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THE STEREOCHEMISTRY OF 2-BENZALCYCLOHEXANONES AND 2-BENZALCYCLOPENTANONES[1]

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Abstract—*trans*-2-Benzal-6-methylcyclohexanone (III) and *trans*-2-benzal-5-methylcyclopentanone (VII) isomerize in the presence of acid to the endocyclic unsaturated isomers 2-benzyl-6-methyl-2-cyclohexenone (II) and 2-benzyl-5-methyl-2-cyclopentenone (VI) respectively. Structure proof and chemical conversions of II are described. Isomerization of III to its *cis* isomer IV was accomplished by light irradiation. It is shown how to distinguish by means of UV, IR and NMR spectra between isomeric *trans* benzalcyclohexanones, *cis* benzalcyclohexanones and cyclohexenones.

DURING their extensive work on the chemistry of cyclanones Cornubert *et al.*[3] observed the formation of two isomers in the aldol condensation of 2-methylcyclohexanone (I) with benzaldehyde. Permanganate oxidation of these products yielded benzoic acid. On this basis the solid isomer, obtained in the base catalyzed aldol reaction, was assigned the structure of *trans*-2-benzal-6-methylcyclohexanone (III) while the liquid isomer resulting from condensation in the presence of hydrochloric acid was described[3] as *cis*-2-benzal-6-methylcyclohexanone (IV). Analogous *cis* and *trans* benzalketone structures were assigned to several other isomer pairs obtained in condensations of cyclohexanones and cyclopentanones with benzaldehyde. In the light of our experience with endo and exocyclic unsaturated 1-tetralones[4] and in view of the well known generalization[5] about the relative stability of endo- versus exocyclic double bonds this assignment seemed questionable. This and the scarce knowledge about the formation and the chemistry of *cis*-2-benzalcyclanones[6] made a re-examination of the chemistry of the benzalcyclohexanone III and the benzalcyclopentanone VII desirable.

trans-2-Benzal-6-methylcyclohexanone (III) was obtained according to Cornubert.[3] Its UV absorption maximum[7] at 284 mμ (ϵ 16,000) and ozonolysis to benzoic acid support the early structure assignment. The spectrum of the liquid isomer of III,

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[1] [a] For a preliminary account of part of this study see A. Hassner and T. C. Mead, *Tetrahedron Letters* No. 25, 1223 (1962);

[b] This work was supported by Public Health Service Grant GY-4475 from the National Cancer Institute.

[2] Shell Oil Co. Fellow 1960–61.

[3] R. Cornubert, *Bull. soc. chim. Fr.* (3) **5**, 513 (1938); R. Cornubert and P. Louis, *Ibid.* (5), **5**, 520 (1938).

[4] A. Hassner and N. H. Cromwell, *J. Amer. Chem. Soc.* **80**, 893 (1958).

[5] H. G. Brown, J. Brewster and H. Schechter, *J. Amer. Chem. Soc.* **76**, 467 (1954); H. C. Brown, *J. Org. Chem.* **22**, 439 (1957); R. B. Turner and R. H. Garner, *J. Amer. Chem. Soc.* **80**, 1424 (1958); A. C. Cope, D. Ambros, E. Ciganek, C. F. Howell and Z. Jacura, *Ibid.* **82**, 1750 (1960).

[6] D. H. R. Barton, A. Head and P. May, *J. Chem. Soc.* 935 (1957).

[7] The generalizations of R. B. Woodward (*J. Amer. Chem. Soc.* **64**, 72 (1942)) and of H. French and M. E. T. Holden (*Ibid.* **67**, 1240 (1945)) predict an absorption maximum at 288 mμ; *trans* benzalacetone likewise absorbs at 288 mμ.

λ_{max} 234 mμ (ϵ 9,000), obtained by acid catalyzed condensation of 2-methylcyclohexanone (I) with benzaldehyde or by isomerization of III in the presence of hydrogen chloride, indicated an endocyclic unsaturated structure as in II.[8] The IR spectra of isomers II and III are characteristically different in the carbonyl and double bond region (see below). Phenylacetic acid and α-methylglutaric acid as products of ozonolysis of the liquid isomer are best accounted for by the structure 2-benzyl-6-methyl-2-cyclohexenone (II) rather than by IV. The isolation of benzoic acid[3] in the permanganate oxidation of II is most likely a result of side chain oxidation of phenylacetic acid.

Further evidence for structure II is furnished by lithium aluminium hydride reduction of II to 2-benzyl-6-methyl-2-cyclohexenol (XII) which except for benzenoid absorption is transparent in the UV. Alcohol XII, an allylic alcohol, can be converted back to ketone II by means of manganese dioxide. By contrast, *trans*-2-benzal-6-methylcyclohexanol (IX), obtained by hydride reduction of ketone III, exhibits an UV maximum (244 mμ, ϵ 19,000) characteristic of styrenes.[9] Attempts to prepare common alcohol derivatives of IX and XII were unsuccessful due to facile dehydration in these compounds. Addition of bromine to the unsaturated alcohol IX yielded 2-bromo-2-(α-bromo-benzyl)-6-methylcyclohexanol (XI), the stereochemical structure of which is best represented as XIa on the following grounds. The methyl group in III, IX and XI as well as the large bromobenzyl group in XI can be assumed to be equatorially[10] disposed leaving the configuration of the hydroxyl group in IX and XI to be determined. An axial hydroxyl in XI would be *trans* to the C_2-bromine and treatment of XI with base should give rise to an epoxide. On the other hand, the formation of a ketone from dibromoalcohol XI would indicate on equatorial hydroxyl, *cis* to the C_2-bromine, as in XIa. The product obtained from XI upon heating with dilute sodium hydroxide was in fact the unsaturated ketone III, obviously the result of hydrogen bromide elimination from a primarily formed saturated β-bromoketone.

Chromic acid oxidation of dibromoalcohol XI yielded 2-(α-bromobenzal)-6-methylcyclohexanone (X) identical with the product of bromination of *trans*-2-benzal-6-methylcyclohexanone (III). In both cases of preparation of bromoketone X an equivalent of hydrobromic acid was found in the mother liquors from the product, indicating facile loss of the halogen acid from a dibromoketone intermediate. Analogously addition of chlorine to III leads to 2-chloro-(2-α-chlorobenzal)-6-methyl-cyclohexanone. The exocyclic unsaturated structure of X was indicated by the inertness of the bromine in X to base and by a bathochromic shift of 12 mμ in the UV, characteristic of halogen substitution on a conjugated carbonyl system.[11] Heating of bromoketone X above its melting point resulted in elimination of hydrogen bromide and formation among others of 2-benzyl-6-methylphenol (XIII). The latter was synthesized for comparison by palladium dehydrogenation of 2-benzyl-6-methyl-2-cyclohexenone (II).

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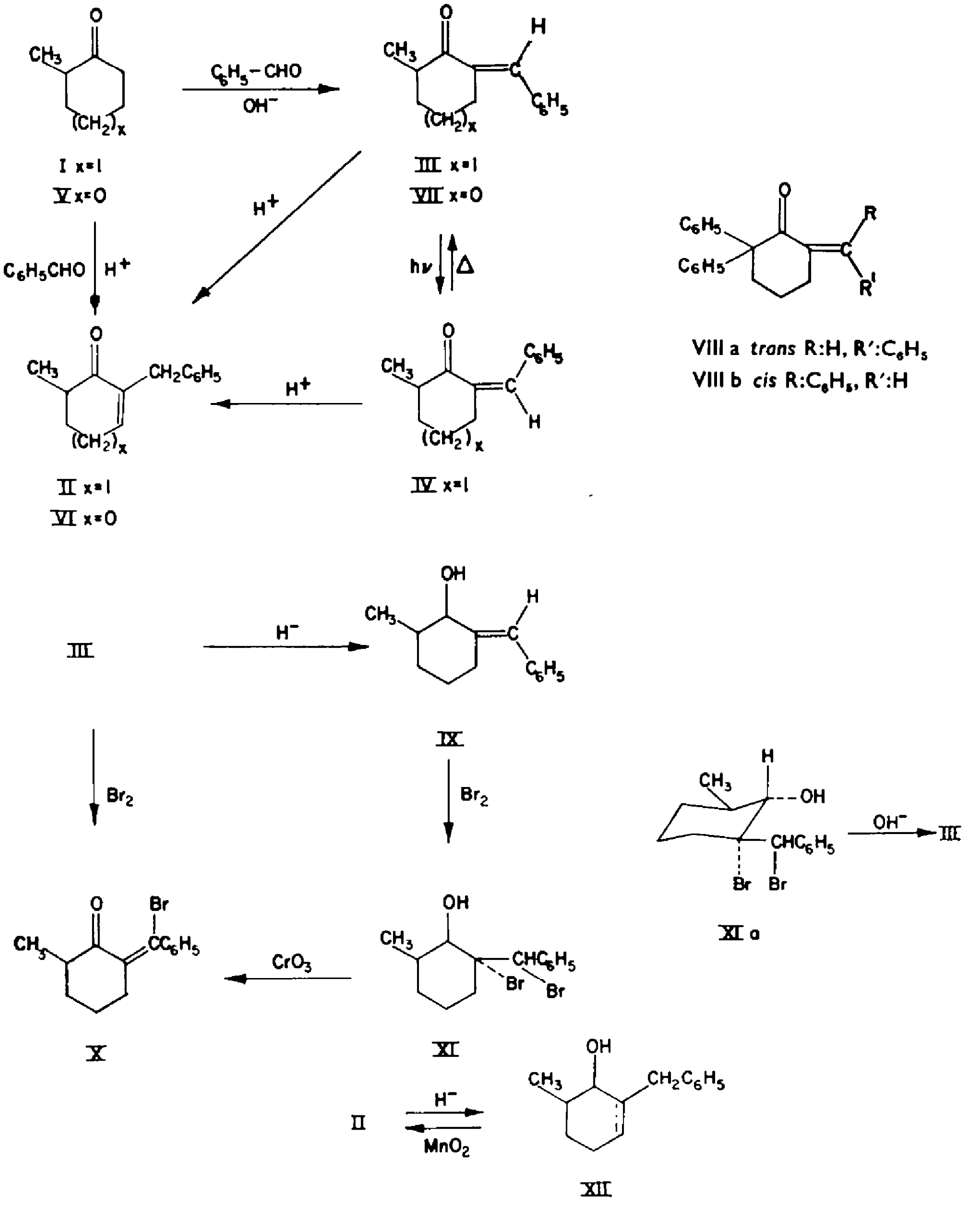
[8] From Woodward's rules (cf. ref. 7) one can predict a maximum at 237 mμ. An absorption maximum of 235 mμ, ϵ 9,600 is reported for 2-methyl-2-cyclohexenone by H. O. House and R. L. Wasson, *J. Amer. Chem. Soc.* **79**, 1490 (1957).

[9] α-Methylstyrene absorbs at 251 mμ, ϵ 17,000, cf. A. Gillam and E. Stern *Electronic Absorption Spectroscopy* p. 277. Arnold, London (1958).

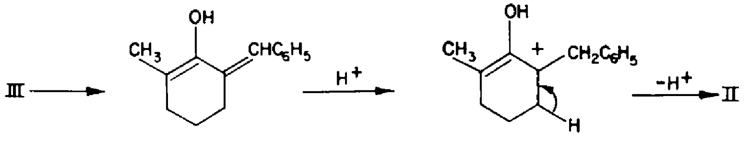
[10] E. L. Eliel, *Stereochemistry of Carbon Compounds* Ch. 8, McGraw-Hill, New York (1962); See also ref. 4.

[11] A. L. Nussbaum, O. Mancera, R. Daniels, G. Rosenkranz and C. Djerassi, *J. Amer. Chem. Soc.* **73**, 3263 (1951).



Acid isomerization of an exo- to an endocyclic unsaturated cyclohexanone (cf. III → II) also could be accomplished in the corresponding cyclopentanone system. Thus, heating of *trans*-2-benzal-5-methylcyclopentanone (VII) with hydrogen chloride in cyclohexanol led to the isomer 2-benzyl-5-methyl-2-cyclopentenone (VI) previously[3] described as the *cis* isomer of VII. The assigned structure of the cyclopentenone VI, which is also obtainable through acid catalyzed aldol condensation of 2-methylcyclopentanone (V) with benzaldehyde, was obvious from UV (λ_{max} 227 mμ, ε 7,900) and IR spectra (see below) comparison with those of the benzalcyclopentanone VII (λ_{max} 297 mμ, ε 22,000). These findings raise the possibility that all "*cis* 2-benzalketones" reported by Cornubert[3] actually possess an isomeric endocyclic unsaturated ketone structure.[12]

It is difficult to conceive of a path of isomerization of VII to VI or of III to II via 1,4-addition of hydrogen chloride and indeed no such addition products could be isolated. A plausible explanation for the change of exo- to endocyclic unsaturated isomers involves the less expected protonation at the benzal carbon to form a carbonium ion alpha to the carbonyl or more likely enolization of ketone III to XIV, followed by protonation at the benzal carbon (cf. XV). A preferred loss of a ring proton leading to the less conjugated system (II rather than III) has been observed before[4] and is probably stereoelectronically motivated.



XIV XV

Although even *cis*-2-benzal-6-methylcyclohexanone (IV) is converted by acid into endo isomer II, the exo to endo isomerization described is not universally applicable. Thus, 2-benzal-6,6-diphenylcyclohexanone, 2-(p-chlorobenzal)-6-methylcyclohexanone or 2-benzal-4,4-dimethyltetralone were recovered unchanged from treatment with hydrogen chloride in cyclohexanol. Cornubert had already shown that α,α-disubstituted cyclic ketones formed only one benzal derivative (presumably the *trans* isomer) which was not isomerized by acid. An explanation might be provided by the assumption that further substituents destabilize the endo relative to the exo isomer or that an intermediate of type XIV, which cannot form in the case of the α,α-disubstituted ketones, is required for isomerization. We prefer the latter explanation, since, at least in the case of the 4,4-dimethyltetralone, the preferential formation of the endo over the exocyclic unsaturated ketone in elimination reactions has been demonstrated.[4]

The synthesis of authentic *cis*-2-benzal ketones was accomplished by photochemical transformation of the *trans* isomers. Light catalyzed isomerization of *trans* to *cis* olefins is a well established reaction.[13] For benzal cyclic ketones Barton noted such transformations in the triterpene series[6] but did not characterize the photoisomers. UV irradiation of a methanolic solution of *trans*-2-benzal-6-methylcyclohexanone (III) yields the *cis* isomer IV, λ_{max} 270 mμ, ϵ 6,700, which upon heating reverts to III and upon acid treatment is converted to the endocyclic unsaturated isomer II. The oxime of IV, however, does not isomerize when heated.

The UV spectrum of *cis* benzal ketone IV indicates a lower degree of coplanarity of the chromophore than in the *trans* isomer III. An examination of molecular models of the two isomers (III and IV) reveals that in the *trans* 2-benzalcyclohexanone (III) the entire chromophore can be nearly coplanar; in the *cis* ketone IV a serious steric interaction between the *ortho* hydrogen of the benzene ring and the carbonyl oxygen

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[12] H. W. Wanzlick and W. Menz, *Chem. Ber.* **87**, 475 (1954) have shown that Cornubert's "*cis*" isomer of 2,5-dibenzalcyclopentanone is in fact 2-benzyl-5-benzal-2-cyclopentenone.

[13] W. B. Black and R. E. Lutz, *J. Amer. Chem. Soc.* **77**, 5134 (1955); I. Harrison, R. Hurst and B. Lythgoe, *Proc. Chem. Soc.* 269 (1959).

is unavoidable in a planar conformation and the benzene ring is forced out of coplanarity with the rest of the absorbing system. This condition is reflected both in a decreased intensity and a hypsochromic shift with respect to the *trans* isomer. A similar relationship exists between *cis* and *trans* 2-benzal-6,6-diphenylcyclohexanone (see Table).

TABLE 1. INFRARED[a] AND ULTRAVIOLET SPECTRA[b]

	λ_{max} (mμ)	ϵ	$\nu^c_{C=O}$ (cm^{-1})	$\nu^c_{C=C}$ (cm^{-1})	Δ (cm^{-1})	γ^d
trans 2-Benzal-6-methylcyclohexanone (III)	284	16,000	1666 (s)	1590 (s) 1565 (m)	76	0·9
trans 2-Benzalcyclohexanone	290	11,200	1670 (s)	1588 (s) 1562 (m)	82	0·9
trans 2-Benzal-6,6-diphenylcyclohexanone (VIIIa)	292	17,000	1670 (s)	1590 (s) 1565 (m)	80	1
trans 2-(α-Bromobenzal)-6-methylcyclohexanone (X)	296	15,400	1670 (s)	1596 (s) 1565 (w)	74	0·9
trans 2-(α-Chlorobenzal)-6-methylcyclohexanone	292	13,200	1675 (s)	1598 (s) 1565 (w)	77	0·8
trans 2-(*p*-Chlorobenzal)-6-methylcyclohexanone	286	16,700	1670 (s)	1590 (s) 1558 (m)	80	1
trans 2-Benzal-5-methylcyclopentanone (VII)	297	22,000	1708 (s)	1620 (s) 1565 (w)	88	1·1
trans 2-Benzalcyclopentanone	298	17,000	1722 (s)	1630 (s) 1570 (m)	92	0·9
cis 2-Benzal-6-methylcyclohexanone (IV)	270	6,700	1692 (s)	1628 (w) 1592 (w)	64	0·2
cis 2-Benzal-6,6-diphenylcyclohexanone (VIIIb)	268	7,810	1690 (s)	1628 (w) 1590 (w)	62	0·2
2-Benzyl-6-methyl-2-cyclohexenone (II)	234	9,000	1666 (s)	1600 (m)	66	0·6
2-Benzyl-5-methyl-2-cyclopentenone (VI)	227	7,900	1700 (s)	1635 (m) 1600 (m)	65	0·5

[a] in 10% solution of carbon tetrachloride; [b] in methanol; [c] letters in parenthesis indicate the intensity of the bands s = strong, m = medium, w = weak; [d] $\gamma = \frac{\text{absorbance of C=C}}{\text{absorbance of C=O}}$, see also ref. 15*b* and 16.

The alkali promoted condensation product of 2,2-diphenylcyclohexanone and benzaldehyde is reported[14] to absorb in the UV at 270 mμ, ϵ 6340. This corresponds to the spectrum of the *cis* benzalketone IV; yet a sterically hindered *cis* compound VIIIb would be an unexpected result of a base catalyzed condensation. Furthermore 2-(*p*-chlorobenzal)-6,6-diphenylcyclohexanone, λ_{max} 292 mμ; ϵ 13,460, similarly prepared[14] appeared to be the expected *trans* isomer. That the effect of a *p*-chloro substituent on the UV absorption of the chromophore $-COCH{=}CHC_6H_4X$ is negligible was shown by synthesis of the *p*-chloro analog of 2-benzal-6-methylcyclohexanone (see Table). When the preparation of 2-benzal-6,6-diphenylcyclohexanone[14] was repeated, the product, m.p. 110°, was indeed the *trans* isomer VIIIa, as indicated by

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[14] J. P. Collman, *J. Org. Chem.* **26**, 3162 (1961).

[15] [a] R. L. Erskine and E. J. Waight, *J. Chem. Soc.* 3425 (1960);

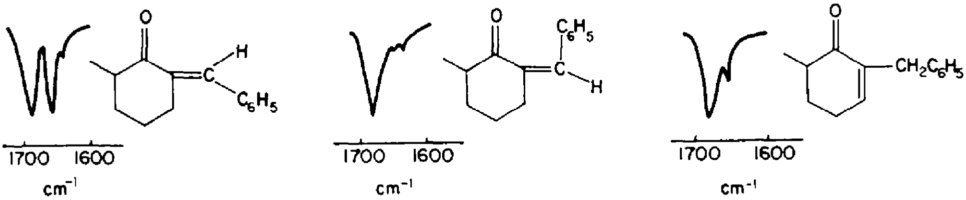
[b] The absorbance ratio γ is a useful quantity even if the half width of the band,[16a] which is sometimes hard to measure, is ignored and if spectra are run in KBr pellets.

[16] It should be borne in mind that, unlike the *transoid* cyclohexenones II and VI, the *cisoid* 2-benzal ketones III, VII and VIII possess a chromophore extended by the phenyl group. Therefore, the Δ and γ values here apply to 2-benzalcycloalkanones and to their endocyclic unsaturated isomers but not necessarily to *cisoid* and *transoid* unsaturated ketones in general. Similarly, in the UV spectra of these isomers the extinction coefficient ϵ is larger for the *cisoid* but more highly conjugated isomer III, than for the *transoid* isomer II; the reverse would be expected in the absence of the phenyl group.

IR and UV spectra. The UV absorption maximum charged from 292 $m\mu$, ϵ 17,000 to 268 $m\mu$, ϵ 7,800 when a solution of VIIIa in methanol was allowed to stand several days in diffuse room light. Presumably Collman's ketone[14] had isomerized on standing in the light before an UV spectrum was taken. UV irradiation of a methanolic solution of VIIIa lead to the isolation of the photo-isomer, *cis*-2-benzal-6,6-diphenylcyclohexanone VIIIb.

Neither *trans*-2-benzal-5-methylcyclopentanone (VII) nor *trans* 2-*p*-chlorobenzal-6-methylcyclohexanone could be isomerized by UV irradiation to the corresponding *cis* isomers. Presumably the photoequilibrium in these systems lies in favour of the *trans* isomer, or possibly a minor impurity may be acting as a quencher.

It has been shown that the intensities of the C=C and of the C=O stretching frequencies differ in *cisoid* and *transoid* forms of α,β-unsaturated ketones.[15,17] We found that IR spectra may be used not only to distinguish between *cisoid* 2-benzalcyclohexanones, e.g. III, and *transoid* 2-benzylcyclohexenones, e.g. II, but also between isomeric *cisoid* benzalcyclohexanones, e.g. III and IV. Typical characteristic curves are shown in Fig. 1. Numerical data for UV and IR spectra are given in Table 1. The values of Δ, which represents frequency differences, in cm^{-1}, between the C=O and the first C=C absorption band and the significance of which has been pointed out earlier,[17a] are in the range of 75–90 cm^{-1} for several *trans* 2-benzalcyclohexanones and cyclopentanones and 60–65 cm^{-1} for *cis* 2-benzalcyclohexanones and for endocyclic unsaturated cyclohexenones.[16] Furthermore, the value of γ, the ratio of absorbance of the C=C band versus absorbance of the C=O band is characteristically different for *cis* and *trans* 2-benzalcycloalkanones.[15b] A combination of IR and UV spectral data can be employed to differentiate between isomers such as described.



III IV II

FIG. 1. Partial infrared spectra of isomeric α, β-unsaturated cyclohexanones.

The NMR spectra of these isomers also yield valuable information.[17d] The vinyl proton in the *cis* benzal ketone VIIIb appears at $3{\cdot}67\tau$. On the other hand the vinyl proton in the *trans* isomer VIIIa, being *cis* to the carbonyl, is deshielded due to the π-electron current of the carbonyl group and is buried in the $2{\cdot}5$–$3\ \tau$ region of the aromatic protons.

EXPERIMENTAL

All m.p.s were taken on a Fisher–Johns m.p. block and are corrected. IR spectra were obtained in KBr pellets or as smears with a Beckmann Model IR-5 instrument. UV spectra were taken in solutions of Fisher "Spectroanalyzed" methanol on a Carey Model 14 spectrophotometer. Elemental analyses were performed by A. Bernhardt, Muelheim, Germany.

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[17] [a] E. A. Brande and C. J. Timmons, *J. Chem. Soc.* 3766 (1955);

[b] R. D. Campbell and N. H. Cromwell, *J. Am. Chem. Soc.* **79**, 3462 (1957);

[c] D. H. R. Barton and C. R. Narayanan, *J. Chem. Soc.* 963 (1958).

[d] For a very recent report on this subject see D. N. Kevill, E. D. Weiler and N. H. Cromwell, *J. Org. Chem.*, **29**, 1276 (1964).

trans-2-*Benzal-6-methylcyclohexanone* (III)

This unsaturated ketone, m.p. 61–62° (lit.[3] m.p. 61°) was prepared by condensing benzaldehyde with I in the presence of base, essentially following the method of Cornubert,[3] or better that of Johnson.[18]

2-*Benzyl-6-methyl-2-cyclohexenone* (II)

a. *By acid isomerization of* III. A solution of III in cyclohexanol previously saturated with HCl was heated at 60–65° for 5 hr. Workup with water and ether followed by fractional distillation gave II boiling at 143–146°/4·5 mm, $n_D^{11°}$ 1·5525 (lit.[19] b.p. 172–174°/19 mm, $n_D^{13°}$ 1·5546) in 70% yield. Gas chromatography indicated essentially one component. The semicarbazone of II, m.p. 183–185° (lit.[19] m.p. 183°) could be hydrolyzed back to II.

The isomerization was also carried out in n-butanol solution at 60° or in cold 80% H_2SO_4.

b. *By acid catalysed condensation of* I. Condensation of 2-methylcyclohexanone (0·3 m) with benzaldehyde (0·3 m) in cyclohexanol in the presence of HCl at 65° under N_2 resulted in formation in 83% yield of II contaminated with some isomer III, as evidenced from spectra. The product, b.p. 121·5–122°/0.9 mm was converted to pure II by further heating with HCl in cyclohexanol followed by fractional distillation.

Ozonolysis of trans-2-*benzal-6-methylcyclohexanone* (III)

Ozone-rich oxygen (using a Montgomery "Controlled Ozone" apparatus, type MLP, at 5 lbs press. and 500 mamp) was bubbled for 30 min into a solution of 20 g III in 100 ml ethyl acetate, cooled in a dry ice-acetone bath. The solution was allowed to warm to room temp, then ethyl acetate was removed under red. press. while acetic acid was added to keep a constant volume. The acetic acid solution was added to a solution of 113 g 30% H_2O_2, 5 ml H_2SO_4 and 200 ml water and the resulting solution was refluxed 2 hr. After further workup the base soluble material was chromatographed on silica gel (Eagle, mesh 25–200). Elution with 50% ether in benzene afforded 7·6 g benzoic acid (60% yield) identified by IR and by an underpressed mixed m.p. with authentic benzoic acid. A mixture of dicarboxylic acids, eluted with more polar solvents, was not further investigated.

Ozonolysis of 2-benzyl-6-methyl-2-cyclohexenone (II)

Cyclohexenone II (20 g) ozonized by the procedure described above afforded 6·1 g phenylacetic acid (51%). An additional 2·0 g organic acid were eluted from silica gel with 10% methanol in ether. This acid mixture was esterified with diazomethane and the resultant ester mixture was examined on a Perkin–Elmer Model D Vapor Phase Fractometer (Column D, "Ucpn" oil, at 172° and 15 lbs press.). Eight peaks were discernible. By comparison with the retention time of authentic dimethyl ester of α-methylglutaric acid under these conditions, the chromatogram of the ester mixture clearly revealed the presence of dimethyl α-methylglutarate to the extent of ca. 10%.

trans-2-*Benzal-trans-6-methylcyclohexanol* (IX)

A solution of 1·6 g $NaBH_4$ in 20 ml 0·2N NaOHaq was added dropwise, over 20 min, to 5 g III in 50 ml methanol. The temp was held between 20 and 25° by intermittent ice bath cooling. Stirring was continued for an additional 2 hr. After removal of solvent under red. press., 50 ml water was added and the mixture extracted thrice with 50 ml portions of ether. The dried ethereal extracts were evaporated to afford 2 g (40%) IX as a waxy solid, λ_{max} 244 mμ; ε 19,000.

Alcohol IX resisted purification by recrystallization and did not form derivatives with common hydroxyl group reagents including N-benzoylimidazole. The alcohol appears to dehydrate under these conditions. It was converted back to ketone III by oxidation with manganese dioxide. Compound IX was analyzed as its dibromo derivative XI.

2-*Benzal-6-methylcyclohexanol dibromide* (XI)

A mixture of 15 g (0·074 m) IX, 100 ml CCl_4 and 1 g $CaCO_3$ was kept at 0–10° while a solution of 13 g (0·075 m) Br_2 in 30 ml CCl_4 was added dropwise over 30 min. The Ca salts were removed by

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[18] W. J. Johnson, *J. Amer. Chem. Soc.* **65**, 1320 (1943).

[19] R. Cornubert and A. Haller, *Bull. soc. chim. Fr.* (5) **39**, 1638 (1926).

filtration and the filtrate was washed with 10% $NaHSO_3$aq. The dried organic layer was evaporated to leave 24 g (89%) of a tan solid. Crystallization from benzene afforded colorless needles of XI (75%), m.p. 133–134°. (Found: C, 46·48; H, 5·25; Br, 43·85; Calc. for $C_{14}H_{18}OBr_2$: C, 46·43; H, 5·01; Br, 44·14%).

2-(α-*Bromobenzal*)-6-*methylcyclohexanone* (X)

a. *From* 2-*benzal*-6-*methylcyclohexanone* (III). To a solution of 28·5 g III in 150 ml CCl_4 there was added 5 g $CaCO_3$. The mixture was cooled to 5° and 22·7 g Br_2 was added dropwise over a period of 20 min, with stirring. Filtration and evaporation of the filtrate yielded 40 g brownish powder, smelling strongly of HBr. Two crystallizations from ethanol–water afforded 37 g (90%) white needles, m.p. 118°; λ_{max} 296 mμ (ε 15,400). (Found: C, 60·00; H, 5·50; Br, 28·60; Calc. for $C_{14}H_{15}BrO$: C, 60·20; H, 5·37; Br, 28·64%).

b. *By oxidation of* 2-*benzal*-6-*methylcyclohexanol dibromide* (XI). A solution of 4·4 g (12 mmole) dibromide XI in 25 ml glacial acetic acid was added to an ice-cold solution of 0·8 g CrO_3 (8 mmole) in 3 ml water and 25 ml acetic acid and the mixture was stirred for 16 hr until the color changed from red to reddish green. Workup with water and extraction with ether gave 2·2 g brown powder which crystallized from ethanol–water afforded 2 g (60%) of m.p. 118°, identical with material obtained by route a.

Alkali treatment of 2-*benzal*-6-*methylcyclohexanol dibromide* (XI)

When the dibromo alcohol XI (1·87 g) was dissolved in 20 ml 95% ethanol containing 3·6 ml 10% NaOHaq (2 equiv.), a mild exothermic reaction was observed. The solution was stirred for 3 hr at room temp and made barely acidic with HNO_3. Evaporation to dryness under red. press. was followed by addition of 30 ml ether to the residue. The ethereal solution was washed with water, dried and evaporated to yield 600 mg (58%) of III.

2-*Benzyl*-6-*methyl*-2-*cyclohexenol* (XII).

This alcohol was prepared by $NaBH_4$ reduction of II in a fashion similar to that described for the synthesis of IX. The yield of once distilled alcohol, b.p. 140–143°/1·5 mm was 63%. No derivatives of IX could be obtained due to the ease of dehydration. The allylic nature of the alcohol was demonstrated by its ready oxidation to ketone II with activated MnO_2.

Oxidation of XII *with manganese dioxide*

A solution of 1 g XII in 25 ml CCl_4 was stirred with 5 g active MnO_2 for 48 hr. The inorganic residue was removed by filtration and the filtrate was evaporated to give in essentially quantitative yield II, identical by IR and UV spectrum with the authentic material.

2-*Benzyl*-6-*methylphenol* (XIII)

a. *By dehydrobromination of* 2-(α-*bromobenzal*)-6-*methylcyclohexanone* (XI). Bromoketone (XI; 1·0 g) was heated at 145° under red. press. for 1 hr. The initially clear melt evolved a gas and gradually darkened. Chromatography on 30 g neutral alumina (City Chemical Co.) and elutions with 2:1 Skellysolve F (b.p. 45–60°)–benzene afforded 100 mg of a ketone, the IR spectrum of which was identical to that of II. Elution with pure benzene yielded 500 mg (70%) of a waxy solid with an intense phenolic odor. This material proved to be XIII, m.p. 49° (lit.[20] m.p. 50°).

Since the reported[20] preparation of XIII from *o*-cresol was unsuccessful in our hands we prepared phenol XIII for comparison by the following route.

b. *By dehydrogenation of* 2-*benzyl*-6-*methyl*-2-*cyclohexenone* (II). A mixture of 2 g II with 0·4 g 10% Pd—C was heated under N_2 at 250° for 14 hr. The cooled mixture was taken up in 50 ml ether and filtered. Evaporation of the solvent from the filtrate gave 1·9 g (95%) XIII, m.p. 49–50°, identical in all respects to the product of thermal decomposition of bromoketone (XI).

2(α-*Chlorobenzal*)-6-*methylcyclohexanone*

Into a solution of 20 g III in 150 ml CS_2 at 0° Cl_2 was bubbled for 4 hr. The solvent was removed under red. press. and the residue was dissolved in 200 ml ether. Evaporation of the dried ether

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[20] P. Schorigen, *Ber. Dtsch. Chem. Ges.* **58**, 2033 (1925).

solution afforded 31·1 g yellow oil which solidified on standing for 48 hr. Repeated recrystallizations from ethanol–water furnished pure 2-(α-chlorobenzal)-6-methylcyclohexanone, m.p. 118°. (Found: C, 71·68; H, 6·51; Cl, 15·21; Calc. for $C_{14}H_{15}ClO$: C, 71·63; H, 6·44; Cl, 15·10%).

trans-2-*Benzal-5-methylcyclopentanone* (VII)

This benzal ketone was prepared by ethoxide catalyzed condensation of V with benzaldehyde according to the method of Cornubert and Louis;[8] m.p. (lit.[8] m.p. 58°).

2-*Benzyl-5-methyl-2-cyclopentone* (VI)

Cyclopentenone (VI), allegedly the *cis* isomer of VII, b.p. 109–111°/0·95 mm was prepared by the HCl catalyzed condensation of V with benzaldehyde as previously described. The semicarbazone of VI melts at 181° (lit.[8] m.p. 181°).

cis-2-*Benzal-6-methylcyclohexanone* (IV)

A solution of 20 g *trans* isomer III 150 ml absolute methanol was irradiated with a Hanovia 100 watt UV lamp (type 608A) through quartz. The heat generated by the light source kept the solution under reflux. Aliquot samples were taken at 1 hr intervals and the course of the reaction was followed by UV spectra. After 9 hr the maximum at 284 mμ had entirely disappeared and a maximum of lower intensity was present at 270 mμ. The solvent was removed under red. press. and the residual liquid was distilled at 156° and 4·5 mm to give 17 g (85% of the *cis* isomer IV). A rapid, short path distillation is necessary, because the photo-isomer IV reverts to the *trans* isomer on prolonged heating. Compound IV was converted with hydroxylamine hydrochloride and sodium acetate in ethanol to cis-2-*benzal-6-methylcyclohexanone oxime*, m.p. 107°; mixed with oxime of *trans* ketone III it gave a m.p. depression of 13°. The oxime unlike the parent ketone IV was not isomerized to its *trans* isomer on heating overnight at 150°. (Found: C, 78·03; H, 7·86; N, 6·69; Calc. for $C_{14}H_{17}ON$: C, 78·10; H, 7·69; N, 6·51.)

Thermal isomerization of cis-2-*benzal-6-methylcyclohexanone* (IV).

When 1 g *cis* isomer IV was heated at 225° for 2 hr it was quantitatively converted into crude *trans* isomer III. Two crystallizations from ethanol–water gave 0·7 g (70%) pure III identified by spectra and m.p. experiments.

Acid isomerization of IV

A solution of 1 g IV in 15 ml methanol containing 2 drops conc. HCl was heated under reflux overnight. The solvent was removed under red. press. The residual liquid was essentially pure II identified by IR and UV spectra.

trans-2-*Benzal-6,6-diphenylcyclohexanone* (VIIIa)

A solution of 2·3 g 2,2-diphenylcyclohexanone and 1·6 g freshly distilled benzaldehyde in 65 ml 1% ethanolic KOH was allowed to stand 3 days. Filtration afforded 1·6 g VIIIa, m.p. 107°. The freshly prepared ketone has an absorption maximum at 293 mμ (ε 17,500). When a 10^{-5}M solution was allowed to stand 4 days in diffuse room light, the absorption maximum dropped to 270 mμ (ε 8,450). Reported for *trans*-2-benzal-6,6-diphenylcyclohexanone, m.p. 109–110°, λ_{max} 268 mμ (ε 7,810).[14]

cis-2-*Benzal-6,6-diphenylcyclohexanone* (VIIIb)

A solution of 2·0 g *trans* isomer VIIIa in 200 ml absolute methanol was irradiated from 15 hr with UV light as described for the preparation of IV. Compound VIIIb, m.p. 117–119° was obtained in quantitative yield λ_{max} 268 mμ (ε 7,800). (Found: C, 88·63; H, 6·74; Calc. for $C_{25}H_{22}O$: C, 88·72; H, 6·55%).

2-(p-*Chlorobenzal*)-*6-methylcyclohexanone*

To a solution of sodium ethoxide (2·3 g Na in 300 ml ethanol), there were added *p*-chlorobenzaldehyde (14·06 g) and 2-methylcyclohexanone (11·2 g). The resultant solution was poured into an 800 ml beaker and agitated overnight with a mechanical vibrator. The viscous yellow solution was poured into 600 ml water and extracted thrice with 250 ml portions benzene. The combined organic layers were washed with 5% H_2SO_4aq and 10% Na_2CO_3aq in 250 ml portions. The solvent was removed under red. press. and the residue distilled *in vacuo*. Ten grams of a yellow oil were collected between 120 and 158° (3 mm). The material solidified on standing to a wax. Recrystallization from Skellysolve F (b.p. 45–60°) afforded 7·3 g (32%) 2-*p*-chlorobenzal)-6-methylcyclohexanone, m.p. 61–62·5°, λ_{max}^{MeOH} 286 mμ (ϵ 16,700). It was analyzed as its oxime.

2-(p-*Chlorobenzal*)-*6-methylcyclohexanone oxime*

One gram of the ketone described above treated with hydroxylamine dihydroxylamine hydrochloride in pyridine gave an 87% yield of the oxime, m.p. 147–150° (dec). (Found: C, 67·44; H, 6·31; Calc. for $C_{14}H_{16}ClNO$: C, 67·33; H, 6·46%).