Experimental

Umbellulone (I).—Umbellulone was isolated from the oil of the California Bay Tree by the bisulfite addition method of Wienhaus and Todenhöfer.[8,9] The product had b.p. 99.0–99.8° at 15 mm., showed a single peak on the gas chromatogram obtained from a 12′ × 8 mm. silicone oil on Celite gas chromatography column, and had an infrared absorption which was identical with that of a highly purified sample prepared by Eastman and Oken.[9]

Photolysis.—Small (1–6 ml.) samples of umbellulone were photolyzed in soft-glass or quartz test tubes filled with nitrogen.

Irradiation of a 5-ml. sample of umbellulone for 48 hours with radiation from a H400 General Electric mercury arc lamp gave a quantitative yield of thymol, while illumination for only 20 hours of a similar sample but in a quartz test tube gave identical results. Irradiation for 50 hours in the quartz test tube using a 2537 Å. source (Mineralite) gave a mixture of 90% starting material and 10% thymol. Illumination for 50 hours in quartz with a 75 watt tungsten incandescent lamp produced only traces of thymol.

In all cases the extent of reaction and the identity of products were established by liquid–vapor partition chromatography and infrared absorption spectroscopy.

Pyrolysis.—Umbellulone was pyrolyzed in a tube furnace at 280 ± 2° in small, sealed Pyrex tubes (*ca.* 10 cm. × 8 mm.). Sample sizes were *ca.* 0.5 ml. and the duration of the heating was 18 hr. The crude reaction mixture was seeded with a crystal of thymol (m.p. 50.5–51.0°) (Eastman Kodak Co.). After centrifugal filtration to remove the thymol which crystallized, the mother liquors were analyzed on a 12′ × 8 mm. silicone oil on Celite gas chromatography column and were found to be approximately one-third *sym*-thymol and two-thirds thymol. The *sym*-thymol collected at the exit of the column melted at 37–38°. A sample five times recrystallized from pentane melted at 49.5–50.0°. A mixture of thymol and *sym*-thymol was liquid at 25°.

***sym*-Thymol** (VI).—3-Methyl-5-isopropylcyclohex-2-en-1-one was prepared from isobutyraldehyde and acetoacetic ester according to the method of Knoevenagel.[6a] Our product boiled at 120–122° at 15 mm. (reported[6a] 124° at 15 mm.) and had an infrared spectrum very similar to that of piperitone. The ketone was aromatized using N-bromosuccinimide and dehydrohalogenation. In a typical run the ketone (5 cc., 4.7 g., 0.03 mole) was dissolved in carbon tetrachloride (30 cc.). N-Bromosuccinimide (6.2 g., 0.035 mole) was added and a reflux condenser attached. The flask was illuminated with a 250 watt flood lamp which produced a reddish color in the solution which persisted until the reaction was complete. The reaction mixture was filtered to remove the succinimide and the carbon tetrachloride was distilled off under reduced pressure after the solution had been dried with sodium sulfate. The residual oil was separated on the silicon gas chromatography column. The major product (0.2 g.) was *sym*-thymol. The *sym*-thymol collected at the exit of the column melted at 39.5–41.0°. It was recrystallized five times from pentane to produce a white solid (0.13 g.) melting at 49.5–50.0°. Knoevenagel[6b] reported a melting point of 54°. However, Carpenter and Easter[10] found that *sym*-thymol prepared by the Knoevenagel synthesis melted at 50.0–50.5°. A mixed melting point of the synthetic *sym*-thymol and *sym*-thymol from umbellulone showed no depression. The infrared spectra of the two samples were identical, and markedly different from that of thymol.

Anal.[11] Calcd. for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.81; H, 9.60.

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

[9] R. H. Eastman and A. Oken, THIS JOURNAL, **75**, 1029 (1952).

[10] M. S. Carpenter and W. M. Easter, *J. Org. Chem.*, **20**, 401 (1955).

[11] Analyses by Microchemical Specialties Co., Berkeley, Calif.

STANFORD, CALIF.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Optical Rotatory Dispersion Studies. XXI.[1] Effect of Ring Size[2]

BY CARL DJERASSI AND G. W. KRAKOWER[3]

RECEIVED JULY 14, 1958

The rotatory dispersion curves of a series of 3-methylcycloalkanones were determined, all of them possessing the same absolute configuration (R) at the single asymmetric center. The sign of the Cotton effect was found to be identical in the five- and six-membered rings and was then inverted in the case of the seven-membered ketone. No further change was encountered up to and including 3-methylcyclopentadecanone (IV). The synthetic work in the nine-membered series (XV–XVIII) involved acyloin condensation of (+)-β-methylazelaic acid dimethyl ester, produced by anodic coupling, while 3-methylcycloheptanone was formed by diazomethane ring expansion of 3-methylcyclohexanone. This ring expansion produced both 3-methyl- and 4-methylcycloheptanone, rotatory dispersion being used to differentiate between the two structures since the 4-methyl isomer VI exhibited a plain dispersion curve in contrast to the anomalous one of 3-methylcycloheptanone (V).

Our investigations of the application of rotatory dispersion to organic chemical problems[4] have encompassed many areas including the determination of absolute configuration, the detection of conformational distortion and the location of carbonyl groups. One field which has as yet not been examined systematically is the effect of ring size upon the shape of the optical rotatory dispersion curve and the present paper is concerned with experimental work along those lines.

The reference compound for the entire investigation was (+)-3-methylcyclohexanone (II) which is available in one step by acid-catalyzed retroaldolization[5] of (+)-pulegone (I), whose absolute configuration is known.[6,7] The rotatory dispersion of (+)-3-methylcyclohexanone (II) has already been recorded in the literature[8] and we have confirmed (see Fig. 1) that it is characterized by a single positive Cotton effect curve.[9] The next lower

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[1] Paper XX, N. J. Leonard, J. A. Adamcik, C. Djerassi and O. Halpern, THIS JOURNAL, **80**, 4858 (1958).

[2] Supported by grant No. CY-2919 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

[3] Taken from Part II of the Ph.D. dissertation of G. W. K.

[4] For pertinent review of the first ten papers in this series see C. Djerassi, *Bull. soc. chim. France*, 741 (1957). For additional references to later papers see ref. 1.

[5] See J. L. Simonsen and L. N. Owen, "The Terpenes," Cambridge University Press, Cambridge, 1953, 2nd ed., Vol. I, p. 371.

[6] See E. J. Eisenbraun and S. M. McElvain, THIS JOURNAL, **77**, 3383 (1955).

[7] See A. J. Birch, *Ann. Repts., Chem. Soc.*, **47**, 192 (1950), and J. A. Mills and W. Klyne in W. Klyne's "Progress in Stereochemistry," Academic Press, Inc., New York, N. Y., 1954, Vol. I, Chapter 5.

[8] H. S. French and M. Naps, THIS JOURNAL, **58**, 2303 (1936).

[9] For nomenclature see C. Djerassi and W. Klyne, *Proc. Chem. Soc.*, 55 (1957).

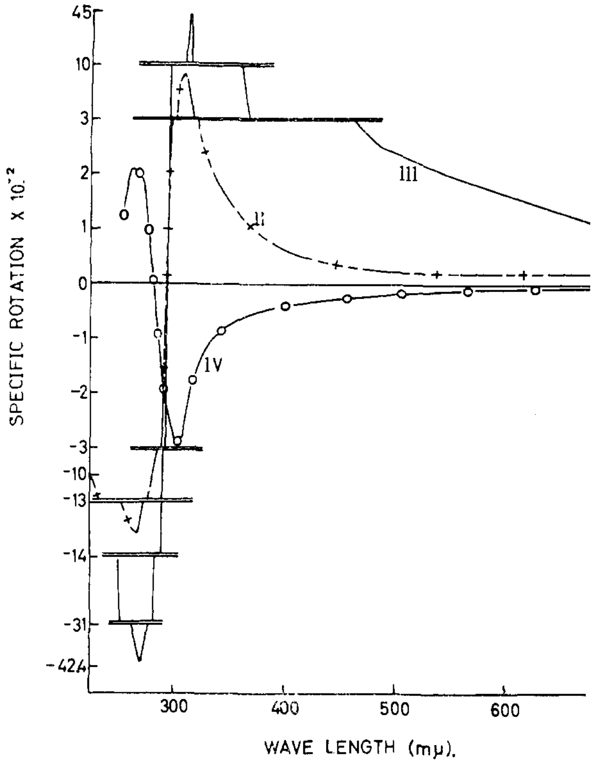

Fig. 1.—Optical rotatory dispersion curves (methanol solution) of (+)-3-methylcyclohexanone (II), (+)-3-methylcyclopentanone (III) and (−)-muscone (IV).

homolog, (+)-3-methylcyclopentanone (III), has been synthesized,[6,10] from (+)-pulegone (I) without disturbing the asymmetric center and the rotatory dispersion curve (Fig. 1) of this ketone exhibits a positive Cotton effect curve of rather high amplitude.[9] Since both (+)-3-methylcyclohexanone (II) and (+)-3-methylcyclopentanone (III) are derived from (+)-pulegone (I), the absolute configuration of the asymmetric center in all three ketones is (R).[11]

A third readily available 3-methylcycloalkanone is the naturally occurring (−)-muscone (3-methylpentadecanone) (IV)[12] whose absolute configuration (R) was established by its synthesis[13] from β-methylglutaric acid monomethyl ester of established stereochemistry. The optical rotation of (−)-muscone (IV) has already been measured[13] at four different wave lengths down to 404.6 mμ and the values were found to be progressively more negative. This indicated that the compound most likely possessed a negative Cotton effect curve and when its rotatory dispersion was determined more precisely in our laboratory[14] throughout the relevant ultraviolet region, (−)-muscone was found (Fig. 1) to have a negative Cotton effect curve of rather small amplitude.

The results summarized in Fig. 1 demonstrate the striking fact that the rotatory dispersion curve of the large membered ring ketone IV possesses a Cotton effect curve of *opposite sign* as compared to the corresponding five- (III) and six-membered (II) ketones in spite of the fact that all of them contain only a single asymmetric carbon atom of identical absolute configuration (R) and which is separated from the carbonyl group in each instance by one carbon atom. Therefore for potential assignments of absolute configurations of cycloalkanones by rotatory dispersion means, it was clearly desirable to determine at what ring size—between six (II) and fifteen (IV)—this inversion of the Cotton effect occurred and since no such ketones were known, a synthetic program had to be undertaken.

In view of the above observation that inversion of the Cotton effect can occur in a homologous series of cyclic ketones with identical absolute configuration but differing in the size of the ring, it was indispensable that the synthetic ketones had to be of known absolute configuration. This essentially eliminated syntheses involving resolution of the final ketone and required synthetic routes starting with precursors of established absolute configuration. For the cycloheptanone series, it was felt that the diazomethane ring expansion procedure[15] could be employed, especially since it has been claimed[16] that treatment of optically active 3-methylcyclohexanone with diazomethane yielded only 3-methylcycloheptanone (V) rather than the expected mixture[15,17] of 3- (V) and 4-methyl-(VI)-cycloheptanone.

Since the diazomethane ring expansion fulfilled the requirement of not affecting the asymmetric center, it was applied to (+)-3-methylcyclohexanone (II) and yielded a mixture of cycloheptanones and cyclooctanones. The cycloheptanone fraction was separated readily and was fractionated carefully. While the boiling point and refractive index of the various fractions did not differ significantly and only one peak was observed upon vapor phase chromatography, differences in the optical rotation were noted. As demonstrated in Fig. 2, the rotatory dispersion curves of two cycloheptanone fractions of identical boiling point were found to be completely different, one of them exhibiting a negative Cotton effect curve while the other one possessed only a plain curve. Both fractions were shown to be methylcycloheptanones by elementary analysis, infrared examination and formation of semicarbazones (melting points not completely identical but undepressed upon admixture). We conclude, therefore, that contrary to the earlier report,[16] both 3-methylcycloheptanone (V) and 4-methylcycloheptanone (VI) were produced. The product with the negative Cotton effect curve is assigned the 3-methyl structure V while the material with the plain curve is believed to be the 4-methyl isomer VI, since model experiments with aliphatic ketones and aldehydes[18,19] showed that

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(10) For leading references see G. H. Stempel, W. O. Forshey and G. S. Schaffel, THIS JOURNAL, **67**, 344 (1945).

(11) According to the new convention of R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

(12) L. Ruzicka, *Helv. Chim. Acta*, **9**, 1008 (1926).

(13) S. Ställberg-Stenhagen, *Arkiv Kemi*, **3**, 517 (1951).

(14) The measurements were carried out on a sample of natural (−)-muscone kindly provided by Dr. M. Stoll, Firmenich and Cie., Geneva, Switzerland.

(15) C. D. Gutsche, *Org. Reactions*, **8**, 364 (1954).

(16) M. Mousseron and G. Manon, *Bull. soc. chim. France*, 392 (1949).

(17) See D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

(18) C. Djerassi and L. E. Geller, to be published.

(19) See P. A. Levene and A. Rothen, *J. Chem. Phys.*, **4**, 48 (1936)

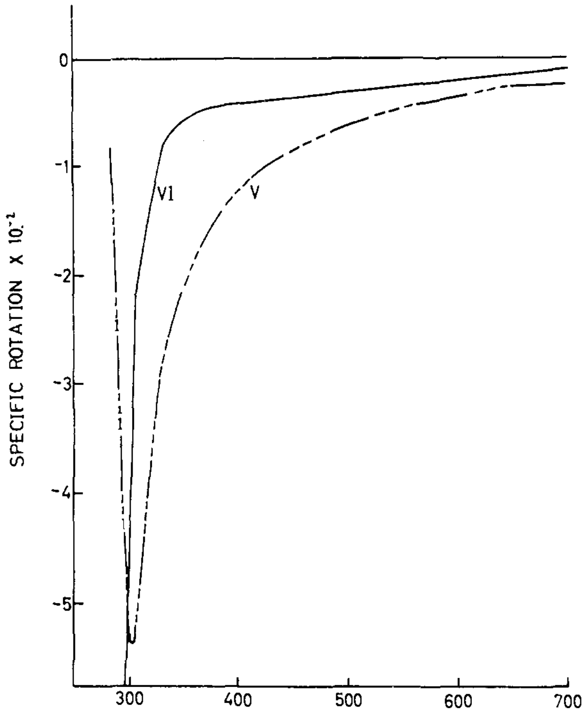

Fig. 2.—Optical rotatory dispersion curves (methanol solution) of (—)-3-methylcycloheptanone (V) and (—)-4 methylcycloheptanone (VI).

separation of the asymmetric center from the carbonyl function by two carbon atoms resulted in a tendency toward a plain[9] dispersion curve. This structure assignment to the methylcycloheptanone mixture arising from diazomethane ring expansion of 3-methylcyclohexanone (II) by means of rotatory dispersion affords still another illustration of the utility of this physico-chemical tool.

While it appears from the above observation (Fig. 2) that inversion of the Cotton effect curve occurs already at the stage of the seven-membered ketone[20] it was, nevertheless, important to examine at least one example of a medium-sized ring ketone in order to see whether this trend continued or was perhaps reversed due to the well-known[21] *trans*-annular effects operating in such rings.

One of the best syntheses for medium-sized rings[21] is the acyloin condensation[22] and it was decided to utilize this procedure for the preparation of an optically active cyclononanone. In order to fulfill the above-mentioned criterion of known absolute configuration, we employed (+)-citronellal (VII) which was oxidized to (+)-citronellic acid (VIII) and then transformed into its methyl ester IX. Ozonization now produced (+)-methyl hydrogen β-methyl adipate (X) where the asymmetric center possesses the (R) configuration. This half-ester was selected as one component for the synthesis of the requisite azelaic acid for the acyloin condensation. It was planned to prepare the acid by anodic coupling[23] and for that purpose, benzyl[24] hydrogen glutarate (XI) was selected as the other partner in order to facilitate the separation of the three possible products formed during anodic coupling of two different esters. The primary products (XIIa, XIII and XIVa) were debenzylated catalytically and the neutral product, β,β'-dimethylsebacic acid dimethyl ester (XIII), removed by ether extraction from alkaline solution. The acidic fraction, consisting of suberic acid (XIIb) and the monomethyl ester of β-methylazelaic acid (XIVb), was separated by fractional distillation followed by further purification *via* the dimethyl ester, thus affording the desired (+)-β-methylazelaic acid dimethyl ester (XIVc). Acyloin condensation[22] produced (—)-β-methylazeloin, which may possess either structure XVa or XVb, and which was characterized by conversion to (—)-β-methylazelil (4-methylcyclononane-1,2-dione) (XVII). As shown in Fig. 3, both compounds are characterized by negative Cotton effect curves[25] and this also applied to the corresponding methylcyclononanone (XVIII).

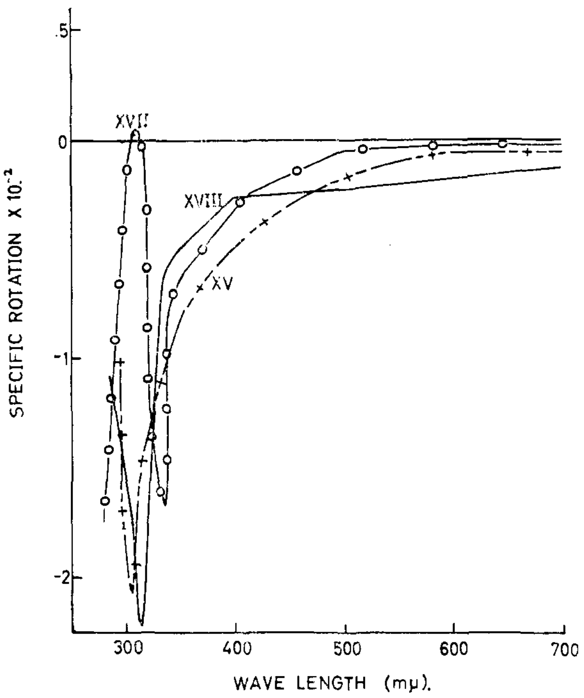

Fig. 3.—Optical rotatory dispersion curves (methanol solution) of (—) β-methylazeloin (XV), (—)-β-methylazelil (XVII) and (—)-3(or 4)-methylcyclononanone (XVIII).

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(20) If the "octant rule" (C. Djerassi, W. Klyne, W. Moffitt, A. Moscovitz, and R. B. Woodward, in preparation) can be applied to cycloheptanones, then it would be predicted that the boat form of V would exhibit a negative, and the chair form of V a positive Cotton effect.

(21) See V. Prelog in A. Todd's "Perspectives in Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 96–133.

(22) (a) V. L. Hansley, U. S. Patent 2,228,268; (b) V. Prelog, L. Frenkiel, M. Kobelt and P. Barman, *Helv. Chim. Acta*, **30**, 1741 (1947); (c) M. Stoll and J. Hulstkamp, *ibid.*, **30**, 1815, 1822, 1837 (1947).

(23) See W. S. Greaves, R. P. Linstead, B. R. Shephard, S. L. S. Thomas and B. C. L. Weedon, *J. Chem. Soc.*, 3326 (1950), and succeeding papers by R. P. Linstead, *et al.*

(24) The use of a benzyl half-ester, which aids in the separation of the products from a mixed anoding coupling reaction, has been introduced by L. Dolejs and L. Novotny, *Coll. Czech. Chem. Comm.*, **19**, 716 (1954), and by R. P. Linstead, B. C. L. Weedon and B. Wladislaw, *J. Chem. Soc.*, 1097 (1955). See also F. Sorm, M. Streibl, V. Jarolim, L. Novotny, L. Dolejs and V. Herout, *Chemistry & Industry*, 252 (1954).

(25) The rotatory dispersion of (steroidal) ketols is discussed in detail by C. Djerassi, O. Halpern, V. Halpern, O. Schindler and C. Tamm, *Helv. Chim. Acta*, **41**, 250 (1958).

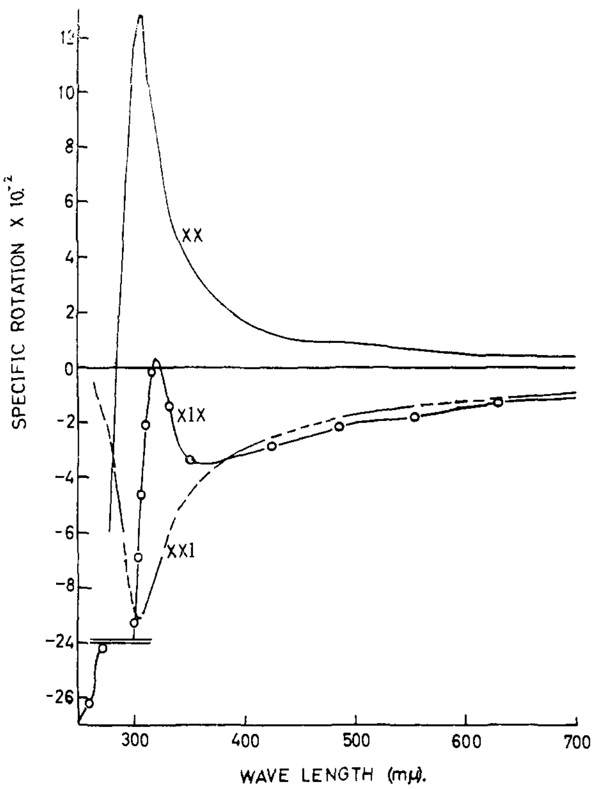
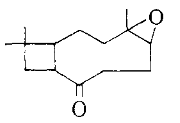


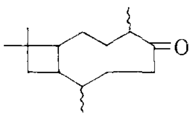
Fig. 4.—Optical rotatory dispersion curves (methanol solution) of 5,6-oxido-6,10,10-trimethylbicyclo[7:2:0]undecan-2-one (XIX), 2,6,10,10-tetramethylbicyclo[7:2:0]undecan-5-one (XX) and 2,8,8-trimethylbicyclo[5:2:0]nonan-5-one (XXI).

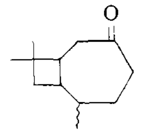
As far as the conversion of the keto XV to the corresponding ketone XVIII is concerned, the first experiments were conducted using the zinc-acetic acid procedure.[22b,c] The results were not too satisfactory and recourse was taken to the recently developed calcium–ammonia reduction,[26] which has been used with such success for the deacetoxylation of steroidal ketol acetates.[26,27] Indeed, when (−)-β-methylazeloin (XVa and/or XVb) was transformed into its acetate (XVIa and/or XVIb) and then treated with calcium in liquid ammonia, a ketone (XVIII) was obtained uncontaminated by acyloin, alcohol or acetate.

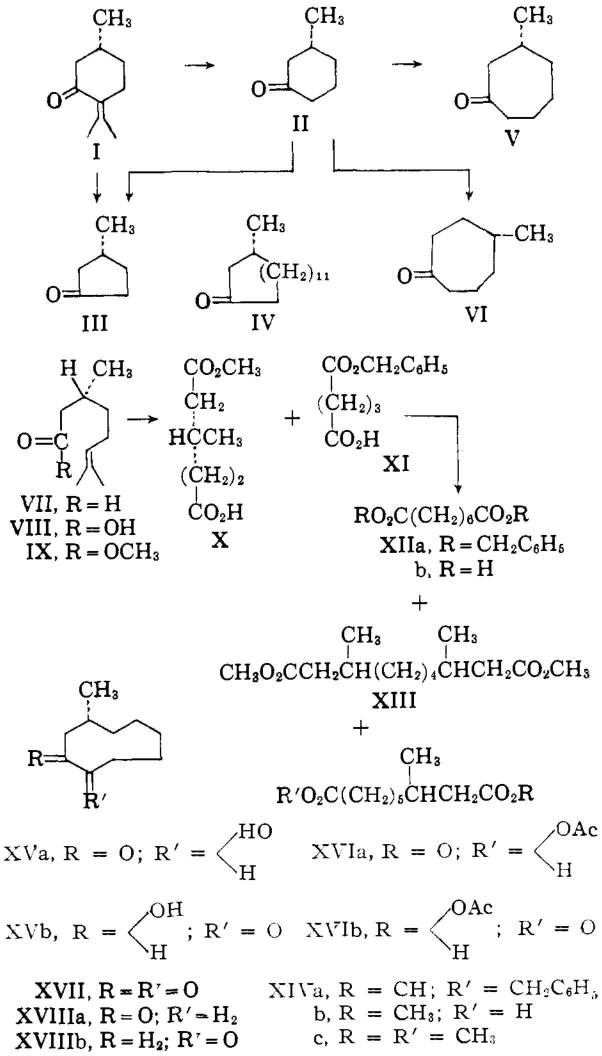
Using the argument employed above in the structure assignment of 3-methylcycloheptanone (V), the fact that an anomalous rotatory dispersion curve was produced indicates that the ketone should be largely 3-methylcyclononanone (XVIIIa) rather than the 4-methyl isomer XVIIIb. Unfortunately, this cannot be done with the same degree of certainty because it is quite possible that the "distance factor"[18] is rendered meaningless by operation of a *trans*-annular effect.[1,28] Nevertheless, the rotatory dispersion curves collected in Fig. 3 suggest strongly that the negative Cotton effect observed in the seven- (V) and fifteen- (IV) membered ketones applies also to the intermediate ring sizes.

In Fig. 4 are collected the rotatory dispersion curves of three ketones, XIX,[29] XX[30a] and XXI,[30b] which are related to caryophyllene. They represent further examples of anomalous dispersion curves exhibited by 7- and 9-membered ketones in which an asymmetric center is not more than one carbon atom removed from the carbonyl group.


XIX


XX


XXI



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[26] J. H. Chapman, J. Elks, G. H. Phillipps and L. J. Wyman, *J. Chem. Soc.*, 4344 (1956).

[27] J. S. Mills, H. J. Ringold and C. Djerassi, This Journal, **80**, 6118 (1958).

[28] It should be noted that M. Stoll and A. Commarmont, *Helv. Chim. Acta*, **31**, 1435 (1948), reduced an analogous ketol by the zinc procedure in the 15-membered series and obtained an inseparable mixture of 3- and 4-methylcyclopentadecanone.

[29] W. Treibs, *Ber.*, **80**, 56 (1947). We are indebted to Prof. D. H. R. Barton (Imperial College of Science and Technology) for a sample.

[30] (a) F. Sorm, unpublished observation. (b) F. Sorm, L. Dolejs and J. Pliva, *Coll. Czech. Chem. Comm.*, **15**, 186 (1950).

Experimental[31]

(+)-**3-Methylcyclohexanone** (II).—Freshly distilled (+)-pulegone (I)[32] (250 g.) was heated under reflux with 1000 cc. of water and 200 cc. of concd. hydrochloric acid and the acetone so formed was removed continuously by slow distillation through a fractionating column. The product was then steam distilled, the distillate was extracted with ether and after washing, drying and evaporating the ether, (+)-3-methylcyclohexanone (II)[33] was fractionally distilled; yield 120 g., b.p. 164–166°, $n^{23}D$ 1.4448, α_D +12.75° (neat), λ_{max}^{capill} 5.84 μ; R.D. (Fig. 1) in methanol (*c* 0.212): $[\alpha]_{700}$ +2°, $[\alpha]_{589}$ +5°, $[\alpha]_{309}$ +977°, $[\alpha]_{270}$ −1352°, $[\alpha]_{240}$ −960°.

(+)-**3-Methylcyclopentanone** (III) was prepared according to the literature directions[6,10] by thermal cyclization of the barium salt of (+)-β-methyladipic acid, obtained by ozonolysis of (+)-pulegone (I), and its infrared spectrum was shown to be identical with that of an authentic sample kindly supplied by Dr. E. J. Eisenbraun[6]; R. D. (Fig. 1) in methanol (*c* 0.062): $[\alpha]_{650}$ +124°, $[\alpha]_{589}$ +153°, $[\alpha]_{312.5}$ +4490°, $[\alpha]_{270}$ −4270°, $[\alpha]_{250}$ −3063°.

(−)-**Muscone** (IV),[14] R.D. (Fig. 1) in methanol (*c* 0.069): $[\alpha]_{700}$ −4°, $[\alpha]_{589}$ −7°, $[\alpha]_{305}$ −314°, $[\alpha]_{265}$ +210°, $[\alpha]_{255}$ +106°; R.D. in octane (*c* 0.115): $[\alpha]_{700}$ −17°, $[\alpha]_{589}$ −31°, $[\alpha]_{317.5}$ −229°, $[\alpha]_{315}$ −209°, $[\alpha]_{310}$ −226°, $[\alpha]_{290}$ +35°.

Ring Expansion of (+)-**3-Methylcyclohexanone** (II).—The ring expansion of 37 g. of (+)-3-methylcyclohexanone (II) was carried out with 80 g. of *p*-tolylsulfonylmethylnitrosamide[34] exactly as described for the similar reaction[35] with cyclohexanone. The steam-volatile material (13 g.) was fractionated through a Podbielniak spiral column with the results summarized in Table I.

TABLE I

FRACTIONAL DISTILLATION OF METHYLCYCLOHEPTANONES

Fraction	Wt., g.	B.p. °C.	Mm.	n_D[a]	α_D (neat)
1	1.937	80–86	20	1.4560	−16.75°
2	3.340	79–81	15	1.4560	−26.00
3	3.790	84–85	20	1.4561	−37.60
4	1.310	87–96	16	1.4581	−28.65
5	0.775	97–100	16	1.4620	+18.10

[a] The first three measurements were made at 24°, the last two at 26°.

Analysis of fraction 1 by vapor phase chromatography[36] showed it to be contaminated with a small amount of starting ketone II. Consequently, it was separated by vapor phase chromatography into two fractions, 1a and 1b, the former consisting of pure 3-methylcyclohexanone (II). Fraction 3 was homogeneous by vapor phase chromatography and a mixture of fractions 1b and 3 showed only a single peak in the vapor phase chromatogram. The infrared spectra were virtually identical except for very minor differences in the fingerprint region; λ_{max}^{capill} 5.86 μ. Fraction 1b exhibited a plain rotatory dispersion curve (Fig. 2) in methanol solution (*c* 0.071): $[\alpha]_{700}$ −10°, $[\alpha]_{589}$ −58°, $[\alpha]_{300}$ −450°, $[\alpha]_{290}$ −1035°; therefore it is considered to be (−)-**4-methylcycloheptanone** (VI), whose racemate has already been obtained by Adamson and Kenner.[17]

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18; O, 12.68. Found: C, 76.36; H, 11.28; 0, 12.30.

The semicarbazone was prepared by the sodium acetate method in methanol solution and was recrystallized from dilute methanol, m.p. 166–169°.

Anal. Calcd. for $C_9H_{17}N_3O$: C, 58.98; H, 9.35; N, 22.93. Found: C, 58.41; H, 9.22; N, 23.20.

Fraction 3, assigned the (−)-**3-methylcycloheptanone** (V) structure, exhibited the following rotatory dispersion curve (Fig. 2) in methanol solution (*c* 0.159): $[\alpha]_{700}$ −25°, $[\alpha]_{589}$ −38°, $[\alpha]_{305}$ −624°, $[\alpha]_{290}$ −218°.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.95; H, 11.03.

The semicarbazone was recrystallized from aqueous ethanol, m.p. 160–163°; when mixed with the semicarbazone of VI, the m.p. was 163–167°.

Anal. Calcd. for $C_9H_{17}N_3O$: C, 58.98: H, 9.35; N, 22.93. Found: C, 58.99; H, 9.28; N, 22.87.

(+)-**Methyl Citronellate** (IX).—(+)-Citronellal (VII)[37] (77 g.) was added to a solution[38] of 187 g. of silver nitrate in 600 cc. of water and 200 cc. of ethanol. After cooling to below 20°, a solution of 124 g. of sodium hydroxide in 800 cc. of water was added with stirring over a period of 2 hr. and stirring was then continued at room temperature for 15 hr. The insoluble material was removed by filtration and washed with ethanol and ether and the basic filtrate was extracted with ether to remove unreacted starting material (7.5 g.). Acidification of the aqueous solution with hydrochloric acid, extraction with ether and distillation of the crude citronellic acid[39] (VIII) (73 g.) through a 6-inch Vigreux column yielded 65 g., b.p. 148–155° (15 mm.), $n^{28}D$ 1.4510. The entire 65 g. was heated under reflux for 16 hr. with 32 g. of methanol, 100 cc. of methylene chloride and 1 cc. of concd. sulfuric acid, diluted with water and the organic layer was separated, washed, dried and fractionally distilled. The fraction (48 g.) with b.p. 101–102° (20 mm.), $n^{26}D$ 1.4401, corresponded to (+)-**methyl citronellate** (IX), while a higher boiling fraction (11 g.), b.p. 110–150° (21 mm.), was largely recovered citronellic acid. The analytical sample of the methyl ester IX was prepared in a small scale experiment by diazomethane methylation of citronellic acid (VIII) and exhibited b.p. 145° (70 mm.), $n^{28}D$ 1.4386, α_D +4.1° (neat).

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94; O, 17.37. Found: C, 71.13; H, 10.85; O, 17.93.

(+)-**Methyl Hydrogen** β-**Methyladipate** (X).—A solution of 48 g. of methyl citronellate (IX) in 500 cc. of ethyl acetate was cooled in a Dry Ice–acetone-bath, a stream of ozone was passed through until a blue color developed and then let stand overnight. The solution was concentrated *in vacuo* to a volume of 100 cc. and added dropwise with stirring to a cooled mixture of 50 cc. of 30% hydrogen peroxide, 50 g. of potassium bicarbonate and 200 cc. of water and stirred overnight. After separating into neutral and acidic components, the latter (24 g.) was fractionally distilled through a Podbielniak spiral column and afforded 18.5 g. of the desired ester X, b.p. 127–130° (1.8 mm.), $n^{27}D$ 1.4411, α_D +4.8° (neat), λ_{max}^{capill} 5.79 and 5.89 μ.

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.16; H, 8.10; 0, 36.74; mol. wt., 174. Found: C, 55.41; H, 8.03; 0, 36.75; neut. equiv., 175.

Mixed Electrolysis of (+)-**Methyl Hydrogen** β-**Methyladipate (X) and Benzyl Hydrogen Glutarate (XI)**.—A mixture of 44.4 g. of benzyl hydrogen glutarate (XI)[40] and 34.8 g. of (+)-methyl hydrogen β-methyladipate (X) was diluted with sufficient absolute methanol to give 130 cc. of solution and one-half of it was added to the electrolysis cell[41] which con-

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[31] Melting points and boiling points are uncorrected. We are indebted to Miss B. Bach for the infrared spectra and to Mr. W. Closson, Mr. L. A. Mitscher, Mrs. T. Nakano, Mrs. V. Halpern and Mrs. J. Osiecki for the rotatory dispersion curves. The microanalyses were preformed by Dr. A. Bernhardt, Mülheim, Germany.

[32] Obtained from A. M. Todd Co., Kalamazoo, Mich.; b.p. 113–114° (25 mm.), $n^{26}D$ 1.4842, λ_{max}^{EtOH} 252.5 mμ, log ϵ 3.81; R.D. in dioxane (*c* 0.058): $[\alpha]_{700}$ +3°, $[\alpha]_{589}$ +9°, $[\alpha]_{365}$ +388°, $[\alpha]_{362.5}$ +371°, $[\alpha]_{357.5}$ +405°, $[\alpha]_{297.5}$ −1481°, $[\alpha]_{294}$ −1433°, $[\alpha]_{290}$ −1510°, $[\alpha]_{285}$ −845°.

[33] For constants see R. Adams, C. M. Smith and S. Loewe, THIS JOURNAL, **64**, 2087 (1942).

[34] T. J. De Boer and H. J. Backer, *Org. Syntheses*, **34**, 96 (1954).

[35] T. J. De Boer and H. J. Backer, *ibid.*, **34**, 24 (1954).

[36] The vapor-phase chromatogram was conducted with a Wilkins Aerograph apparatus using a 3 meter column (0.66 cm. diameter) packed with 1:1 silicone grease on Celite (No. 545) at a temperature of 164° and a flow rate of 40 cc. of helium per minute.

[37] This material was obtained from Fritzsche Bros., New York City, and upon redistillation exhibited the following properties: b.p. 104–108° (21 mm.), $n^{24}D$ 1.4490; R.D. in methanol (*c* 0.167): $[\alpha]_{700}$ +9°, $[\alpha]_{589}$ +11°, $[\alpha]_{312.5}$ +122°, $[\alpha]_{275}$ +12°, $[\alpha]_{260}$ +49°.

[38] See M. Delépine and P. Bonnet, *Compt. rend.*, **149**, 39 (1909).

[39] M. V. Trikojus and D. E. White, *J. Proc. Roy. Soc. N.S. Wales*, **66**, 284 (1932).

[40] K. Mislow and W. C. Meluch, THIS JOURNAL, **78**, 5920 (1956).

[41] The cell consisted of a 500-cc. 3-necked flask equipped with a reflux condenser and electrodes fitted into a ground-glass joint. The electrodes were held 2 mm. apart and were made from platinum foil measuring 2 × 4 cm.; d.c. line current of 100 v. and 1–2 amp. was used, the current being controlled by a variable resistance of 10–1000 ohms.

tained 0.46 g. of sodium in 300 cc. of absolute methanol. Current was passed through the solution for 2 hr. (vigorous evolution of carbon dioxide), the temperature being kept below 50° while stirring with a magnetic stirrer. The anode became gradually coated with gummy, polymeric material and this could be corrected by periodically reversing the polarity of the electrodes or by removing and cleaning them. The other half of the original ester solution was submitted to identical treatment and the two solutions were combined and the methanol was removed. After addition of water, extraction with ether, washing with sodium hydroxide and water, the ether extract was dried, evaporated and the residue (36 g.) fractionally distilled. A total of 10 fractions was collected ranging from b.p. 86–92° (4.5 mm.) to 185–205° (1 mm.) without, however, effecting a very sharp separation of the three esters XIIa, XIII and XIVa.

Consequently, the middle fractions (16 g., b.p. 129° (5 mm.)–180° (1 mm.)) were dissolved in 20 cc. of absolute ethanol and debenzylated catalytically with 10% palladized charcoal at room temperature and atmospheric pressure for 16 hr. The catalyst was filtered, the solvent was removed and the residue (15 g.) was divided into neutral (9.5 g.) and acidic (5.0 g.) material.

The neutral fraction was shown to be the expected symmetrical coupling product of X, namely **β,β′-dimethylsebacic acid dimethyl ester (XIII)** by analysis of a sample distilled at a bath temperature of 100° and 0.05 mm.

Anal. Calcd. for $C_{14}H_{26}O_4$: C, 65.08; H, 10.14; methoxyl, 24.03. Found: C, 64.62; H, 9.90; methoxyl, 24.12.

The acidic fraction, consisting of suberic acid (XIIb) and β-methylazelaic acid monomethyl ester (XIVb), was fractionally distilled at 0.005 mm., but analysis indicated that no complete separation had been achieved. Therefore, the higher boiling fraction (1.4 g., bath temperature 115° (0.005 mm.)) richest in the desired monomethyl ester XIVb was methylated with diazomethane in ether solution and the crude **(+)-β-methylazelaic acid dimethyl ester (XIVc)** was distilled at a bath temperature of 150° and 1 mm., yielding 1.15 g. of the required ester, $\alpha_D + 2.28°$ (neat), $\lambda_{max}^{CHCl_3}$ 5.78 μ.

Anal. Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63; O, 27.79. Found: C, 62.43; H, 9.51; O, 28.24.

(−)-β-Methylazeloin (XV).—The acyloin condensation was conducted in an apparatus and under conditions similar to those recommended by Allinger.[42] A solution of 4.9 g. of (+)-β-**methylazelaic** acid dimethyl ester (XIVc) in 100 cc. of toluene was added dropwise over a period of 17 hr. to a refluxing and vigorously stirred mixture of 200 cc. of toluene containing a few grams of sodium dispersion[43] in toluene, nitrogen being passed through the system at all times. After heating for an additional 6 hr., the mixture was cooled in ice and excess sodium was decomposed by the addition of 1:1 acetic acid–toluene, followed by water. The toluene layer was separated, dried over magnesium sulfate and the toluene removed carefully by distillation through a column. The residue was distilled at a bath temperature of 150° and 20 mm. to give 1.20 g. of (−)-β-methylazeloin (XV), $\lambda_{max}^{CHCl_3}$ 2.92 and 5.87 μ; R.D. (Fig. 3) in methanol (*c* 0.065): $[\alpha]_{700}$ −5°, $[\alpha]_{589}$ −14°, $[\alpha]_{305}$ −209°, $[\alpha]_{295}$ −103°. The liquid gave a purple color with ferric chloride, turning gray on standing and exhibited a positive test for α-ketols with bismuth oxide.[44]

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66; O, 18.80. Found: C, 70.82; H, 10.55; O, 18.61.

Treatment of a few drops of (−)-β-methylazeloin (XV) with Brady reagent[45] in methanol solution and recrystallization from ethyl acetate afforded the red colored **bis-2,4-dinitrophenylhydrazone of (−)-β-methylazelil (XVII)**, m.p. 220–221.5°.

Anal. Calcd. for $C_{22}H_{24}N_8O_8$: C, 50.00; H, 4.58; N, 21.20; O, 24.22. Found: C, 49.35; H, 4.64; N, 21.26; O, 24.26.

(−)-β-Methylazelil (4-Methylcyclononane-1,2-dione) (XVII).—(−)-β-Methylazeloin (XV) (340 mg.) was added to a boiling solution of 372 mg. of bismuth oxide[44] in 10 cc. of glacial acetic acid and heating was continued for 10 min. The metallic bismuth was filtered, the filtrate was diluted with water, extracted with ether and the washed and dried ether solution was evaporated. Distillation of the residue at a bath temperature of 130° and 30 mm. afforded (−)-β-methylazelil (XVII), which was characterized by conversion to the 2,4-dinitrophenylosazone, m.p. 221–223°, undepressed upon admixture with the sample described above; R.D. (Fig. 2) in methanol (*c* 0.125): $[\alpha]_{700}$ O°, $[\alpha]_{589}$ −2°, $[\alpha]_{335}$ −117°, $[\alpha]_{302.5}$ +2°, $[\alpha]_{285}$ −170°.

(−)-3-(or 4)-Methylcyclononanone (XVIII).—A 135-mg. sample of the above-described (−)-β-methylazeloin (XV) was converted into its acetate XVI by the acetic anhydride–pyridine procedure and distilled at a bath temperature of 120–130° and 25 mm. The entire acetate (XVI), dissolved in 2 cc. of toluene, was added dropwise over a period of 5 min. to a solution of 200 mg. of calcium metal in 20 cc. of liquid ammonia cooled in a Dry Ice–acetone-bath. After stirring for an additional 15 min., bromobenzene[26] in toluene was added to discharge the blue color, followed by much water. Extraction with ether, washing with ammonium chloride solution, drying over magnesium sulfate and evaporation of the ether left a colorless oil, which was distilled at a bath temperature of 120–150° and 20 mm., $\lambda_{max}^{CHCl_3}$ 5.85 μ and no absorption corresponding to hydroxyl or acetate groups; R.D. (Fig. 3) in methanol (*c* 0.073): $[\alpha]_{700}$ −15°, $[\alpha]_{589}$ −19°, $[\alpha]_{315}$ −228°, $[\alpha]_{287.5}$ −114°.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 78.25; H, 11.67.

An alternate and less satisfactory synthesis involved removal of the hydroxyl group of XV with zinc.[22b,c] A solution of 216 mg. of (−)-β-methylazeloin (XV) in 2 cc. of glacial acetic acid was heated under reflux with 500 mg. of zinc foil, 0.5 cc. of concd. hydrochloric acid was added followed by a second portion of acid after 35 min. This was repeated twice more, the total reflux time being 2 hr. and 40 min. The product was isolated in the usual manner by ether extraction and distilled at 90–110° and 20 mm., but its infrared spectrum still showed the presence of a hydroxyl group. Consequently the material was passed through a column of alumina and eluted with pentane and benzene. The combined eluates were distilled at a bath temperature of 130° and 20 mm.; its infrared spectrum was substantially identical with that of the sample prepared by the calcium–ammonia reaction.

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(42) N. L. Allinger, *Org. Syntheses*, **36**, 79 (1956).

(43) Kindly supplied by Dr. Thomas Coffield, Ethyl Corporation, Detroit, Mich.

(44) W. Rigby, *J. Chem. Soc.*, 793 (1951).

(45) O. L. Brady, *ibid.*, 756 (1931).