule. In the present paper we consider the oxidation of 2-carene, which contains a vinylcyclopropane fragment in the molecule [2-6], by this reagent.

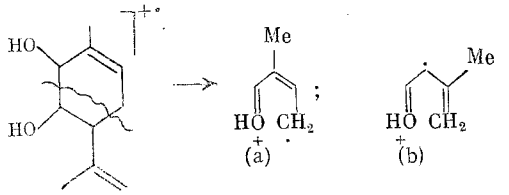
Unlike in the case of 3-carene, the action of $Tl(OAc)_3$ on 2-carene leads to a more complex mixture of products. The following were isolated from the products of the saponification of the primary reaction mixture: 2-p-tolylpropanol-2 (I), p-menth-1,8-diene-3-ol (II) [3], p-menth-1-en-3β,8-diol (III) [6], p-menth-1-en-3α,8-diol (IV), p-menth-1-en-3-on-8-ol (V) [6], p-menth-1,8-dien-5,6-diol (VII), and 2,3-dihydroxy-1,8-cineole (VIII)



The structures of the newly prepared (VII) and (VIII) follow from their IR, PMR, and mass spectral data. The PMR spectrum of compound (VII) contains signals from the protons of the CH_3 groups attached to the double bonds (δ = 1.7, 1.76 ppm, 6H), from the carbinol protons (δ = 4.1 ppm), from the proton of the trisubstituted double bond (δ = 5.15 ppm, 1H), and from the protons of the terminal double bond (δ = 4.90 ppm, 2H). The IR spectrum (ν, cm^{-1}) contains absorption bands due to secondary OH groups (1010, 1040, 1055, 1085, 3240, and 3380), and the trisubstituted (850, 1680, 3020) and terminal (890, 1640, 3090) double bonds. In the IR spectrum of a 10^{-3} M solution of (VII) in CCl_4 there are intense bands in the OH group valence vibration region at 3562 and 3573 cm^{-1} with a shoulder at around 3615-3620 cm^{-1}. The band at 3562 cm^{-1} belongs to the OH group at C^6 which forms an intramolecular hydrogen bond with the neighboring hydroxyl group while the band at 3573 cm^{-1} belongs to the OH group on C^5 which interacts with the π-electrons of the terminal double bond [7]. The band at 3620 cm^{-1} belongs to the free OH group on C^5 since it can occur both in a free form as well as in a form bound to the π-electrons of the isopropenyl group [8]. According to the mass spectral data, (VII) has a molecular mass of 168 and contains two hydroxyl groups which are indicated by the presence of peaks due to the ions $[M - H_2O]^+$ 150 [1, 2] and $[M - 2H_2O]^+$ 132 [11]. After exchange with D_2O, the molecular ion peak is shifted toward higher masses by two units [9]. In the case of (VII), the route leading to ions (a) and (b) with the same mass m/z = 84 is a favorable route for dissociative ionization. Since the mass of both of the ions is the same, the intensity of the peak corresponding to them at m/z = 84 must be significant [11]

A. M. Butlerov Chemical Institute, Kazan State University; V. I. Ul'yanova-Lenin Kazan' Aviation Institute. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 8, pp. 1824-1828, August, 1983. Original article submitted July 21, 1982.

0568-5230/83/3208-1651$07.50



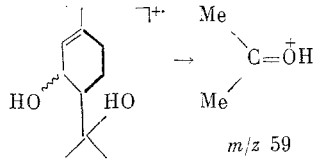
The 2,3-dihydroxycineole structure (VIII) has been proposed for the compound with the composition $C_{10}H_{18}O_3$. In the PMR spectrum signals are observed from the protons of three CH_3 groups attached to carbon atom bearing oxygen (δ, ppm: 1.26, 1.21, 1.03) and from two carbinol protons (4.26 ppm). The mass spectrum showed that (VIII) has a molecular mass of 186 and contains two OH groups, $[M - H_2O]^+$ 168 (0.40) and $[M - 2H_2O]^+$ 150 (0.62). After exchange with D_2O the molecular ion peak was displaced by two units of mass toward higher masses. The appearance in the mass spectrum of an ion peak with m/z = 60 corresponding to an ion with the composition $C_2H_4(OH)_2$ which is shifted by two mass units toward greater masses in the deuteroanalog indicated a vicinal arrangement of the OH groups. It followed from these data that, apart from the two alcoholic oxygen atoms in molecule (VIII), it contains a further oxygen atom which is probably in the form of an ether.

It would be expected from a consideration of Dreiding models, subject to the assumption that the six-membered ring in (VIII) has a boat conformation and the $(CH_3)_2CO$ group occupies a flagstaff position, that the lateral vicinal OH groups, situated in an exo,cis- or endo, cis-position, could be linked by an intramolecular hydrogen bond. The IR spectra of a 10^{-3} M solution of (VIII) in CCl_4 exhibits intense bands at 3538 and 3635 cm^{-1} in the region of the valence vibrations of an OH group forming a hydrogen bond with a second hydroxyl group and which acts as a proton donor while the second band corresponds to an intramolecularly hydrogen bonded OH group acting as a proton acceptor [10]. This assignment of the bands is the most likely, but the possibility that a hydrogen bond is formed between a hydroxyl group and the bridging oxygen atom cannot be completely precluded although the distance between the latter and the hydrogen of an exo-hydroxyl group, as measurements on Dreiding models have shown, is significantly greater than that between the two hydroxyl groups.

The p-menth-1-en-3α,8-diol structure (IV) was ascribed to the compound of composition $C_{10}H_{18}O_2$ on the basis of the presence of a CH_3 group attached to the carbon atom with a double bond [δ, ppm: 1.7 (3H)], a $(CH_3)_2CO$ group [1.2, 1.36 (6H)], and a triply substituted double bond [5.53 doublet (1H)]. In the IR spectra absorption bands are present which are due to secondary and tertiary OH groups (1030, 1060, 1080, 1110, 1145, 1170, 1190, and 3350 cm^{-1}) and a trisubstituted double bond (850, 1675, and 3015 cm^{-1}). The molecule (IV) is an epimer of p-menth-1-en-3β,8-diol (III) which has been identified in the products of this reaction [6]. There were two bands in the IR spectrum of a 10^{-3} M solution of (IV) in CCl_4 in the region of the valence vibrations of the OH group: a broad intense band at 3525 cm^{-1} and a less intense band at 3610 cm^{-1}. The latter band is assigned to the tertiary hydroxyl group, a proton acceptor. The intense band at 3525 cm^{-1} belongs to the secondary OH proton donor since there was no band due to a free secondary hydroxyl group observable in the spectrum.

A consideration of the Dreiding models under the assumption that the six-membered ring has a half-chair conformation showed that, when there is a trans-orientation of the secondary OH and the hydroxyisopropyl groups, an intramolecular hydrogen bond can only arise when the two groups are in a diequatorial position. The higher frequency of the CO valence vibrations (1030, 1065 cm^{-1}) in comparison with p-menth-1-en-3β,8-diol (1000, 1020 cm^{-1}) [6] is also indicative of an equatorial orientation of the OH group. A trans-diequatorial orientation of the OH group on C^3 and of the hydroxyisopropyl group in (IV) follows from this and a cis-axial-equatorial orientation, giving a stronger hydrogen bond (3514 cm^{-1}) [6] in the case of (III).

The mass spectra of both the p-menth-1-en-3,8-diol's are in accord with the structures which have been proposed for (III) and (IV). The molecular ion peak is practically absent from these spectra, which is evidence of the low stability of the molecular ions. This is explained by the well-known fact that the molecular ions of tertiary alcohols are less stable than those of secondary alcohols. The presence of two OH groups is confirmed by the peaks $[M - H_2O]^+$ 152 (0.35) and $[M - 2H_2O]^+$ 134 (1.8). The appearance in the mass spectra of both the diols of an intense peak with m/z 59 confirms the presence of hydroxyisopropyl groups in them



m/z 59

Possible routes for the formation of the compounds which have been identified in the reaction products are shown in the reaction scheme. Like $Hg(OAc)_2$, $Tl(OAc)_3$ can attack both a double bond and a three-membered ring [11-13]. Hence, the formation of p-menth-1,8-dien-3-ol (II), and the p-menth-1-en-3,8-diols (III) and (IV) can be represented both as the result of an attack on the double bond of the 2-carene molecule by the reagent followed by an allylic rearrangement and as the result of an attack on just the cyclopropane ring.

Compound (VII) could have been formed as the result of a successive attack on the cyclopropane ring and the double bond or a simultaneous attack on these fragments. Decomposition of the acetoxonium cation which has been formed (IX) by water in AcOH (see Experimental) leads to the cis-hydroxyacetate (VI). The formation of (VIII) can be explained by assuming that the OH group at C^8 acts as an internal nucleophile in the stabilization of the carbocation (X) which is formed during the successive attack of $Tl(OAc)_3$ on the cyclopropane ring and the double bond. The acetoxonium cation (XI) which has been formed initially yields the cis-hydroxyacetate (XII).

Hence, $Tl(OAc)_3$ stereospecifically attacks both the double bond and the three-membered ring of 2-carene, leading to the predominant formation of diol ethers and not to the formation of the products of allylic acetohydroxylation, as in the case of oxidation by $Hg(OAc)_2$ and $Pb(OAc)_4$.

EXPERIMENTAL

The IR spectra were recorded on a UR-10 instrument, the PMR spectra on Varian T-60 and Varian HA-100 instruments, and the mass spectra on a MI-1305 mass spectrometer with direct introduction of the substance into the ionization source and rapid recording of the mass spectra at an ionizing potential of 50 V and a sample input temperature of ~20°C. The sum of the intensities of all the peaks was taken as 100. The compounds were deuterated by mixing the sample with D_2O in the admission system and subsequently pumping off the water in vacuo. Melting points were determined in a Kofler apparatus. The GLC analysis was carried out using a Chrom-4 instrument (5% polyethyleneglycol sebacinate on Chromosorb G, N_2 carrier gas). "L Chemapol" grade SiO_2 was used for the adsorption chromatography and Silufol for the TLC. The 2-carene was prepared according to [14] and the $Tl(OAc)_3$ according to [15].

Oxidation of 2-Carene. Thirty grams of 2-carene, maintained at a temperature of 25-27°C by cooling, was added dropwise to a solution of $Tl(OAc)_3$ consisting of 50 g of Tl_2O_3 in 400 ml of glacial acetic acid. The mixture was kept for three days and nights at 20°C, diluted with water, and extracted with ether. The extract was washed with a solution of $NaHCO_3$, with water, dried over $MgSO_4$, and evaporated down. The reaction products (33.1 g) were saponified by heating (6 h at 80°C) with an alcoholic solution of alkali (15.63 g NaOH in 80 ml H_2O and 210 ml C_2H_5OH). The saponification products (20.1 g) were subjected to chromatography on SiO_2. Upon elution with petroleum ether, 3 g of 2-carene were obtained and 0.5 g of p-menth-1,8-dien-3-ol (II) was obtained when the elution was carried out with a petroleum ether–ether mixture (8:2). IR spectrum (ν, cm^{-1}): 850, 890, 960, 1010, 1030, 1150, 1220, 1240, 1380, 1440, 1645, 1680, 2730, 3015, 3080, 3350. p-Nitrobenzoate, mp 107-109°C. It gave no depression of the melting point when mixed with the p-nitrobenzoate of p-menth-1,8-dien-3-ol (II) prepared in [3].

2-p-Tolylpropanol-2 (I). (0.4 g) was isolated by elution with a mixture of petroleum ether and ether (8:2). IR spectrum (ν, cm^{-1}): 820, 870, 960, 1100, 1170, 1260, 1360, 1380, 1520, 3020, 3050-3080, 3400. The 3,5-dinitrobenzoate had a double melting point and there was no depression of the melting point when it was mixed with the 3,5-dinitrobenzoate of 2-p-tolylpropanol-2 [16].

cis-p-Menth-1,8-dien-5,6-diol (VII). 0.3 g of (VI) was isolated from the fractions eluted with a mixture of petroleum ether and ether (7:3). mp 72-73.5°C, $[\alpha]_D^{20} = -29.1°$ (C 2.3, C_6H_6). IR spectrum (ν, cm^{-1}): 850, 890, 910, 1010, 1040, 1055, 1080, 1140, 1160, 1210, 1260, 1380, 1460, 1640, 1680, 3020, 3080, 3250, 3380. PMR spectrum (CCl_4, δ, ppm): 1.7 s, 1.76 s ($2CH_3$, 6H), 4.1 s (CHO, 2H), 4.89 d ($C=CH_2$, 2H). 5.15 (C=CH, 1H).

Mass Spectrum of (VII): 169(0.07), 168(0.22), 153(0.062), 151(0.18), 150(1.2), 133(1.4), 132(11), 131(2.2), 119(1.9), 118(1.4), 117(10), 116(1.9), 115(4.5), 109(0.61), 108(1.4), 107(0.84), 105(1.1), 93(3.5), 92(2.8), 91(7.0), 85(3.5), 84(11), 83(3.5), 79(1.5), 77(2.2), 69(1.4), 65(2.0), 64(0.93), 63(1.1), 62(0.71), 57(0.69), 56(1.2), 55(1.2), 53(1.5), 52(0.62), 51(1.5), 50(0.46), 44(0.31), 43(1.7), 42(0.6), 41(4.2), 39(3.7).

p-Menth-1-en-3α,8-diol (IV). 1.85 g of (IV) was prepared from the fractions eluted with a mixture of petroleum ether and ether (7:3). $[\alpha]_D^{20}$ +163° (C 2.46, C_2H_5OH). IR spectrum (ν, cm^{-1}): 800, 850, 905, 960, 1030, 1060, 1110, 1140, 1170, 1190, 1220, 1240, 1290, 1380, 1670, 3010, 3300. PMR spectrum (CCl_4, δ, ppm): 1.2 s, 1.36 s (9,10-CH_3, 6H), 4.33 s (C^3H, 2-OH, 3H, splits into a doublet and shifts upon dilution), 5.53 d (C^2H, 1H).

Mass Spectrum of (IV): 155(0.03), 154(0.07), 153(0.29), 152(0.35), 134(1.8), 133(0.19), 132(0.22), 124(0.53), 119(3.4), 117(0.66), 115(0.4), 111(0.8), 110(2.0), 109(3.1), 105(0.66), 95(0.92), 94(7.9), 93(3.0), 92(1.6), 91(5.0), 85(0.26), 84(0.5), 83(0.4), 82(1.6), 81(0.9), 80(1.3), 79(9.7), 78(1.0), 77(3.9), 69(0.9), 67(0.8), 65(1.4), 60(2.4), 59(10.5), 58(1.0), 57(0.26), 55(0.9), 54(0.6), 53(1.0), 52(0.4), 51(1.0), 46(1.0), 45(5.9), 43(8.8), 41(4.0), 39(3.1), 31(1.6).

p-Menth-1-en-3-on-8-ol (V). 0.43 g of CrO_3 was carefully added to a solution of 0.55 ml of pyridine in 7.1 ml of CH_2Cl_2 and mixed for 15 min. A solution of 0.12 g of (IV) was then added. 0.1 g of (V) was obtained. The IR and PMR spectra were similar to the corresponding spectra of (V) which had previously been prepared by the oxidation of p-menth-1-en-3β,8-diol (III) [6].

p-Menth-1-en-3β,8-diol (III). A mixture of two products (III) and (IV) (2.96 g) was isolated during elution with a mixture of petroleum ether and ether (6:4, 5:5). Repeated chromatography of this mixture yielded pure (III) with mp 79-81.5°C which did not give any depression of the freezing point when mixed with a sample of p-menth-1-en-3,8-diol [6]. The IR and PMR spectra were identical.

Mass Spectrum of (III): 153(0.05), 152(0.3), 150(0.13), 135(0.76), 134(4.0), 120(1.3), 119(9.1), 109(1.7), 105(1.3), 94(8.9), 91(8.7), 79(11), 77(5.3), 65(2.3), 60(2.5), 59(11), 53(1.1), 51(1.4), 45(2.3), 43(7.6), 41(5.0), 39(3.7), 31(1.5), 29(8.9).

2,3-Dihydroxy-1,8-cineole (VIII). 0.55 g of (VIII) was isolated from the fractions eluted with a mixture of petroleum ether and ether (3:7). mp 99.5-101°C (petroleum ether 70-100°C). IR spectrum (ν, cm^{-1}): 770, 820, 830, 940, 980, 1000, 1040, 1060, 1090, 1140, 1160, 1380, 1390, 3300. PMR spectrum (CCl_4, δ, ppm): 1.03 s, 1.21 s, 1.26 s (3-CH_3, 9H), 1.56 multiplet (2-CH_2), 3.81 (2-OH, 2H), 4.26 d (2H).

Mass Spectrum of (VIII): 187(0.06), 186(0.40), 169(0.10), 168(0.40), 153(0.27), 151(0.15), 150(0.62), 128(1.8), 127(2.0), 126(3.7), 111(3.5), 110(1.5), 109(4.7), 108(5.7), 93(3.7), 91(2.2), 71(5.5), 69(7.0), 60(2.7), 59(2.7), 55(4.0), 53(1.5), 45(2.0), 43(1.8), 42(2.7), 41(9.0), 39(4.5).

CONCLUSIONS

2-p-Tolylpropanol-2, p-menth-1,8-dien-3-ol, p-menth-1-en-3α,8-diol, p-menth-1-en-3β,8-diol, p-menth-1-en-3-on-8-ol, p-menth-1,8-dien-5,6-diol, and 2,3-dihydroxy-1,8-cineole are formed during the oxidation of 2-carene by thallium (III) acetate.

LITERATURE CITED

1. V. V. Ratner, Z. G. Isaeva, I. P. Povodyreva, Yu. Ya. Efremov, and B. A. Arbuzov, Izv. Akad. Nauk SSSR, Ser. Khim., 1136 (1983).
2. G. Ohloff and W. Giersch, Helv. Chim. Acta, 51, 1328 (1968).
3. B. A. Arbuzov, V. V. Ratner, Z. G. Isaeva, and M. G. Belyaeva, Dokl. Akad. Nauk SSSR, 205, 1115 (1972).
4. B. A. Arbuzov, V. V. Ratner, Z. G. Isaeva, E. Kh. Kazakova, and M. G. Belyaeva, Izv. Akad. Nauk SSSR, Ser. Khim., 2752 (1971).
5. B. A. Arbuzov and Z. G. Isaeva, Usp. Khim., 45, 1339 (1976).
6. B. A. Arbuzov, V. V. Ratner, Z. G. Isaeva, M. G. Belyaeva, and I. P. Povodyrova, Izv. Akad. Nauk SSSR, Ser. Khim., 1049 (1979).
7. L. I. Bellamy and R. Pace, Spectrochim. Acta, 22, 525 (1966).
8. T. Shishibori, Bull. Chem. Soc. Jpn., 41, 1170 (1968).

9. Yu. Ya. Efremov, Dokl. Akad. Nauk SSSR, 178, 1080 (1968).
10. S. I. Angyal and R. I. Joung, J. Am. Chem. Soc., 81, 5467 (1959).
11. H.-J. Kabbe, Liebigs Ann. Chem., 656, 204 (1962).
12. A. Banerji, I. Banerji, and R. Das, J. Sci. Ind. Res., 33, 510 (1974).
13. A. South, Jr. and R. J. Ouellette, J. Am. Chem. Soc., 90, 7064 (1968).
14. S. P. Acharay and H. C. Brown, J. Am. Chem. Soc., 89, 1928 (1967).
15. L. Fieser and M. Fieser, Reagents for Organic Synthesis, Vol. 3, Wiley, New York (1967).
16. Z. G. Isaeva, B. A. Arbuzov, V. V. Ratner, and I. P. Povodyreva, Izv. Akad. Nauk SSSR, Ser. Khim., 466 (1965).

CONTROL OF REGIOSELECTIVITY IN CYCLIZATION OF AZADIKETONES TO 3-KETOPIPERIDINE SYSTEMS: SYNTHESIS AND STEREOCHEMISTRY OF 1,2,5- AND 1,5,6-TRIMETHYLPIPERID-3-ONES

G. T. Katvalyan and É. A. Mistryukov

UDC 542.91+541.63:547.824

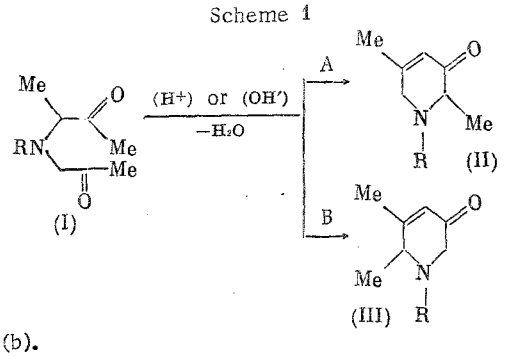
In the course of synthesis of 4,5-dehydro-3-ketopiperidines by cyclization of azadiketones [1], we have shown that in their cyclization the carbonyl on the least-substituted segment assumes the electrophile function and nothing can change the tendency to react in this direction. Thus the azadiketone (I) in both acidic and basic conditions gives regioisomer (II) exclusively, in the formation of which the acetonyl carbonyl participates as the electrophile and the ketobutyl segment as the nucleophile (direction A), just as if direction B were completely blocked [2].

In the present communication we describe methods of regulating the regioselectivity of this reaction, making it possible to obtain compounds important for proposed syntheses of precursors of biologically important compounds.

By replacing the t-butyl substituent on nitrogen by the less bulky methyl group [ketone (Ia)] the regioselectivity of the reaction decreases substantially and it now goes appreciably in direction B (the ratio (II):(III) = 78:22 under acidic cyclization conditions).

The regioselectivity decreases still more on forming a ketal from the acetonyl carbonyl. Starting with compound (IV) under acid conditions, about 40% of the other regioisomer (IIIa) is now formed. Such an effect of use of the ketal is evidently linked with cyclization by intermediate formation of the enol ether, which is a nucleophilic segment.

Scheme 1



R = Me (a), *t*-Bu (b).

Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 8, pp. 1829-1832, August, 1983. Original article submitted November 24, 1982.

