Notes A department for short papers of immediate interest.

Thermal Carbonylation of Cyclohexene

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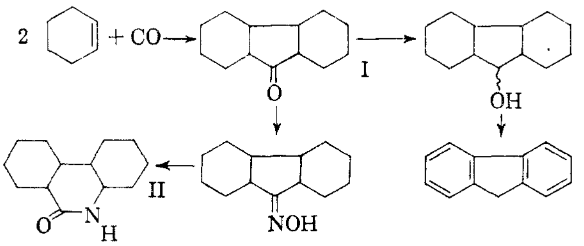
During the course of an investigation of certain carbonylation reactions, a mixture of cyclohexene, carbon monoxide, and hydrogen was processed in a stainless steel autoclave at 300° and about 800 atmospheres pressure. In addition to the normal hydroformylation products, hexahydrobenzaldehyde and cyclohexylcarbinol, a high-boiling carbonyl compound (I), b.p. 122.5–123°/5 mm., the elemental analysis of which corresponded to the formula $C_{13}H_{20}O$, was obtained in low yield. It seemed logical to assume that this material was dicyclohexyl ketone, arising from the addition of two moles of alkene to one mole of carbon monoxide and one mole of hydrogen.[1] However, further work (*vide infra*) revealed that I could be prepared by thermal reaction of cyclohexene and carbon monoxide only, and this, therefore, pointed to a perhydrofluorenone structure. We wish to present evidence favoring this structural assignment.

Compound I exhibited a carbonyl band in the infrared at 5.75 microns, indicative of a cyclopentanone-type ketone or an aldehyde[2] rather than a normal, unstrained ketone carbonyl. Furthermore, the oxime of I, which resisted recrystallization to a sharp melting point, also appeared to possess a five-membered ring containing the carbon-nitrogen double bond, as indicated by the $\rangle\mathrm{C{=}N}-$ infrared band at 5.95 microns,[3] and depressed the melting point of authentic dicyclohexyl ketoxime. These data suggested that I was a mixture of stereoisomeric perhydrofluorenones and that treatment with hydroxylamine yielded a mixture of isomeric oximes. In addition to analytical and spectral data in support of the proposed structure for I, the oxime was subjected to the Beckmann rearrangement in polyphosphoric acid and found to yield a lactam (II). II did not melt sharply, again indicating stereoisomers, but had the correct analysis and the expected infrared spectrum for a perhydrophenanthridone.[4] The possibility that I may have been an aldehyde, such as 2-cyclohexylhexahydrobenzaldehyde, was ruled out, since aldoximes generally give primary amides under these mildly acidic Beckmann conditions.[5] Moreover, spectral evidence (*vide supra*) contradicted the presence of a normal aldoxime group and I gave a negative Fehling's test. As a means of further identification I was reduced to perhydrofluorenol with lithium aluminum hydride and the crude product converted directly to fluorene by dehydrogenation over palladium.



Having established the novel nature of this reaction, efforts were directed toward defining optimum conditions for obtaining I. It was found that conventional carbonylation catalysts such as cobalt carbonyl did not affect the yield of I, and that best results could be achieved merely by processing cyclohexene and carbon monoxide at 350°C. for about eight hours (see experimental section). Although metal carbonyls were occasionally formed when the reaction was carried out in stainless steel autoclaves, the use of platinum-lined vessels was equally effective. This observation establishes the noncatalytic nature of the carbonylation. In the absence of hydrogen the normal hydroformylation products were not found. However, a hydrocarbon fraction, corresponding to (x)-cyclohexylcyclohexene[6] was obtained. Infrared data indicated that 1-cyclohexylcyclohexene was not a major component (little absorption at 11.9 to 12.7 microns).[7] The presence of 3- or 4-cyclohexylcyclohexene was suggested by a band attributable to *cis* unsaturation at 14.4 microns[7] in the infrared spectrum. Attempted hydrogenation of the cyclohexylcyclohexene fraction with palladized charcoal in a Parr hydrogenator yielded phenylcyclohexane and bicyclohexyl, resulting from a disproportionation *via* hydrogen transfer.[8] As expected, the cyclo-

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[1] W. F. Gresham, R. E. Brooks, and W. E. Grigsby, U. S. Patent **2,473,995**; G. Natta, P. Pino, and R. Ercoli, *J. Am. Chem. Soc.*, **74**, 4496 (1952).

[2] L. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley & Sons, New York, 1954, p. 114.

[3] L. Cross and A. Rolfe, *Trans. Far. Soc.*, **47**, 354 (1951).

[4] Ref. 2, pp. 176, 178.

[5] E. C. Horning and V. L. Stromberg, *J. Am. Chem. Soc.*, **74**, 5151, 5153 (1952).

[6] V. Mark and H. Pines, *J. Am. Chem. Soc.*, **78**, 5946 (1956).

[7] Ref. 2, p. 31.

[8] R. P. Linstead, E. A. Braude, P. W. D. Mitchell, K. R. H. Wooldridge, and L. M. Jackman, *Nature*, **169**, 100 (1952).

hexylcyclohexene can be obtained in the absence of carbon monoxide.[6] In two of the reactions of cyclohexene and carbon monoxide small amounts of fluorene were unexpectedly obtained. It is possible that under the rather strenuous reaction conditions simultaneous hydrogenation and dehydrogenation of I may yield fluorene.

The paucity of information relating to the pure stereoisomeric perhydrofluorenones precluded further attempts on our part along these lines. Whereas Linstead and coworkers[9] studied the pyrolysis of the six stereoisomeric perhydrodiphenic acids to perhydrofluorenones, the resolution of the resulting pyroketone mixtures into individual isomers was possible only by tedious separation of the mixed oximes. It appeared, however, that ketone I may be of the *syn*-series[9] since the melting points of the oxime and semicarbazone obtained from I correspond closely to the derivatives of the *syn*-pyroketone mixture.

In studying the scope of this reaction, cyclopentene and carbon monoxide yielded an analogous cyclic ketone, but no reaction occurred with a variety of aliphatic olefins.

EXPERIMENTAL

Boiling points and melting points are uncorrected. All infrared spectra were obtained using a Perkin-Elmer Model 21 double beam spectrometer.

Carbonylation of cyclohexene. A typical reaction involved the heating of 324 g. of cyclohexene at 350° for 6–8 hr. in a stainless steel autoclave under 700 atm. carbon monoxide pressure. Distillation of the pale yellow product gave several fractions having the following boiling point ranges: (1) 75–80°; *ca.* 200 g.; (2) 48–71°/3 mm., 4.6 g.; (3) 78–80°/3 mm., 23 g.; (4) 81–115°/3 mm., 6.0 g.; (5) 115°/3 mm., 23 g.; (6) 116–122°/3 mm., 11 g.; 30 g. pot residue. Fraction 1 was mainly unreacted cyclohexene with trace quantities of both benzene and cyclohexane as indicated by vapor phase chromatography using a column heated to 100°, with dinonyl phthalate supported on Celite as adsorbent, and helium as carrier gas.

Fraction 3, boiling point 78–80°/3 mm., n_D^{24} 1.4920–1.4928, was a clear mobile liquid. The infrared spectrum showed medium intensity bands at 3.3, 6.05, and 14.35 microns and little absorption at 11.9 to 12.7 microns. The presence of unsaturation was further indicated by the rapid decolorization of bromine in carbon tetrachloride. Hydrogenation of the olefin in absolute ethanol with 5% palladium on carbon at 25° and 60 p.s.i.g. in a Parr apparatus did not yield the anticipated bicyclohexyl. Instead, a mixture of bicyclohexyl and phenylcyclohexane, as confirmed by infrared analysis and vapor phase chromatography, was obtained.

Perhydrofluorenone (I). Fraction 5, boiling point 115°/3 mm. or 122.5–123°/5 mm., n_D^{24} 1.5038, was a clear, pale yellow, viscous liquid possessing a strong mint-like odor. The yield was approximately 6%. A strong absorption band at 5.75 microns was present in the infrared.

Anal. Calcd. for $C_{13}H_{20}O$: C, 81.1; H, 10.4. Found: C, 81.3; H, 10.6.

The *semicarbazone* of I was prepared[10] and after two recrystallizations from aqueous ethanol melted at 198–199°.

Anal. Calcd. for $C_{14}H_{23}ON_3$: C, 67.5; H, 9.3; N, 16.9. Found: C, 67.8; H, 9.4; N, 16.6.

The *oxime* was also prepared in the usual manner[10] and after several recrystallizations from aqueous methanol melted at 143–144.5°. (Another sample of oxime had m.p. 152–154° after three recrystallizations.) A mixed melting point with dicyclohexyl ketoxime, m.p. 163–163.5° (reported[11]: m.p. 158–159°), was 118–125°. Pertinent infrared spectral bands were found (KBr pellet) at 3.05 microns (strong: O—H stretching) and 5.95 microns (weak; >C=N— stretching). Authentic dicyclohexyl ketoxime shows >C=N— stretching at *ca.* 6.1 microns.

Anal. Calcd. for $C_{13}H_{21}OH$: C, 75.3; H, 10.2; N, 6.8. Found: C, 75.7; H, 10.2; N, 6.9.

A Beckmann rearrangement of the oxime was conducted by allowing 0.8 g. of oxime to stand overnight in 10 ml. of polyphosphoric acid and then warming on a steam bath for 1 hr. The burgundy-colored solution was diluted with water and 0.7 g. of solid material collected. This product after recrystallization from aqueous methanol gave white crystals, m.p. 164–165°. A strong band in the infrared spectrum (KBr pellet) was noted at 6.0 microns (lactam >C=O) and weak bands were present at 3.15 and 3.25 microns (N—H stretching).

Anal. Calcd. for $C_{13}H_{21}ON$: C, 75.3; H, 10.2; N, 6.8. Found: C, 75.2; H, 10.2; N, 6.9.

For dehydrogenation of perhydrofluorenone to the aromatic parent, fluorene, I was first reduced to a carbinol. Approximately 2 g. of the ketone was added dropwise to excess lithium aluminum hydride in ether. After the initial vigorous reaction, the mixture was kept at room temperature overnight, cautiously treated with methanol, and then decomposed with 15% sulfuric acid. The ether layer was washed with 5% sodium bicarbonate solution and water, then dried over sodium sulfate. Removal of the ether by means of gentle heating under a stream of nitrogen left a colorless oil, which showed a strong infrared band at 2.9 microns and no carbonyl absorption. This material was heated for 2 hr. at 305° with 2 g. of 5% palladium-on-carbon, using nitrogen to sweep out the reaction tube. The mixture was extracted with hot ethanol; the solution was then filtered to remove catalyst and diluted with water to incipient crystallization. Cooling produced an initial crop (*ca.* 0.5 g.) of colorless solid, m.p. 109–111°, which, after recrystallization from methanol, melted at 113.5–114°. This material was identified as fluorene by comparing its infrared spectrum with an authentic sample, and a mixture melting point, which was undepressed.

Perhydrofluorenone (I) gave a negative Fehling's test and upon oxidation with alkaline permanganate gave an unresolvable mixture of acids.

Similar yields of cyclohexylcyclohexene and perhydrofluorene were obtained when platinum-lined autoclaves were employed and also when cobalt carbonyl was added as a catalyst.

Fluorene. In each of two reactions, as much as 3 g. of a white solid was obtained from the pot residues following distillation. Recrystallization from aqueous ethanol gave a product melting at 113–114°. Infrared comparison and a mixed melting point (no depression) with an authentic sample showed this material to be fluorene.

Carbonylation of cyclopentene. Employing the same procedure and conditions used with cyclohexene, cyclopentene (231 g.) was processed with carbon monoxide. A hydrocarbon, b.p. 46–48°/5 mm. and a ketone (15 g.; 5.4% yield), b.p. 99–99.5°/5 mm., were obtained. The former showed bands due to olefinic unsaturation at 3.3, 6.05, and 12.5

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(9) S. B. Davis, W. E. Doering, P. Levine, and R. P. Linstead, *J. Chem. Soc.*, 1423 (1950).

(10) S. M. McElvain, *The Characterization of Organic Compounds*, Revised Edition, MacMillen Company, New York, 1953, p. 204.

(11) C. M. Hill and M. E. Hill, *J. Am. Chem. Soc.*, **75**, 2765 (1953).

microns, and a strong band at 5.78 microns was present in the spectrum of the ketone.

Anal. Calcd. for $C_{11}H_{18}O$: C, 80.5; H, 9.8. Found: C, 80.8; H, 9.7.

The colorless semicarbazone was prepared[10] and recrystallized from 25% ethanol, m.p. 188–189°.

Anal. Calcd. for $C_{12}H_{19}ON_3$: C, 65.2; H, 8.6. Found: C, 65.2; H, 8.6.

The 2,4-dinitrophenylhydrazone derivative formed as orange flakes, m.p. 144–145° (from 95% ethanol).

Anal. Calcd. for $C_{17}H_{20}O_4N_4$: C, 59.3; H, 5.8; N, 16.3. Found: C, 59.6; H, 6.0; N, 16.6.

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The Diels-Alder Reaction of Steroidal 20-Methylene-Δ^{16}-pregnene Derivatives with Maleic Anhydride

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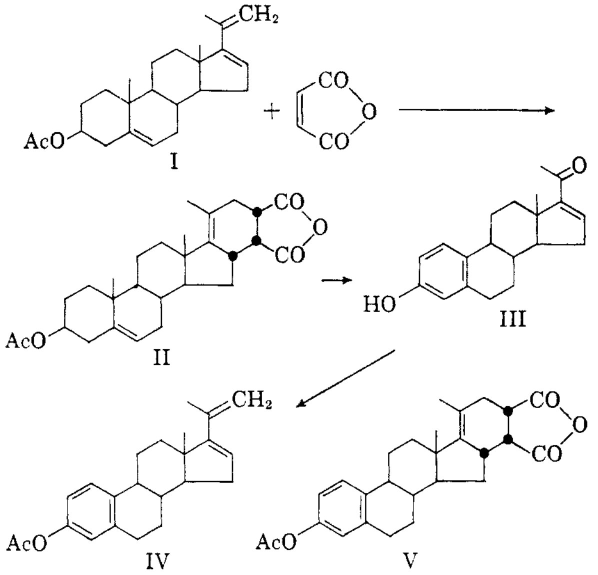
We have recently described[1] the synthesis of 20-methylene-$\Delta^{5,16}$-pregnadien-3β-ol acetate (I) by treatment of the corresponding 20-ketone with triphenylphosphine-methylene. The novel $\Delta^{16,20(22)}$-diene system present in I should permit its condensation with dienophiles in a Diels-Alder type of reaction to produce substances containing an additional ring (or rings) fused to the 16 and 17 positions of the steroid nucleus. Indeed when the triene I was allowed to react with maleic anhydride in boiling benzene, an adduct was obtained stereospecifically in excellent yield, which on the basis of the elemental analysis and spectral properties must be the pentacarbocyclic compound II. The β-configuration of the hydrogen substituent at C-16 is based on the expectation that attack of the dienophile proceeds from the less hindered α-side of I.[2] The β-hydrogen configuration at the other two new asymmetric centers follows from the rule of maximum accumulation of unsaturation in the transition state of the complex formed in the Diels-Alder reaction.[3]

In the 19-nor steroid series, 17-acetyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol (III)[4] on treatment with triphenylphosphinemethylene and subsequent acetylation yielded the 19-nor-20-methylene-Δ^{16}-derivative IV, which was smoothly converted to the adduct V by means of maleic anhydride in boiling benzene. The Diels-Alder reaction between 20-methylene-Δ^{16}-pregnenes and maleic anhydride therefore appears to be general.[5]



EXPERIMENTAL[6]

Adduct II from 20-methylene-$\Delta^{5,16}$-pregnadien-3β-ol acetate (I) and maleic anhydride. A solution containing 100 mg. of the triene I (m.p. 124.5–126°)[1] and 100 mg. of freshly sublimed maleic anhydride in 10 cc. of dry benzene was boiled under reflux for 6 hr., cooled, and diluted with water. The organic layer was washed with 2% sodium hydroxide solution and water and was then dried and evaporated. The solid residue (108 mg.) showed m.p. 235–245° and after one crystallization from ether gave the analytical sample of the adduct II as needles with constant m.p. 255–256°, $[\alpha]_D$ −26°, ν_{max} 1860, 1780 cm.$^{-1}$ (5-membered cyclic anhydride) and 1735 cm.$^{-1}$ (acetate), no high-intensity absorption in the ultraviolet.

Anal. Calcd. for $C_{28}H_{36}O_5$: C, 74.30; H, 8.02. Found: C, 74.23; H, 7.88.

17-Isopropenyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol acetate (IV) *from 17-acetyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol* (III). A 1*N* ethereal solution of butyllithium (10 cc.) was added to a suspension of 3.57 g. (10 millimoles) of methyltriphenylphosphonium bromide in 50 cc. of ether with swirling under nitrogen. The mixture was shaken in nitrogen for 2 hr., and a solution of 590 mg. (2 millimoles) of 17-acetyl-$\Delta^{1,3,5(10),16}$-estratetraen-3-ol (III)[4] in 30 cc. of dry ether was then added. The mixture was shaken for a further 4 hr. and allowed to stand overnight at room temperature. Tetrahydrofuran was then added at the same time as the ether was distilled off until most of the latter had been replaced. The mixture was boiled

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[1] F. Sondheimer and R. Mechoulam, *J. Am. Chem. Soc.*, **79**, 5029 (1957).

[2] *Cf.* L. F. Fieser, *Experientia*, **6**, 312 (1950).

[3] *Cf.* K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937).

[4] C. Djerassi, G. Rosenkranz, I. Iriarte, J. Berlin, and J. Romo, *J. Am. Chem. Soc.*, **73**, 1523 (1951).

(5) Since our work was completed, two patents have appeared describing the Diels-Alder reaction between 20-acetoxy-$\Delta^{16,20}$-pregnadiene derivatives and maleic anhydride [R. H. Mazur and G. P. Mueller, U. S. Patent **2,753,343**, July 3, 1956; *Chem. Abstr.*, **51**, 2070 (1957); R. H. Mazur, U. S. Patent **2,753,359**, July 3, 1956; *Chem. Abstr.*, **51**, 4436 (1957)].

(6) Melting points are uncorrected. Rotations were determined at 20–25° in chloroform solution. Ultraviolet spectra were measured on a Unicam Model S.P. 500 spectrophotometer and infrared spectra (in chloroform solution) on a Baird double beam recording spectrophotometer with sodium chloride prism. Analyses were carried out in our microanalytical laboratory under the direction of Mr. Erich Meier.