[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

# The Base-catalyzed Dimerization of 3-Substituted Cyclohexenones

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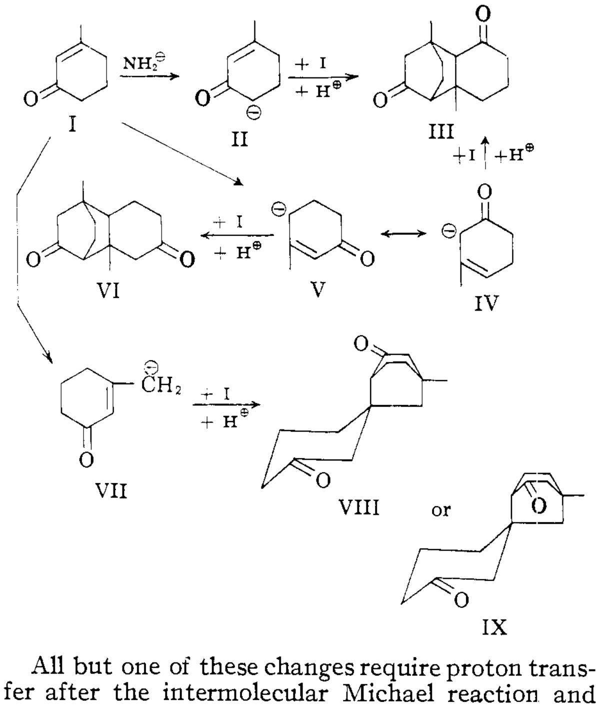
The self-condensation of 3-methylcyclohex-2-en-1-one in the presence of sodium amide in boiling ether solution yields a tricyclic saturated diketone. The structure of this dimer was established rigorously. Under identical conditions analogous dimeric compounds are formed from isophorone and 3,5-dimethylcyclohex-2-en-1-one. In the latter case, the dimer is shown to be produced in a rate-controlled process because on exposure to sodium amide in boiling *n*-decane it is converted to an unsaturated hydroxyketone stabilized by intramolecular hydrogen bonding which had previously been prepared from the monomer and sodium hydroxide under drastic conditions. Self-condensation of 3-phenylcyclohex-2-en-1-one gives an unsaturated hydroxyketone. The product formed is the only one of the nine mechanistically permissible structures which is stabilized by intramolecular hydrogen bonding.

In the course of a study concerning the structures of the photodimers of 3-substituted cyclohexenones[1] it became necessary to reinvestigate the constitutions of the dimers obtainable by base catalysis. The instability of cyclohexenones to basic reagents was first noted by Knoevenagel[2] who reported the formation of crystalline dimers from 3,5-dimethylcyclohex-2-en-1-one (XXIII) and 3-methyl-5-phenylcyclohex-2-en-1-one. In both cases the self-condensation was initiated by potassium hydroxide. Under similar conditions piperitone yields a mixture of two stereoisomeric dipiperitones.[3,4] All of these dimers are undoubtedly unsaturated hydroxyketones, but their structures have been the subject of considerable controversy.[2-5] As a result of the elegant investigations of Taylor[6,7] it is now known that dipiperitone is XXVI and that XXV represents the 3,5-dimethylcyclohexenone dimer. Undoubtedly also, the dimerization of 3-methyl-5-phenylcyclohex-2-en-1-one leads to an analogous structure.

A second type of self-condensation was discovered by Ruzicka.[8] When 3-methylcyclohex-2-en-1-one (I) was treated with excess sodium amide in boiling ether a mixture of two oily isomeric compounds, $C_{14}H_{20}O_2$ was formed. Although he was unable to separate these substances, his experiments seemed to suggest that they were an unsaturated hydroxyketone and a saturated diketone for which he proposed structure III. The behavior of 3,5-dimethylcyclohex-2-en-1-one (XXIII) and isophorone (XXI) parallels that of 3-methylcyclohex-2-en-1-one (I) and analogous structures were proposed for these non-crystalline dimers.

Our own investigations to be discussed in this paper were concerned mainly with the preparation and proof of structure of the saturated diketones formed by self-condensation of 3-methylcyclohex-2-en-1-one (I), 3,5-dimethyl-cyclohex-2-en-1-one (XXIII) and isophorone (XXI). We have confirmed the observation of Ruzicka[8] that I undergoes a rapid change in the presence of a suspension of sodium amide in ether. The resulting reaction mixture could be separated into two components: (1) a crystalline substance tentatively identified as a tetramer (6%) and (2) a solid dimer $C_{14}H_{20}O_2$ (53%) which was characterized by a bis-2,4-dinitrophenylhydrazone and a monosemicarbazone. The latter derivative may well be identical with a substance which was assumed previously[8] to be the semicarbazone of an unsaturated hydroxyketone, although a direct comparison of specimens was not possible. The infrared spectrum of the dimer exhibited a single carbonyl band at 1715 cm.$^{-1}$, but no bands associated with hydroxyl groups and double bonds were detectable. The absence of unsaturation was confirmed by a negative color reaction with tetranitromethane and lack of significant end absorption at 200 m$\mu$. On these grounds this self-condensation product must be a saturated tricyclic diketone.

If we make the reasonable assumptions that (a) dimerization involves two Michael additions and (b) that no small nor medium rings are closed in these two processes, three possible structures emerge. Thus carbanions II and IV both lead to III. The second resonance form (V) of IV furnishes VI, while anion VII proceeds to the spiro structures VIII or IX.



All but one of these changes require proton transfer after the intermolecular Michael reaction and

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[1] A. Mustafa, *Chem. Revs.*, **51**, 1 (1952).

[2] E. Knoevenagel and E. Reinecke, *Ber.*, **32**, 418 (1899).

[3] W. Treibs, *ibid.*, **63**, 2738 (1930); *J. prakt. Chem.*, **138**, 299 (1933).

[4] L. H. Briggs, C. W. Harland, C. Ralph and H. A. Simmonds, *J. Chem. Soc.*, 3788 (1953).

[5] A. R. H. Cole, *Chemistry & Industry*, 661 (1954).

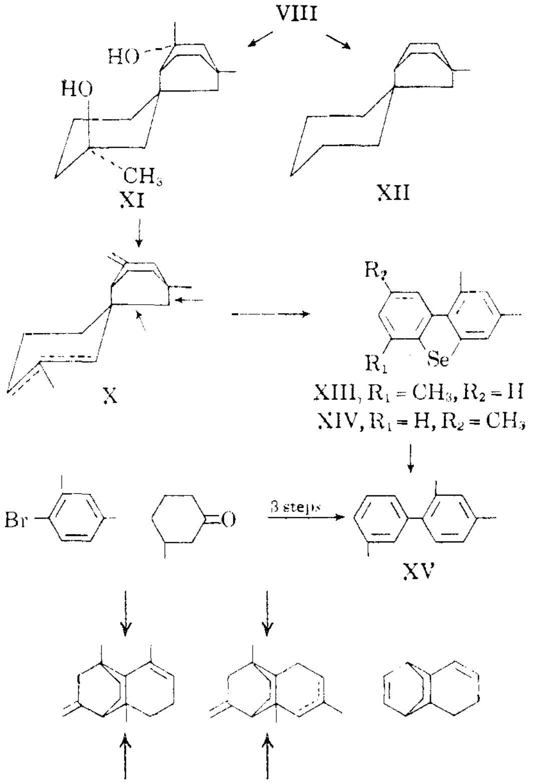
[6] W. I. Taylor, *ibid.*, 252 (1954).

[7] W. A. Ayer and W. I. Taylor, *J. Chem. Soc.*, 2227 (1955).

[8] L. Ruzicka, *Helv. Chim. Acta*, **3**, 781 (1920).

in the absence of hydroxylic solvent the starting material must serve as proton source. If this hypothesis were correct the two 3-methylcyclohexanone moieties must still be present in the structure of the dimer. This was confirmed by the following observations. Treatment of the dimer with excess methylmagnesium iodide produced the ditertiary diol XI which was converted to the corresponding diene by dehydration with either iodine in boiling benzene or with hot acetic anhydride. The ultraviolet spectrum of the diene demonstrated the absence of conjugation and the infrared spectrum with peaks at 1645, 877 and 800 cm.$^{-1}$ was in agreement with the presence of a terminal methylene and a trisubstituted double bond. Although rearrangements of bicyclo[2,2,2]octanes to bicyclo[3,2,1]-octanes are known[9–12] this seems excluded in the present case because dehydration of XI with thionyl chloride in pyridine, a reaction known not to involve carbonium ion intermediates, led to the same diene (X). If the diketone is VIII, as will be shown in the sequel, approach of the Grignard reagent from the less hindered side should lead to a diol XI with an axial hydroxyl in the non-bridged ring and a $\psi$-equatorial hydroxyl in the bicyclo[2,2,2]-octane ring. Such tertiary alcohols dehydrate to endocyclic and exocyclic olefins, respectively.[13–16] Dehydrogenation of the diene X with selenium produced a substance $C_{15}H_{14}Se$ which developed an intense blue color when dissolved in concentrated sulfuric acid. The same compound became also available by direct dehydrogenation of the diol XI with selenium. Both its ultraviolet light absorption[17] (see Experimental) and its color reaction[18] are typical of dibenzoselenophene.[19] The presence of this ring system was confirmed by treatment with Raney nickel[20] which yielded a liquid hydrocarbon $C_{15}H_{16}$ with $\lambda_{max}$ 242 m$\mu$, log $\epsilon$ 4.08, indicative of the presence of a substituted biphenyl. If our views on the structure of the dimer were correct, the $C_{15}H_{16}$ hydrocarbon should be 2,4,3′-trimethylbiphenyl (XV). An authentic sample of this substance whose synthesis is described in the Experimental section was identical with XV obtained by degradation of VIII. The substituted dibenzoselenophene must thus be either XIII or XIV. Attempts to dehydrogenate X with palladium failed, but dehydrogenation with sulfur led to a poorly defined sulfur-containing substance[21] which on desulfurization with Raney nickel was converted to XV in 10% over-all yield.

The conversion of the diketone to 2,4,3′-trimethylbiphenyl (XV) does not allow an unambiguous differentiation between the three possible structures for the dimer because bond cleavages at any of the indicated positions in X, XVI and XVII (see arrows) could eventually lead to XV. However, the formation of XIII/XIV is in better agreement with expression VIII for the dimer because bicyclohexadiene (XVIII) which is structurally closely related to the two dienes XVI and XVII derived from III and VI is converted to naphthalene rather than biphenyl on dehydrogenation.[22] Nevertheless, more rigorous evidence in favor of VIII was desirable.



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[9] W. v. E. Doering and M. Farber, THIS JOURNAL, **71**, 1514 (1949).

[10] M. S. Newman and Y. T. Yu, *ibid.*, **74**, 507 (1952).

[11] H. M. Walborsky, *Experientia*, **9**, 209 (1953).

[12] W. C. Wildman and D. R. Saunders, THIS JOURNAL, **76**, 946 (1954).

[13] D. H. R. Barton, A. da S. Campos-Neves and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956).

[14] J. D. Cocker and T. G. Halsall, *ibid.*, 4262 (1956).

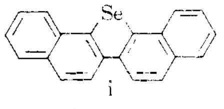
[15] M. Stoll, *Helv. Chim. Acta*, **38**, 1587 (1955).

[16] G. Büchi and K. Biemann, *Croatica Chem. Acta*, **29**, 163 (1957).

[17] E. Sawicki, *J. Org. Chem.*, **19**, 1163 (1954), and earlier papers cited.

[18] N. M. Cullinane, A. G. Rees and C. A. J. Plummer, *J. Chem. Soc.*, 151 (1939).

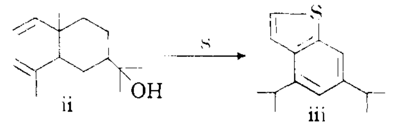
[19] The formation of products containing selenium from dehydrogenation reactions is not novel. *E.g.*, L. Ruzicka (*Helv. Chim. Acta*, **19**, 422 (1936)) reports the formation of a compound $C_{20}H_{12}Se$ from treatment of *trans*-$\beta$-decalone with selenium which we believe to be i. The new carbon–carbon bond may be formed by bimolecular ketone reduction yielding the pinacol.



i

[20] For deselenizations with this reagent see G. E. Wiseman and E. S. Gould, THIS JOURNAL, **76**, 1706 (1954); H. Hauptmann and W. F. Walter, *ibid.*, **77**, 4929 (1955); Ng. P. Buu-Hoi and N. Hoan, *J. Chem. Soc.*, 3745 (1952).

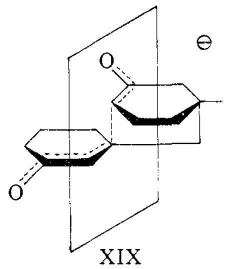
[21] This situation again is not without analogy. For example, dehydrogenation of elemol (ii) [for structure proof see V. Sykora, V. Herout and F. Sorm, *Coll. Czech. Chem. Comm.*, **20**, 220 (1955)] produced a substituted thionaphthene $C_{14}H_{18}S$ [L. Ruzicka and A. G. van Veen, *Ann.*, **476**, 70 (1929)] which we believe to be iii because it is the most stable of the four theoretically possible structures.



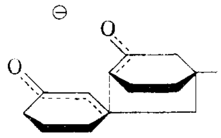
[22] F. Hofmann, *Chem. Ztg.*, **57**, 5 (1933).

Equilibration of the dimer with sodium ethoxide in deuteroethanol resulted in the introduction of 5.82 D atoms per molecule. That the immediate environment of one of the carbonyl groups consists of two methylenes also was demonstrated in the following way. Condensation of VIII with a limited amount of isoamyl nitrite gave an oximinoketone $\lambda_{max}$ 243 m$\mu$, $\epsilon$ 8000. In the presence of excess reagent a bis-oximinoketone $\lambda_{max}$ 273 m$\mu$, $\epsilon$ 10400, was formed.[23] These findings are accommodated by both VI and VIII but not by III. It is apparent that VI has two C-methyl groups while VIII has only one. Although the diketone afforded 0.64 C-methyl on Kuhn–Roth oxidation it seemed hazardous to exclude VI on this finding. The nuclear spin resonance spectra of the diketone and the corresponding saturated hydrocarbon were measured, but due to poor resolution in the methyl region the number of C-methyls could not be evaluated.

It may be noted that the saturated tricyclic hydrocarbon XII derived from VIII has a plane of symmetry whereby the hydrocarbon corresponding to VI does not. It thus became necessary to resolve the dimer and to convert one enantiomer to the hydrocarbon. Attempts to resolve the diketone with *l*-menthyl hydrazide,[24] *l*-($\alpha$-phenylethyl) semioxamazide,[25] *l*-$\alpha$-phenylethyl semi-carbazide[26] and *d*-tartaramide hydrazide[27] failed. Resolution finally was accomplished by catalytic reduction of the dimer to a hydroxyketone,[28] conversion to the acid phthalate, separation of the diastereomeric brucine salts, regeneration of the acid phthalate, hydrolysis to the ketol and chromic acid oxidation to the optically active diketone VIII which had an observed rotation of $-1.04°$ (*c* 0.4023 g. in 1.5 ml. of chloroform). Its infrared spectrum in solution was superimposable on that of the racemic diketone. Wolff–Kishner reduction of optically active VIII gave a hydrocarbon (XII) which had an observed rotation of $-0.003 \pm 0.007°$ (*c* 0.3058 g. in 1.5 ml. of chloroform) and an infrared spectrum identical with that of the hydrocarbon XII obtained by Wolff–Kishner reduction of racemic VIII. Gas chromatographic analysis of XII showed less than 0.5% impurity. Consequently we may formulate the dimer as VIII or IX. There is no experimental evidence available which would allow a distinction between the *syn*-(IX) and *anti* isomer VIII but we prefer VIII on the following grounds: In the transition state XIX the carbon–carbon double bond of the enolate and the carbon–carbon double bond of the $\alpha,\beta$-unsaturated ketone describe a plane which allows for maximum orbital overlap. Furthermore, the two oxygen atoms bearing partial negative charges are at maximum distance. In XX, however, the four carbon atoms concerned do not describe a plane and the two oxygen atoms are in close proximity.



XIX



XX

We next reinvestigated the self-condensation of isophorone (XXI) in the presence of sodium amide. Chromatographic purification of the product gave a crystalline dimer $C_{18}H_{28}O_2$ which has an infrared band at 1718 cm.$^{-1}$ and six activated hydrogen atoms as determined by deuterium exchange. The substance is a saturated diketone for which we propose structure XXII.

Similarly, treatment of 3,5-dimethylcyclohex-2-en-1-one (XXIII) with sodium amide in boiling ether gave two crystalline dimers, both in approximately 25% yield and less than 4% of the hydroxyketone XXV. Isomer A (m.p. 110°) gave 1.37 C-methyl groups on Kuhn–Roth determination and had $\lambda_{max}$ 292 m$\mu$, $\epsilon$ 74. Isomer B (m.p. 114°) gave 1.50 C-methyl groups and possessed $\lambda_{max}$ 292 m$\mu$, $\epsilon$ 52. The infrared spectra of both isomers exhibit a band at 1710 cm.$^{-1}$ (cyclohexanone) and are virtually identical except for the 1200-1300 cm.$^{-1}$ region. The two compounds under discussion, however, are definitely different as also evidenced by the formation of two unlike 2,4-dinitrophenylhydrazones. Both isomers gave hexadeuterio compounds and based on these arguments we wish to propose structure XXIV. At which one of the two possible centers the isomers differ is unknown, but it seems clear that they are not *syn–anti* isomers (like VIII and IX). If this were so, one would anticipate the appearance of two isomeric diketones also from 3-methylcyclohex-2-en-1-one (I), which is contrary to our findings.

As previously mentioned, the hydroxyketone XXV is formed in good yield on treatment of 3,5-dimethylcyclohex-2-en-1-one (XXIII) with 70% aqueous alkali at 170°. To determine whether the observed difference between alkali and sodium amide catalysis (at 35°) might be due to the considerable difference in reaction temperature, the dimerization of XXIII was investigated in boiling *p*-cymene (176°). 3,5-Dimethylphenol (XXVII) was formed in 62% yield. When boiling *n*-decane was used as solvent, 3,5-dimethylphenol (61%), the hydroxyketone XXV (19%) and the diketones XXIV (4%) were produced. Therefore, the phenol is the main product at high temperature and the observed dehydrogenation is reminiscent of the conversion of 1,4-dihydronaphthalene to naphthalene in the presence of phenyllithium[29a]; that only minor quantities of dimeric products appear can be attributed to the reversibility of the Michael reaction.[29b] It then became of interest to ascertain

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[23] Bis-oximinocyclohexanone prepared by the method of W. Borsche, *Chem. Zentr.*, **80**, II, 1549 (1909), has $\lambda_{max}$ 271 m$\mu$, $\epsilon$12000.

[24] R. B. Woodward, T. P. Kohman and G. C. Harris, THIS JOURNAL, **63**, 120 (1941).

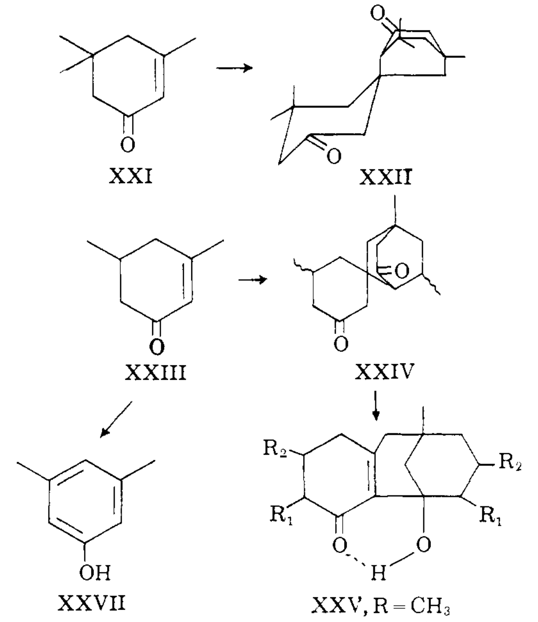
[25] N. J. Leonard and J. H. Boyer, *J. Org. Chem.*, **15**, 42 (1950).

[26] I. V. Hopper and F. J. Wilson, *J. Chem. Soc.*, 2483 (1928).

[27] F. Nerdel and E. Henkel, *Ber.*, **85**, 1138 (1952).

[28] The scale model of VIII suggests the preferred reduction of the carbonyl group in the non-bridged ring, possibly by catalyst approach from the $\alpha$-side of the molecule assuming that VIII indeed represents the most stable conformation.

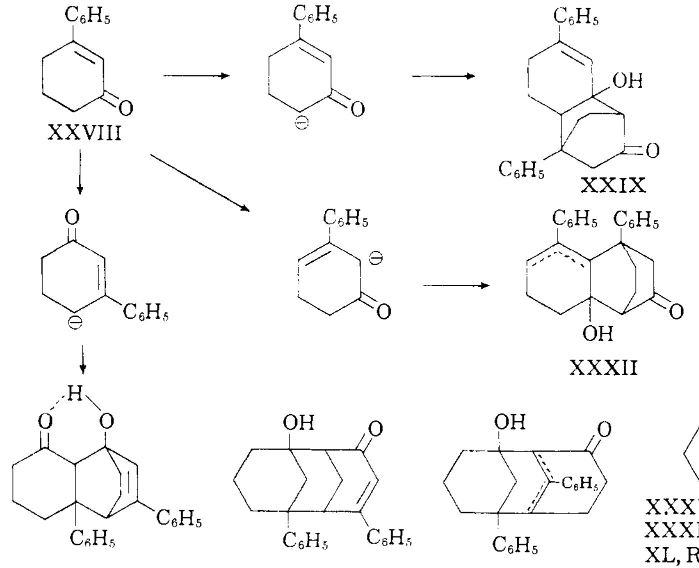
[29] (a) H. Gilman and C. W. Bradley, THIS JOURNAL, **60**, 2333 (1938); (b) S. A. Julia, A. Eschenmoser, H. Heusser and N. Tarköy, *Helv. Chim. Acta*, **36**, 1885 (1953), and earlier literature cited.



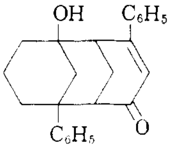
XXI XXII XXIII XXIV XXVII

XXV, R = $CH_3$

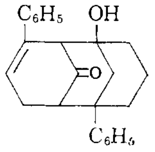
XXVI, R = $(CH_3)_2CH$



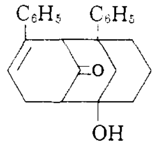
XXVIII XXIX XXXII XXXV XXXVI XXXVII



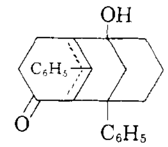
XXX



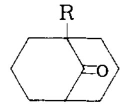
XXXI



XXXIII



XXXIV

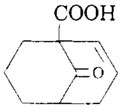


XXXVIII, R = Br

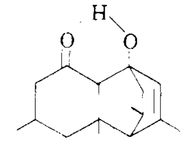
XXXIX, R = $CONH_2$

XL, R = COOH

XLI, R = $COOC_2H_5$



XLII



XLIII

whether either the hydroxyketone XXV or the diketones XXIV represent the product(s) of a rate-controlled process.

Treatment of XXIVb with sodium amide in boiling *n*-decane resulted in the formation of 50% of XXVII and 30% of XXV.[30] Therefore, the hydroxyketone XXVII is the more stable dimer and arises from the diketone XXIV by the sequence: (a) retro-Michael reaction, (b) aldol condensation and (c) isomerization of the $\beta,\gamma$-unsaturated ketone to the more stable conjugated isomer.

It is clear that the methyl group plays a decisive role in the self-condensation of the 3-methylcyclohex-2-en-1-ones and further support for the correctness of this statement was adduced from a study of the dimerization of 3-phenylcyclohex-2-en-1-one (XXVIII). When it was treated with sodium amide in ether, a self-condensation product was isolable in only 2% yield, which seems to represent the equilibrium concentration because prolonged reaction times did not increase the yield. The dimer had infrared bands at 3400 cm.$^{-1}$ (in KBr, sharp and intense) (OH); 1695 cm.$^{-1}$ (in KBr, broad )(C=O); 1650 cm.$^{-1}$ (in $CS_2$) (C=O); 1625 cm.$^{-1}$ ($C_6H_5C$=C); and $\lambda_{max}^{EtOH}$ 248 m$\mu$, $\epsilon$ 15800. If it is assumed that this dimer is produced by intermolecular Michael addition, followed by intramolecular aldol condensation[31] without closure of small or medium rings, nine structures are derivable.

Two of these (XXXIV and XXXVII) violate Bredt's rule, while two others (XXX and XXXVI) are excluded by the ultraviolet light absorption of the dimer, which is in agreement with the presence of a phenylcyclohexene chromophore,[32] but not with a 3-phenylcyclohex-2-en-1-one moiety. Its carbonyl absorption in the infrared fails to agree with the predicted values for XXXI and XXXIII because some closely related 9-oxo-bicyclo[3,3,1]-nonanes had the following carbonyl absorptions: XXXVIII, with equatorial bromine, 1725 cm.$^{-1}$ (in KBr); XXXIX, 1720 cm.$^{-1}$ (in KBr); XL, 1720 cm.$^{-1}$ (in KBr); XLI, 1720 cm.$^{-1}$ (in KBr); 1725 cm.$^{-1}$ (in $CCl_4$); XLII, 1720 cm.$^{-1}$ (in KBr).[33] We reject structure XXXII for the dimer since the ultraviolet absorption observed requires coplanarity of the phenylcyclohexene chromophore (see ref. 32) which is not possible in XXXII. A differentiation between the remaining structures XXIX and XXXV seems feasible on the basis of the infrared spectrum, which suggests intramolecular hydrogen bonding between the hydroxyl and carbonyl groups. This requirement is met by XXXV but not by XXIX. *It may be noted that of the*

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[30] We are indebted to Dr. M. Schach von Wittenau for this experiment.

[31] The reverse order of events would lead to a product with two double bonds and entirely different spectral properties.

[32] Phenylcyclohexene itself has $\lambda_{max}$ 248 m$\mu$, $\epsilon$ ~16000; R. B. Carlin and H. P. Landerl, This Journal, **75**, 3969 (1953).

[33] These substances were kindly made available by Prof. A. C. Cope [A. C. Cope and E. S. Graham, *ibid.*, **73**, 4702 (1951); A. C. Cope and M. E. Synerholm, *ibid.*, **72**, 5228 (1950)].

*nine formally possible expressions for the hydroxyketone, XXXV appears to be the most stable one because intramolecular hydrogen bonding is possible only in this structure.* Similarly, of the twelve mechanistically permissible formulas for the dimer of XXIII, only XXV and XLIII can be stabilized by hydrogen bonding. Structure XXV containing the bicyclo[3,3,1]nonene system seems less strained than XLIII with a bicyclo[2,2,2]octene skeleton and therefore more stable.

Treatment of 3-phenylcyclohex-2-en-1-one with sodium amide in boiling *n*-decane produced only 3-hydroxybiphenyl.

**Acknowledgment.**—We are indebted to Eli Lilly and Co. for generous financial support of this investigation.

## Experimental

The activity of adsorbents used for chromatograms was determined according to H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941). Melting points and boiling points are uncorrected. Ultraviolet spectra were measured on a Cary recording spectrophotometer, model II. Infrared spectra, unless otherwise indicated, were measured on a Perkin–Elmer, model 21, recording spectrophotometer with sodium chloride prism. The infrared bands listed are those which are relative to structural arguments and other medium and strong bands. Deuterium analyses by Mr. J. Nemeth, University of Illinois. Microanalyses by Dr. S. M. Nagy and associates, M. I. T.

**3-Methylcyclohex-2-en-1-one** (I) was prepared by the method of Cronyn and Riesser[34] and had b.p. 90.5–91.5° at 23 mm. with $n^{26}\text{D}$ 1.4921.

**Dimerization of 3-Methylcyclohex-2-en-1-one** (I).—A solution of I (275 g., 2.5 moles) in 500 ml. of anhydrous ether was added over a period of 1 hour to a cooled, stirred suspension of sodium amide (150 g., 3.85 moles) in 2 liters of dry ether. The mixture was stirred overnight at room temperature and then poured into iced water. The ether layer was separated and the aqueous layer extracted twice with 200-ml. portions of ether. The combined ether extract was washed several times with water and dried over magnesium sulfate. After removal of the ether *in vacuo*, 233 g. of a brown oil remained. Distillation under reduced pressure yielded 87.5 g. of starting material I and 100 g. of VIII, b.p. 210–222° at 12 mm.; yield based on consumed I is 53%. The product was recrystallized from ether–petroleum ether, m.p. 73–74°.

*Anal.* Calcd. for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.57; H, 9.12; C–Me, 0.64.

The residue of the above distillation was dissolved in hot benzene and on cooling 16.3 g. of white leaflets, m.p. 186°, crystallized from the solution. The infrared spectrum of this compound indicated the presence of hydroxyl and carbonyl groups, but no double bonds could be detected with tetranitromethane. The compound was tentatively identified as a tetramer of I.

*Anal.* Calcd. for $(C_7H_{10}O)_n$: C, 76.32; H, 9.15. Found: C, 75.89; H, 9.21; mol. wt. (Rast), calcd. for $C_{28}H_{40}O_4$ 440, found 417 and 478.

**Monosemicarbazone of the Diketone VIII.**—The diketone (0.4 g.), semicarbazide hydrochloride (0.4 g.) and sodium acetate (0.34 g.) were dissolved in a mixture of ethanol-water (3:1), the mixture heated under reflux for a few minutes and allowed to stand for two days. None of the bis-semicarbazone reported by Ruzicka[8] precipitated and most of the alcohol was therefore removed by evaporation and, on cooling, 0.35 g. (70%) of a monosemicarbazone was obtained. An analytical sample prepared by recrystallization from a small amount of ether had m.p. 210–212° dec.

*Anal.* Calcd. for $C_{15}H_{23}O_2N_3$: C, 64.95; H, 8.36. Found: C, 65.08; H, 8.34.

The compound seems to be identical with the semicarbazone of the alleged hydroxyketone, m.p. 215° dec., reported by Ruzicka.[8]

**Bis-2,4-dinitrophenylhydrazone of the Diketone VIII.**—The derivative was obtained in 78% yield using the conventional method in the form of yellow-orange needles, m.p. 263° dec. after recrystallization from benzene.

*Anal.* Calcd. for $C_{26}H_{28}N_8O_8$: N, 19.30. Found: N, 19.16.

**Diol XI.**—Methyl bromide was bubbled through a flask containing 3.10 g. (0.127 mole) of magnesium turnings in 200 ml. of anhydrous ether. After the magnesium had dissolved completely, the solution was heated gently to drive off excess methyl bromide. A solution of 6.05 g. (0.0275 mole) of the diketone VIII in 200 ml. of anhydrous ether was added slowly and the resulting mixture heated under reflux for 18 hours. The product was isolated in the usual manner, but an infrared spectrum of the crude material indicated the presence of unreacted diketone and the procedure described above was therefore repeated. Purification of the resulting product by crystallization from petroleum ether gave 4.12 g. (60%) of small white needles, m.p. 153.0–153.8°.

*Anal.* Calcd. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.07; H, 11.17.

**Dehydrogenation of the Diol XI with Selenium.**—A mixture of 1.0 g. (0.0397 mole) of the diol and 1.89 g. (0.24 mole) of powdered selenium was heated to 300–320° for 9 hours. An additional portion of 0.6 g. of selenium was then added and the heating was continued for 10 more hours. A petroleum ether extract of the reaction product was chromatographed over alumina (activity I) and the portion eluted with this solvent (0.27 g.) was treated with an alcoholic solution of picric acid. An analytical sample of the picrate recrystallized from acetone–ethanol melted at 120–121°.

*Anal.* Calcd. for $C_{21}H_{17}O_7N_3Se$: C, 50.21; H, 3.41. Found: C, 50.16; H, 3.64.

The picrate was dissolved in hexane and decomposed by passing the solution through a column packed with alumina. The hexane in the filtrate was then removed by evaporation and the residue recrystallized from ether–ethanol as needles, m.p. 86–87°; $\lambda\lambda_{\text{max}}^{\text{EtOH}}$ 243, 269, 279, 285, 316, 329 mμ (ε 63330, 14460, 13130, 11300, 2780, 4315).

*Anal.* Calcd. for $C_{15}H_{14}Se$: C, 65.94; H, 5.16. Found: (1) C, 65.86; H, 5.18. (2) C, 65.78; H, 5.33.

The compound XIII or XIV developed an intense blue color when dissolved in concentrated sulfuric acid. An identical color reaction of diphenylene selenide has been described in the literature.[18]

**Dehydration of the Diol XI.**—A solution of 1 g. of diol XI in 60 ml. of benzene containing 60 mg. of iodine was heated under reflux for four hours. The water formed in the reaction was removed continuously by azeotropic distillation. The product was isolated in the usual manner, dissolved in petroleum ether and passed over a column containing 30 g. of alumina (activity I). Further purification of the product was achieved by distillation through a Hickman flask, b.p. 80° (0.01 mm.), $n^{24}\text{D}$ 1.5093; principal infrared bands at: 2941, 1645, 1471–1429, 1370, 793, 877, 800 cm.$^{-1}$ (in $CCl_4$).

*Anal.* Calcd. for $C_{16}H_{24}$: C, 88.82; H, 11.18. Found: C, 88.52; H, 11.10.

The dehydration of the diol XI could also be effected by treatment with hot acetic anhydride and the infrared spectra of the olefins obtained by the two methods were superimposable.

Attempts to prepare the diacetate of the diol XI by acetylation with ketene in ether at 0° were of no avail. Only hydrocarbon X could be isolated from such reactions.

**Dehydrogenation of X with Selenium.**—The diene (1 g.) and 1.6 g. of finely powdered, black selenium were heated to 310–315° for 8 hours. An additional portion of 0.8 g. of selenium was added and the heating continued for 12 more hours. The selenium-cake was powdered in a mortar and the product extracted with ether in a Soxhlet apparatus. The ether was evaporated and the residue chromatographed over alumina (activity I). Elution with petroleum ether–benzene (8:1) gave 0.08 g. of XIII or XIV identical with the product obtained by dehydrogenation of the diol XI.

**Dehydrogenation of X with Sulfur.**—Diene X (3.0 g.) was mixed with 2.0 g. of sublimed sulfur and heated in a metal-bath to 220°. The temperature was slowly raised to 250°, and after two hours, 1 g. of sulfur was added. In 280 min.,

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[34] M. W. Cronyn and G. H. Riesser, THIS JOURNAL, **75**, 1664 (1953).

2400 ml. of gas ($H_2S$ and $CH_3SH$) had been evolved. The reaction mixture was extracted with acetone in a Soxhlet apparatus, the solvent removed by evaporation and the residue dissolved in a mixture of 20 ml. of benzene and 10 ml. of ethanol. Raney nickel catalyst, prepared from 20 g. of alloy, was added and the mixture heated under reflux for 5 hours. Isolation of the product in the usual manner yielded 0.7 g. of a brown oil which was purified further by chromatography and distillation. The infrared and the ultraviolet absorption spectra of the product (0.25 g.) were identical with the corresponding spectra of 2,4,3′-trimethylbiphenyl (XV) obtained by reduction of trimethyldibenzoselenophene (XIII) or (XIV).

**Deselenization of XIII/XIV.**—The procedure is essentially that developed by Wiseman and Gould.[20] Trimethyldibenzoselenophene (0.16 g.) was dissolved in a mixture of 15 ml. of benzene and 3 ml. of ethanol. After 2.1 g. of Raney nickel catalyst had been added, the mixture was heated under reflux for five hours. Isolation of the product in the usual manner, followed by chromatography over alumina, gave 0.09 g. of XV, b.p. 108° (3 mm.), $n^{24}D$ 1.5731, which does not give a color reaction with concentrated $H_2SO_4$ but does react with tetranitromethane, producing a deep yellow color; ultraviolet spectrum in cyclohexane: $\lambda_{max}$ 242 m$\mu$, log $\epsilon$ 4.08; principal infrared bands (pure liquid): 3030–2857, 1613, 1481, 1449, 1379, 1089, 1040, 840, 820, 793–780, 704 cm.$^{-1}$.

*Anal.* Calcd. for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 92.00; H, 8.27.

**Synthesis of 2,4,3′-Trimethylbiphenyl (XV).**—A solution of 30 g. of 1,3-dimethyl-4-bromobenzene[35] in 100 ml. of anhydrous ether was allowed to react with 3.9 g. of magnesium turnings; 18 g. of 3-methylcyclohexanone in 100 ml. of ether then was added slowly and the reaction mixture was heated under reflux for 6 hours. The product was isolated by the conventional method and then distilled through a Fenske fractionating column: fraction 1, b.p. 121–122° (5.5 mm.), 10.8 g.; fraction 2, b.p. 120° (0.7 mm.), 7 g. Infrared analysis indicated that fraction 1 consisted of 1-(4′-*m*-xylyl)-3-methyl-1-cyclohexene, and fraction 2 of 1-(4′-*m*-xylyl)-3-methyl-1-cyclohexanol. Iodine-catalyzed dehydration of the alcohol gave the olefin in good yield; ultraviolet spectrum in cyclohexane: $\lambda_{max}$ 276 m$\mu$, log $\epsilon$ 2.66.

*Anal.* Calcd. for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.59; H. 10.22.

The olefin (12.8 g.) was mixed with sulfur (4.1 g.) and heated to 210–220° for 200 min. during which time 2730 ml. of gas (calcd. 2860 ml.) was evolved. The product was isolated, purified by chromatography over alumina and distillation through a semimicro column; b.p. 107–108° (3 mm.), $n^{25}D$ 1.5732; ultraviolet spectrum in cyclohexane: $\lambda_{max}$ 242 m$\mu$, log $\epsilon$ 4.08.

*Anal.* Calcd. for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.44; H, 8.25.

The infrared spectrum of a synthetic sample of XV was indistinguishable from the spectrum of XV obtained by degradation of the dimer of 3-methylcyclohex-2-en-1-one (VIII).

**Nitrosation of VIII. A. Oximino-ketone.**—Freshly cut sodium (0.9 g.) was dissolved in pure abs. EtOH (90 ml.). After the sodium had dissolved, the reaction mixture was cooled with ice-water and 4.4 g. of VIII (0.02 mole) added and cooling continued for one additional hour. Then 2.72 g. (0.025 mole) of isoamyl nitrite was added slowly and the reaction mixture allowed to stand overnight. The deep brown solution was poured into 350 ml. of boiling water and refluxing continued for 1 hr. The solution was cooled, extracted with ether, and the ether layer washed with water. The aqueous layer, after acidification with oxalic acid to *p*H 2–3, gave 3.4 g. of crystalline product, while the ether layer yielded 0.9 g. of starting material.

The acidic material was recrystallized twice from methanol and had m.p. 198–199°, $\lambda_{max}^{EtoH}$ 243 m$\mu$ ($\epsilon$ 8000).

*Anal.* Calcd. for $C_{14}H_{19}O_3N$: C, 67.44; H, 7.68; N, 5.62. Found: C, 67.66; H, 7.84; N, 5.61.

B. **Bisoximino-ketone.**—In a 200-ml. flask, equipped with a calcium chloride drying tube, was placed 1.8 g. of sodium and 140 ml. of abs. ethanol. The solution was cooled in an ice-bath, and 4.4 g. of VIII was added. After an additional hour at ice temperature, 5.45 g. of isoamyl nitrite (freshly distilled) was added slowly, and the reaction mixture was allowed to stand overnight. The solution was poured into 550 ml. of water and refluxed for 1.5 hr. After about half the water had been removed by distillation, the solution was acidified to *p*H 2 and heated at reflux for an hour. The product, which was isolated by continuous extraction with ether, 2 g. (45%), was recrystallized four times from methanol as yellow prisms, m.p. >350° (dec. 223°); infrared spectrum (KBr pellet): 860 (strong), 887 (strong), 1007, 1063, 1100, 1197, 1220, 1245, 1337, 1422 and 1447 (broad), 1540, 1600 (broad), 1696, 2920 and 2200 (broad) cm.$^{-1}$; ultraviolet spectrum: 273 m$\mu$ ($\epsilon$ 10400) in ethanol.

*Anal.* Calcd. for $C_{14}H_{18}O_4N_2$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.45; H, 6.48; N, 10.12.

Bis-oximinocyclohexanone, m.p. >350, prepared by the method of Borsche,[23] has a band in the ultraviolet at 271 m$\mu$ ($\epsilon$12000 in ethanol) and its infrared spectrum (in KBr) is similar to that of the bis-oximinoketone of VIII in the 900, 1100 and 1300 to 1700 cm.$^{-1}$ regions.

**Deuterium Exchange of the Dimer VIII.**—A solution of 0.110 g. of VIII, 4 ml. of ethanol-O-*d* and 0.05 ml. of 20% sodium deuteroxide in deuterium oxide was refluxed for 15 min. under nitrogen. The solvent was removed *in vacuo*, 4 ml. of ethanol-O-*d* and 0.05 ml. of deuterium oxide were added to the residue and the solution again refluxed for 15 min. The second step was repeated twice. To the final residue was added 3 ml. of deuterium oxide, and the mixture extracted with 15 ml. of ether. The ether extract was washed with 2 ml. of deuterium oxide and dried over magnesium sulfate. Removal of the ether followed by distillation in a Späth bulb yielded 0.085 g. of a solid (77% yield), which melted 71–72° after one recrystallization from ether–petroleum ether; infrared spectrum (in $CCl_4$): 1185, 1245, 1280, 1382, 1445, 1465, 1475, 1720, 2200, 2880 and 2950 cm.$^{-1}$. Except for the methyl peak at 1382 cm.$^{-1}$, the fingerprint region of the spectrum is entirely different from that of the undeuterated compound.

*Anal.* Calcd. for $C_{14}H_{14}D_6O_2$: 30.0 atom % D. Found: 29.1 atom % D, which is equivalent to 5.82 deuterium atoms per molecule.

**Hydrogenation of the Dimer VIII.**—A mixture of 43 g. of VIII, 3 g. of platinum oxide and 500 ml. of ethanol was placed in a one-liter hydrogenation bomb and the material hydrogenated using an auxiliary tank with an initial pressure of 29 lb. The theoretical amount of hydrogen was absorbed in 45 min. After the catalyst was removed by filtration, the solvent was removed under reduced pressure. The product was recrystallized twice from ethanol, m.p. 100–102°, yield 19 g. (44%).

*Anal.* Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.93. Found: C, 75.29; H, 9.97.

**Conversion of the Ketol to the Acid Phthalate.**—A solution of 19 g. of the ketol, 12.7 g. of phthalic anhydride, 13.7 g. of pyridine and 50 ml. of benzene was refluxed for 3 hr., poured into 100 ml. of ice-water, and extracted with benzene. The benzene solution was washed subsequently with water, 5% hydrochloric acid and water. After removal of the benzene under reduced pressure, the product was recrystallized from benzene–hexane, m.p. 187–188.5°. The yield was 85% after recrystallization.

**Formation of the Brucine Salt from the Acid Phthalate.**—Solutions of brucine (34 g.) in 500 ml. of acetone and 27 g. of the phthalate in 250 ml. of acetone were mixed. When crystals failed to separate after 2 hr. standing in the refrigerator, the volume of the solution was reduced to 400 ml. On standing overnight 13.6 g. of crystals, m.p. 185–198°, precipitated. Two recrystallizations from ethyl acetate–ethanol gave 6.5 g. of material, m.p. 195–204°. From the mother liquors it was possible to isolate an additional 9 g. of salt with the same melting point.

**Regeneration of the Optically Active Acid Phthalate from the Brucine Salt.**—The brucine salt, 3 g., was treated with 100 ml. of 10% hydrochloric acid, the mixture extracted with benzene, washed with water, and dried over magnesium sulfate. Removal of the solvent yielded 1.5 g. of phthalate which, after recrystallization from benzene–hexane, melted at 160–164° and had $[\alpha]^{25}D$ +30.6° (*c* 1.82 in chloroform). In two other experiments specific rotations of +29.5 and +29.6° were obtained.

**Hydrolysis of the Optically Active Acid Phthalate to the Optically Active Ketol.**—The phthalate, 2.7 g., was re-

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(35) Ng. P. Buu-Hoi and P. Cagniant, *Bull. soc. chim. France*, [5] **10**, 151 (1943); A. E. Goddard, *J. Chem. Soc.*, 2315 (1923).

fluxed for 6 hr. with 50 ml. of 15% sodium hydroxide. Extraction with ether yielded 1.67 g. (100%) of ketol as a colorless, viscous oil which could not be induced to crystallize.

**Optically Active Dimer VIII from Oxidation of the Optically Active Ketol.**—To a cooled suspension of 3.0 g. of chromium trioxide in 35 ml. of pyridine was added 2.5 g. of ketol dissolved in 30 ml. of pyridine. The reaction mixture was allowed to stand at room temperature overnight. Extraction with ether, followed by distillation under reduced pressure, yielded 1.92 g. (64%) of product. Chromatography over 50 g. of alumina (Woelm, activity I) and subsequent recrystallization from ether–petroleum ether gave 0.9 g. of VIII, m.p. 58–62°, with an observed rotation of −1.04° (0.4023 g. in 1.5 ml. of chloroform). The infrared spectrum (in $CCl_4$) was identical with that of the racemic dimer VIII.

**Reduction of the Optically Active Dimer VIII to the Hydrocarbon XII.**—To a sodium diethylene glycolate solution (1.2 g. of sodium, 50 ml. of diethylene glycol) was added 0.9 g. of VIII and 2.5 ml. of 95% hydrazine. The solution was heated to 140–150° for 4 hr. An additional 1-ml. portion of hydrazine was added, the temperature raised to 210–215°, and heating continued for 14 hr. The reaction mixture was diluted with water, extracted with petroleum ether, and the crude product chromatographed on 20 g. of alumina (Woelm, activity I). The petroleum ether eluate contained 0.387 g. (44%) of hydrocarbon XII. Distillation in a Hickman flask yielded pure XII, b.p. ~70° at 0.4 mm., which had an observed rotation of −0.003° (0.3058 g. in 1.5 ml. chloroform). The infrared spectrum (in $CCl_4$) was identical with that of the hydrocarbon derived from racemic VIII.

**Reduction of the Racemic Dimer VIII.**—The diketone (0.48 g.) was reduced and isolated using the procedure described above; crude yield 0.317 g. (76%). Chromatography and distillation gave a colorless oil, b.p. 70° at 0.2 mm. and $n^{23}\text{D}$ 1.4988; infrared spectrum (in $CCl_4$): 1375, 1453, no peak in the carbonyl region, 2875, 2920 cm.$^{-1}$.

*Anal.* Calcd. for $C_{14}H_{24}$: C, 87.42; H, 12.58. Found: C, 87.43; H, 12.59.

**3,5-Dimethylcyclohex-2-en-1-one (XXIII)** was prepared using Horning's[36] method with Cronyn's[34] modification and had b.p. 81–82.5° at 8 mm., $n^{25}\text{D}$ 1.4820.

**Dimerization of 3,5-Dimethylcyclohex-2-en-1-one (XXIII).**—Self-condensation of 11.0 g. of XXIII with 6.0 g. of sodium amide was effected by the procedure described previously for 3-methylcyclohex-2-en-1-one (I). Distillation of the crude reaction product yielded 4.91 g. of material, b.p. 165–170° at 1.9 mm., which solidified on standing; yield 60% based on consumed ketone. The distillate was chromatographed on alumina (Alcoa, activity I). Approximately equal amounts of XXIVa, 2.25 g. (25%) (eluted with benzene and benzene–ether mixtures) and XXIVb, 2.52 g. (27%) (eluted with ether–methanol mixtures) were obtained. After recrystallization from ether–petroleum ether, XXIVa melted at 110–110.5° and XXIVb at 114–114.5°; infrared spectra (in $CCl_4$): XXIVa, 1098, 1220, 1260, 1350, 1380, 1450, 1710, 2820 cm.$^{-1}$; XXIVb, 1090, 1210, 1260, 1340, 1370, 1450, 1710, and 2840 cm.$^{-1}$. The spectra are virtually identical except for the 1200–1300 cm.$^{-1}$ region; ultraviolet spectra: XXIVa, 292 mμ (ε 74); XXIVb, 292 mμ (ε 52) (in ethanol).

*Anal.* Calcd. for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found for XXIVa: C, 77.75; H, 9.77. Found for XXIVb: C, 77.43; H, 9.84; C-Me, XXIVa, 1.37; XXIVb, 1.50.

Isomer a formed a 2,4-dinitrophenylhydrazone, m.p. 192–196°, while that derived from b had m.p. 201–203.5°. The melting point of the two was depressed on admixture.

Chromatography of the pot residue from the distillation of the crude dimerization product over alumina (Alcoa, activity I) yielded a dimer, m.p. 115–117° (yield <4%). The infrared and ultraviolet spectra were identical with a sample of XXV prepared by Taylor's method (ref. 7).

*Anal.* Calcd. for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 76.96; H, 9.56.

**Deuterium Exchange of the Dimers XXIVa and b.**—The compounds were deuterated as described above for VIII.

*Anal.* Calcd. for $C_{16}H_{18}D_6O_2$: 25.0 atom % D. Found: XXIVa, 24.33 atom % D; XXIVb, 24.30 atom % D.

**Conversion of the Diketone XXIVb to the Hydroxyketone XXV.**—The diketone XXIVb (500 mg.) was added to 15 ml. of *n*-decane containing 500 mg. of $NaNH_2$ and the mixture heated to reflux for 45 min. After the usual workup, the residue was separated into phenolic and neutral parts by extraction with sodium hydroxide. The phenolic portion (260 mg.) was chromatographed on silica gel to give 67 mg. of pure XXVII, m.p. 62°, which was not depressed on admixture of authentic XXVII. The neutral part (240 mg.) was chromatographed on 9 g. of alumina (Woelm, activity I), which gave 146 mg. of XXV, m.p. 114–119°, after recrystallization from petroleum ether. The mixed melting point with an authentic sample (m.p. 117–119°) was at 116–119°. On admixture of XXIVb the melting point was depressed to 85°.

**Reaction of 3,5-Dimethylcyclohex-2-en-1-one (XXIII) with Sodium Amide in *p*-Cymene.**—To a suspension of sodium amide (3.5 g., 0.087 mole) in 80 ml. of *p*-cymene (freshly distilled from sodium) in a 200-ml. flask equipped with a condenser was added dropwise over a period of 15 min. 3.0 g. (0.024 mole) of XXIII. The reaction mixture was refluxed for 30 min. and then poured into 350 ml. of ice-water. Extraction with benzene, followed by distillation, yielded 3,5-dimethylphenol (XXVII, 2.19 g., 62%) which, after recrystallization from petroleum ether, melted at 64–64.5°, lit.[37] 68°. Its 3,5-dinitrobenzoate prepared in the conventional manner had m.p. 193.5–194°, lit.[37] 195°; infrared spectrum (in $CCl_4$): 680, 830, 945, 1025, 1150, 1165, 1290, 1310, 1475, 1595, 1620, 2880, 2940, 3040, 3380, 3660 cm.$^{-1}$.

*Anal.* Calcd. for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.92; H, 8.53.

**Reaction of 3,5-Dimethylcyclohexen-1-one (XXIII) with Sodium Amide in *n*-Decane.**—In a 200-ml. flask equipped with condenser were placed sodium amide (3.4 g., 0.085 mole), XXIII (5.0 g., 0.04 mole) and 100 ml. of *n*-decane (distilled from sodium). The mixture was refluxed for 30 min. and poured into 200 ml. of ice-water. The decane layer was separated, washed with water, and dried over magnesium sulfate. The water layer was acidified with concd. hydrochloric acid and extracted with ether. The ether extract yielded XXVII (3.0 g., 61%) which after chromatography over alumina (activity VI) and recrystallization from petroleum ether melted at 62–63°. Chromatography of the decane extract over alumina (Merck, acid washed) yielded the hydroxyketone XXV (0.93 g., 19%) which after recrystallization from ethanol–water melted at 106–110°. A mixture with an authentic sample (m.p. 117–119°) prepared by Taylor's[7] method had m.p. 110–116°. Its 2,4-dinitrophenylhydrazone, m.p. 184–186°, showed no depression when mixed with an authentic sample, m.p. 185–188°. From the same chromatogram XXIVb (0.19 g., 4%) was obtained. Recrystallization from ether–petroleum ether gave material with m.p. 112–113° which on admixture of an authentic sample showed no melting point depression. A sharp melting point depression was noted when the compound was mixed with a sample of XXIVa. The 2,4-dinitrophenylhydrazone prepared from the product likewise did not depress the melting point of the derivative of XXIVb.

**Dimerization of Isophorone (XXI).**—To a stirred suspension of 8.4 g. of sodamide in 200 ml. of absolute ether was added 20 g. of isophorone in 150 ml. of ether. The mixture was allowed to reflux for five hours, cooled, poured on ice and extracted with ether. The product was pre-purified by distillation through a Hickman flask, giving 13 g. of unchanged isophorone and 3 g. of a viscous oil, b.p. 117–119° (0.6 mm.), which crystallized. The product was further purified by chromatography over alumina (activity II). An analytical sample had m.p. 121–122° after recrystallization from ether–petroleum ether; principal infrared bands (in $CCl_4$): 2941, 1718, 1460, 1370, 1348, 1285, 1248, 1217, 1136 cm.$^{-1}$.

*Anal.* Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: (1) 78.11; H, 10.18; (2) C, 78.16; H, 10.29.

Dimer XXII does not give a color reaction with tetranitromethane.

**Deuterium Exchange of the Dimer XXII.**—The dimer was deuterated as described above for VIII; 87% recovery.

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[36] E. C. Horning, M. O. Denekas and R. E. Field, *J. Org. Chem.*, **9**, 549 (1944).

[37] R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," fourth edition, John Wiley and Sons, Inc., New York, N. Y., 1956.

*Anal.* Calcd. for $C_{18}H_{22}D_6O_2$: 21.43 atom % D. Found: 21.43 atom % D.

**Dimerization of 3-Phenylcyclohex-2-en-1-one (XXVIII).**—A mixture of 3-phenylcyclohex-2-en-1-one[38] (4.75 g.), sodium amide (1.8 g.) and 30 ml. of ether was refluxed for 19 hr. The reaction mixture was poured into 100 ml. of ice-water and extracted with ether. The solvent was removed *in vacuo* and the product chromatographed on 120 g. of alumina (Alcoa, activity I). From the chromatogram was obtained 3.38 g. (71%) of starting material and 0.10 g. (2.1%) of hydroxy ketone dimer XXXV, which after recrystallization from ethyl acetate melted at 190–192°. Similar results were obtained when the reaction was run in benzene for 36 hr. at 45–60° with high speed stirring; infrared spectrum (in (KBr): 695, 760, 975, 1220, 1320, 1380, 1440, 1475, 1595, 1690, 2610, 2820, and 3400 cm.$^{-1}$. In $CS_2$: 3450, 1650 (!) cm.$^{-1}$; ultraviolet spectrum: 248 m$\mu$ ($\epsilon$ 15,800).

*Anal.* Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.92; H, 7.15.

CAMBRIDGE, MASS.

[38] G. F. Woods and I. W. Tucker, THIS JOURNAL, **70**, 2174 (1948).

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[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

# Ethylenimine Ketones. XIII.[1] Derivatives of *p*-Phenylbenzalacetone. *cis*- and *trans*-1-Cyclohexyl-2-(*p*-biphenylyl)-3-acetylethylenimine

BY NORMAN H. CROMWELL AND ROGER P. CAHOY

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Several phenylhydrazine derivatives of *p*-phenylbenzalacetone, including the phenylhydrazone, a pyrazoline and a pyrazole, have been synthesized. The *cis* and *trans* geometrical isomers of 1-cyclohexyl-2-(*p*-biphenylyl)-3-acetylethylenimine were prepared from the *p*-phenylbenzalacetone dibromide and characterized by their diagnostic behavior with phenylhydrazine and by absorption spectra studies. This is the first pair of arylacetylethylenimines to be reported.

In previous[2] investigations in this Laboratory several pairs of *cis*- and *trans*-arylaroylethylenimines and one pair of *cis*- and *trans*-alkylaroylethylenimines[3] have been prepared by the reaction of primary amines with $\alpha,\beta$-dibromoketones. These geometrical isomers (racemates) have been separated by fractional recrystallization or by chromatographic means and characterized by chemical and physical methods.

The present paper includes the first report of a synthesis and characterization of arylacetylethylenimines. To ensure that the products would be solids, *p*-phenylbenzalacetone was selected as a starting point.[4] Several years ago attempts to prepare 1-benzyl-2-phenyl-3-acetylethylenimine from benzalacetone dibromide resulted in a very unstable, oily product which we were unable to purify by distillation. It was of interest to relate this new class of ethylenimine ketones, by their behavior with phenylhydrazine and a study of their ultraviolet and infrared absorption spectra, to the previously studied series.

*p*-Phenylbenzalacetone (I) was prepared by the base-catalyzed condensation of acetone with *p*-phenylbenzaldehyde, which was prepared by a known method, employing improved techniques of isolation and purification.

The rather unstable bromine addition product of I, 3,4-dibromo-4-(*p*-biphenylyl)-2-butanone (II) reacted rapidly with one mole of cyclohexylamine in dry benzene to give a near quantitative yield of the stable $\alpha$-bromo-*p*-phenylbenzalacetone (III). Under similar conditions with primary amines, previously studied open chain $\alpha$-bromo-$\alpha,\beta$-unsaturated ketones[2,3] have reacted readily to give directly the $\alpha$-bromo-$\beta$-aminoketones and/or the ring closed product, the ethylenimine ketone. It is probable that the 1,4-addition of amines to III is slow because of the considerable resonance stabilization of this conjugated unsaturated system. The ring closure of the intermediate $\alpha$-bromo-$\beta$-cyclohexylamino ketone (A) should proceed with normal ease.

Only after standing at room temperature for 24 hr. did the dibromide II react with three molar equiv. of cyclohexylamine in benzene to give a 92% production of two equiv. of the by-product cyclohexylamine hydrobromide. The *cis–trans* mixture of ethylenimine ketones was separated by fractional crystallization into approximately two parts of the *trans* product Xb to one part of the *cis* isomer Xa. Since only a 68% yield of Xa + Xb was isolated, one cannot decide in what ratio these isomers were actually produced in this reaction.[5]

The assignment of the configurations to Xa and Xb were based initially upon the diagnostic phenylhydrazine reaction which in previous studies has been shown to produce an isolable aminopyrazoline (XI) from a *trans* isomer and only the pyrazole IX from a *cis* form.[6] 1-Phenyl-3-methyl-5-(*p*-biphenylyl)-pyrazole (IX) also was prepared readily

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[1] For paper XII in this series see N. H. Cromwell and G. D. Mercer, THIS JOURNAL, **79**, 3815 (1957).

[2] See ref. 1 and preceding papers in the series.

[3] N. H. Cromwell and R. J. Mohrbacher, THIS JOURNAL, **75**, 6252 (1953).

[4] After this investigation was substantially completed a prior synthesis of *p*-phenylbenzalacetone came to our attention; see R. Trave and G. Bianchetti, *Atti accad. nazl. Lincei, Rend., Classe sci. fis., mat. e nat.*, **11**, 211 (1951); *C. A.*, **49**, 2381 (1955).

[5] In a recent publication (N. H. Cromwell, R. P. Cahoy, W. E. Franklin and G. D. Mercer, THIS JOURNAL, **79**, 922 (1957)) a rationale was developed to explain the ethylenimine ketone *cis/trans* product ratio based on relative group sizes in the intermediate $\alpha$-bromo-$\beta$-aminoketones and favored conformations in transition states. It now appears to the present authors that such a rationale is tenuous, in that it is based upon the probably unwarranted assumption that one can readily assign relative effective size to various chemical groupings in complex systems such as these. Moreover, the application of the rationale led to the unusual, and probably theoretically unsound, conclusion that the protonation step of the 1,4-addition of amines to the $\alpha$-bromo-$\alpha,\beta$-unsaturated ketones involves a pyramidal carbanion (the $\alpha$-carbon); see J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 225. It is hoped that definitive experiments now being carried out in this Laboratory will clarify the stereochemistry of these conjugate addition reactions.

[6] See N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 1044 (1951), for a theoretical discussion of the method.