***cis*-3,5-Dimethylcycloheptanone (VIb).**—The ring expansion of Vb was carried out in an identical manner to that described for the expansion of Va. From 15.0 g. of Vb the following fractions were obtained at 12 mm.: (1) 3.33 g., b.p. 66.5–70.5°; (2) 1.30 g., b.p. 70.5–83.5°; (3) 8.75 g., b.p. 83.5–85.0°; (4) 0.97 g., b.p. 85–94°. Fraction 3 was the desired ketone VIb, $n^{25}\text{D}$ 1.4524, d^{25} 0.9115 g./ml. The semicarbazone, prepared in the usual way and recrystallized once, had m.p. 165.7–166.6°, reported[17] m.p. 166.5°.

Equilibration Studies.—A 100-mg. sample of the ketone to be equilibrated was placed in a small sealed tube with 25 mg. of 10% palladium-on-carbon. The tube, placed in an iron pipe, was heated in a furnace at the desired temperature which was maintained ±3°. The pipe was then removed from the furnace and cooled rapidly by wrapping with a wet towel. The sealed tube was opened to the atmosphere and the catalyst was settled by centrifuging. The liquid was drawn off with a dropper and weighed into a vial and the proper amount of chloroform was weighed in to give the solution for the infrared analysis. The analysis was made in the usual way,[19] and the results are summarized in Table I.

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[Contribution from the Department of Chemistry and Chemical Engineering, Stanford University]

The Photolysis and Pyrolysis of Umbellulone[1]

By James W. Wheeler, Jr., and Richard H. Eastman

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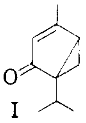
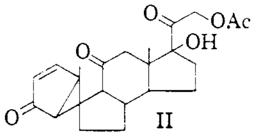
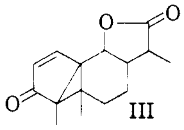
The photolysis of umbellulone produces thymol in essentially quantitative yield, while the pyrolysis of umbellulone produces, in addition to thymol, 5–10% of *sym*-thymol and traces of *p*-cymene.

It has recently been found that the cyclohexadienone systems of prednisone acetate and santonin undergo isomerization to the bicyclo[3.1.0]hexenone system found in umbellulone (I) upon ultraviolet irradiation, prednisone acetate yielding II and santonin (III).[2]


I



II



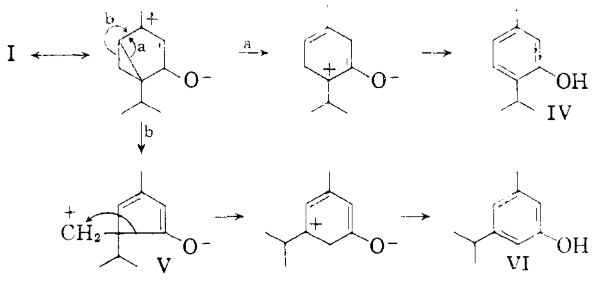
III

We have noted that samples of umbellulone (I) which have been exposed to light invariably contain traces of thymol (IV); and in view of the apparent stability of the umbellulone systems of II and III, it became of interest to determine the course of the photolysis of umbellulone itself.

The photolysis of umbellulone using a variety of sources of radiation (*cf.* Experimental) produces thymol in quantitative yield.

In view of the clear-cut nature of the photolysis, we undertook a reinvestigation of the thermal isomerization of umbellulone, first reported by Semmler[3] to yield thymol, and a vital link in his proof of the structure of umbellulone.[4] Since his observation, the thermal isomerization of umbellulone has continued to be of interest.[5] Contrary to a recent claim,[5c] we have found that the crude pyrolysate from carefully-purified umbellulone contains not only thymol (IV) but also *sym*-thymol (VI) to the extent of 5–10%, and traces of *p*-cymene. Separation of *sym*-thymol from thymol proved difficult, but was achieved by fractional crystallization of the pyrolysate followed by liquid–vapor partition chromatography of the mother liquors. The identity of the *sym*-thymol (m.p. 49.5–50.0°) from the pyrolysis was established by comparison with an authentic sample (m.p. 49.5–50.0°) prepared following the method of Knoevenagel.[6] No depression was observed in a mixed melting point determination, and the two samples had identical infrared absorption spectra.

While the appearance of *sym*-thymol as a pyrolysis product was somewhat surprising,[7] it can be rationalized on the basis of a ring-enlargement in the species V as



It is noteworthy that the pyrolysis and photolysis of umbellulone apparently proceed by different pathways. The results suggest an ionic course for the pyrolysis and a free radical course for the photolysis.

The failure of the umbellulone systems in II and III to undergo facile aromatization on irradiation in analogy to umbellulone may be related to the structural situations in II and III that require the scission of two carbon–carbon bonds for the production of an aromatic system.

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(1) The material of this article is taken from the thesis for the M.S. degree of James W. Wheeler, Jr., at Stanford University.

(2) D. Arigoni, H. Bosshard, H. Bruderer, G. Büchi, O. Jeger and L. J. Krebaum, *Helv. Chim. Acta*, **40**, 1733 (1957); D. H. R. Barton and W. C. Taylor, This Journal, **80**, 244 (1958); D. H. R. Barton, P. de Mayo and M. Shafiq, *Proc. Chem. Soc.*, 205 (1957); *J. Chem. Soc.*, 140 (1958).

(3) F. Semmler, *Ber.*, **40**, 5019 (1907); **41**, 3992 (1908).

(4) The recent synthesis of an isomer of umbellulone [H. E. Smith and R. H. Eastman, This Journal, **79**, 5500 (1957)] having an ultraviolet absorption spectrum identical with that of umbellulone confirmed the structure proposed by Semmler.

(5) (a) E. K. Nelson, U. S. Patent 1,666,342; (b) W. J. Hund, U. S. Patent 1,967,440; (c) R. S. Aries and M. C. Kidder, "Proceedings of Conference on the Cultivation of Drug and Associated Economic Plants in California," California State Department of Education, 1947, p. 218.

(6) (a) H. E. A. Knoevenagel, *Ann.*, **288**, 325 (1895); (b) *Ber.*, **27**, 2347 (1894).

(7) The possibility that *sym*-thymol arose from an impurity in the umbellulone was considered and is rejected on the basis that gas-chromatographically homogeneous umbellulone was employed, and that thymol was the *only* product of photolysis of the same sample of umbellulone.

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.

STANFORD, CALIF.

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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.

[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. 1, 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).