1076. *2-Cyclohexylidenecyclohexanone and 2-Cyclohex-1'-enylcyclohexanone, and the Condensation of the Latter with Diethyl Oxalate.*

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Reaction of 2-(1-chlorocyclohexyl)cyclohexanone (I) with sodium methoxide at temperatures below 10° affords a solid, 2-cyclohexylidenecyclohexanone (II), whereas treatment of compound (I) with sodium hydroxide at room temperature gives a liquid which is shown to be largely 2-cyclohex-1'-enylcyclohexanone (III), together with a small amount of its isomer (II). Condensation of the liquid isomer mixture with diethyl oxalate in the presence of sodium leads to the doubly unsaturated keto-lactone (IX), and not the unsaturated triketone (VI) reported by earlier workers.

CYCLOHEXANONE has long been known to undergo self-condensation to a liquid ketone, $C_{12}H_{18}O$ (A). This condensation can be induced by the action of acids,[1] or bases,[2] or by heat alone.[3] The structure of this ketone has been much disputed, and one of the purposes of this paper is to establish its composition.

Kon and Nutland[4] formulated (A) as the βγ-unsaturated ketone (III), because of its normal molecular refraction, the greater stability of an *endo*-double bond in a cyclohexane ring, and the very high yield of adipic acid on ozonolysis. The presence of only low-intensity absorption in the ultraviolet spectrum of (A) led Evans and Gillam[5] to postulate (III) as the predominant constituent. On the other hand, Kunze[6] believed that (II) represented the true structure of the ketone, because he was able to isolate a dibenzylidene derivative from the reaction of (A) with benzaldehyde. However, Reese[7] subsequently prepared an isomeric solid ketone (B) by treating compound (I) with base at low temperatures, and assigned structure (II) to this product on the basis of its enhanced molecular refraction, and the formation of a diketone on attempting to distil the epoxide made by the action of alkaline peroxide on compound (B), (II → IV → V). The solid ketone (B) was found to be transformed into the liquid (A) on warming. Later studies of the ultraviolet spectrum of (B)[8,9] tended to confirm that it was a trisubstituted αβ-unsaturated ketone, but none of these observations was sufficiently critical to detect the possible presence of small amounts of the isomer (III). Recently, Roginskaia *et al.*[10] examined the liquid and solid ketones using

[1] Wallach, *Ber.*, 1907, **40**, 70; Mannich, *ibid.*, p. 153; Zelinski, Shuiken, and Fataev, *J. Gen. Chem.* (*U.S.S.R.*), 1932, **2**, 761.
[2] Wallach, *Ber.*, 1896, **29**, 2955; Haller and Bauer, *Compt. rend.*, 1911, **152**, 551; Taboury and Godchot, *ibid.*, 1919, **169**, 62; Petrov, *Bull. Soc. chim. France*, 1928, **43**, 1272; Wayne and Adkins, *J. Amer. Chem. Soc.*, 1940, **62**, 3401.
[3] Hurd, Greengard, and Roe, *J. Amer. Chem. Soc.*, 1939, **61**, 3359.
[4] Kon and Nutland, *J.*, 1926, 3101.
[5] Evans and Gillam, *J.*, 1941, 815.
[6] Kunze, *Ber.*, 1926, **59**, 2085.
[7] Reese, *Ber.*, 1942, **75**, 384.
[8] French and Wiley, *J. Amer. Chem. Soc.*, 1949, **71**, 3702.
[9] House and Wasson, *J. Amer. Chem. Soc.*, 1956, **78**, 4392.
[10] Roginskaia, Svetozarskii, Finkel'shtein, and Zil'berman, *J. Gen. Chem.* (*U.S.S.R.*), 1958, **28**, 2266.

Raman, infrared, and ultraviolet spectroscopy, and claimed that all three techniques showed that both compounds (A) and (B) possessed structure (II). In addition, the rather unusual suggestion was made that the cyclohexanone ring of the unstable solid (B) was in the half-boat conformation, while that of the stable liquid (A) was in the half-chair conformation.
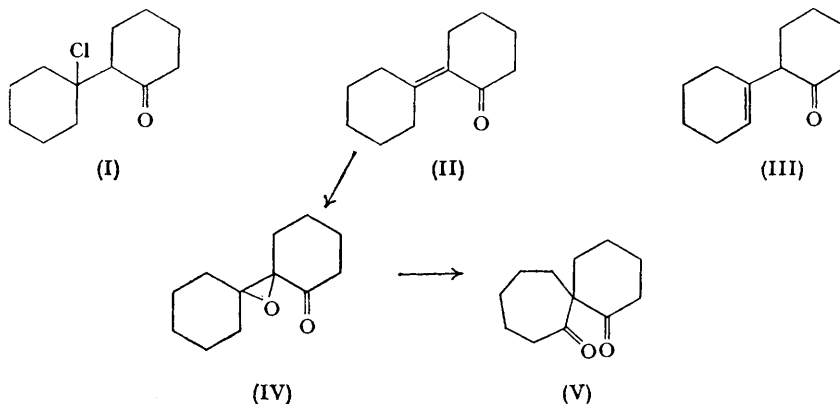
We have made a critical study of the infrared, ultraviolet, and proton magnetic resonance spectra of compounds (A) and (B). We conclude that the solid ketone (B) is homogeneous and possesses structure (II), because its proton magnetic resonance spectrum shows no olefinic proton signal, its infrared spectrum shows only a single carbonyl band at a position (5·93 μ) characteristic of an αβ-unsaturated ketone, and its ultraviolet spectrum exhibits absorption of medium intensity at 254 mμ, indicating a trisubstituted αβ-unsaturated ketone. We believe that the liquid ketone (A) is a mixture of the αβ- and βγ-unsaturated ketones, (II) and (III), respectively, with the latter predominating, probably to the extent of 80—90% of the mixture. Thus, the proton magnetic resonance spectrum shows an olefinic proton signal, the intensity of which, when compared with the integrated intensity of the remaining proton signals, indicates a mixture of (II) and (III) in the ratio 1:4, the infrared spectrum shows a strong band at 5·84 μ, characteristic of an isolated, unstrained ketone, as well as a shoulder at 5·93 μ, and the ultraviolet spectrum exhibits only 12% of the intensity of absorption of compound (II) at 254 mμ.

Very recently, Jäger, Färber, and Poonawalla[11] reported that the liquid ketone (A) condensed with diethyl oxalate in ether solution in the presence of sodium to give a salt which, on acidification, liberated an enolic compound, $C_{14}H_{16}O_3$. No direct evidence was presented in support of a structure for this compound. Nevertheless, it was formulated as (VI) on the assumption that the condensation proceeded by a double Claisen reaction on the αβ-unsaturated ketone (II). These authors believed that this was analogous to the condensations (VII → VIII), reported earlier.[12] However, the reported ease of enolisation of the condensation product and stereochemical requirements of the enol and its derivatives make structure (VI) untenable.
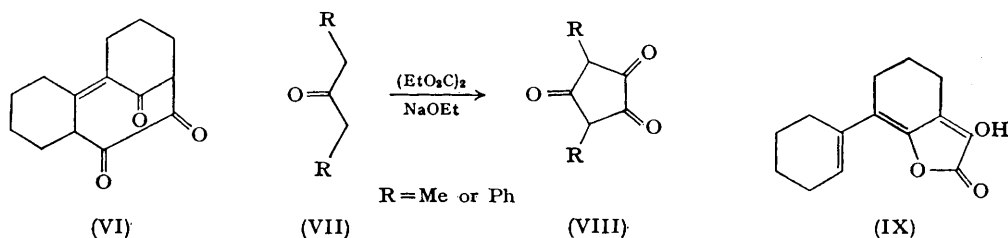
[11] Jäger, Färber, and Poonawalla, *Arch. Pharm.*, 1962, **295**, 205.
[12] Claisen, *Ber.*, 1894, **27**, 1353; Claisen and Ewan, *Annalen*, 1895, **284**, 245.

We have prepared the compound, $C_{14}H_{16}O_3$, described earlier.[11] Although the ferric chloride test was only weakly positive, the enolic nature of the product was evidenced by the strong hydroxylic absorption in its infrared spectrum, by the observation that basification of an alcoholic solution caused a significant bathochromic shift in the ultraviolet spectrum, and by the preparation of an acetate. Further, the infrared spectrum showed strong broad absorption centred at $5 \cdot 78$ μ and medium-intensity absorption at $5 \cdot 96$ and $6 \cdot 22$ μ, which can be ascribed to a carbonyl function and two distinct ethylenic linkages in the molecule. The high intensity and the positions of the ultraviolet absorption, $\lambda_{max.}$ 232 and 325 mμ (ε 6680 and 23,800), indicate extensive conjugation. Finally, the proton magnetic resonance spectrum reveals the presence of one olefinic proton. These observations are all successfully accommodated in the structural expression (IX).
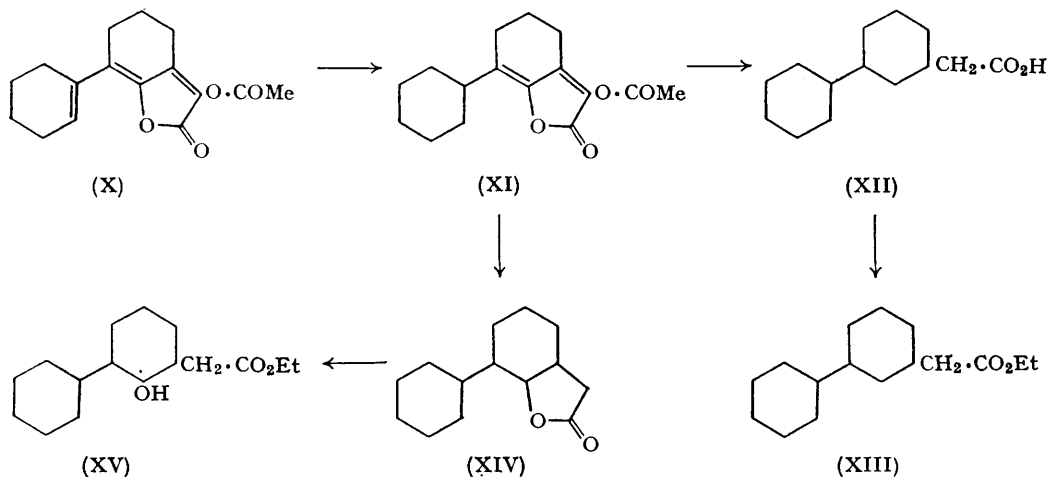
Hydrogenation under moderate pressure of the enol acetate (X) in ethanolic hydro-chloric acid solution in the presence of a large amount of Adams catalyst led to a mixture of products, three of which were isolated. Determination of the constitution of these compounds provided further support for the assignment of structure (IX) to the enolic condensation product.

The major product of the reduction was a sweet-smelling oil, $C_{16}H_{28}O_2$. Its odour, in conjunction with its infrared spectrum, which showed a single sharp band at $5 \cdot 75$ μ, indicated that an ester group was present. The conditions of the reduction made it likely that this would be an ethyl ester, and this was indicated by the proton magnetic resonance spectrum which clearly showed the A_2B_3 pattern of an ethyl group. The proton magnetic resonance and infrared spectra of this ester indicated that it was saturated, and this conclusion was reinforced by the lack of appreciable absorption below 220 mμ in its ultraviolet spectrum, coupled with a negative tetranitromethane test. Accordingly, the ester is ethyl 3-cyclo-hexylcyclohexylacetate (XIII), derived from the enol acetate (X) by simple reduction to (XI), followed by hydrogenolysis of both $>$C:C·O·C:O groups in the molecule, leading to an acid (XII) which is subsequently esterified.

The second most abundant reduction product was a solid, m. p. 60—80°, which after repeated crystallisation melted at 90—91°, and gave analytical data agreeing with $C_{14}H_{22}O_2$. Spectral evidence and a negative tetranitromethane test indicated that it was saturated. In addition its infrared spectrum showed no hydroxyl absorption but had a strong band at $5 \cdot 68$ μ, suggesting the presence of a γ-lactone ring, and, therefore, this compound must be the lactone (XIV), derived from compound (XI) by hydrogenolysis of the enol acetate group and reduction. It is possible that the material, m. p. 60—80°, is a mixture of stereoisomers,

while the recrystallised product is homogeneous, and may be identical with the lactone, m. p. 94°, also having structure (XIV), which was prepared by Rosenmund, Glet, and Pohl.[13]

The third product from the reduction of compound (X) was an oil, $C_{16}H_{28}O_3$. It was in many ways similar to the major reduction product (XIII). Thus, its pleasant smell, together with infrared and proton magnetic resonance spectral data, indicated that it contained an ethyl ester group, and spectral information coupled with a negative tetranitromethane test showed that it was saturated. However, the infrared and proton magnetic resonance spectra also showed the presence of a hydroxyl group. Thus, the compound must be ethyl 3-cyclohexyl-2-hydroxycyclohexylacetate (XV), arising by ethanolysis of the lactone (XIV).

Although Kötz, Blendermann, and Meyer[14] have reported that 2-ethoxalyl-6-methyl-cyclohexanone (XVI) cyclises to the keto-lactone (XVII) on attempted distillation, and Ruzicka and Plattner[15] have achieved an acid-catalysed cyclisation (XVIII → XIX) of the diketo-acid obtained by hydrolysis of the corresponding ethoxalyl-ketone, the formation of the keto-lactone (IX) appears to be the first example of OC-diacylation by diethyl oxalate under relatively mild basic conditions.
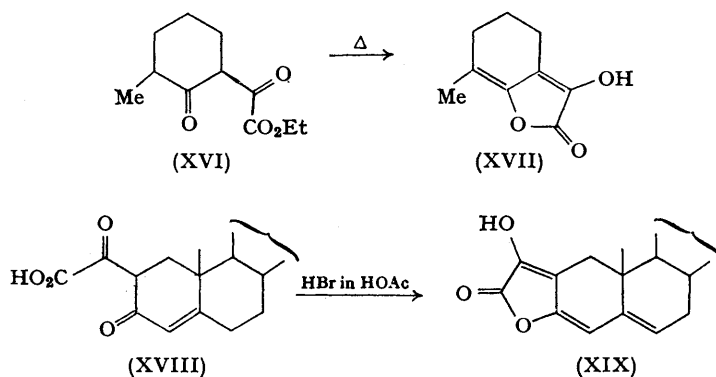
Amongst the many possible anions present (see Chart) the relative insolubility of the salt of compound (XX) under the reaction conditions must be such as to cause its precipitation.

CHART
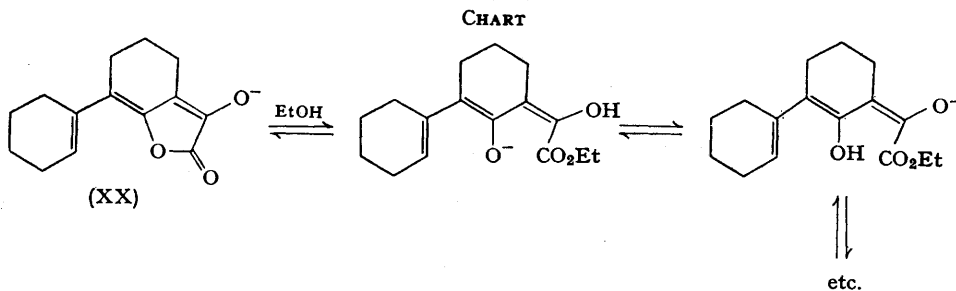
These conditions are very critical because on several occasions the salt did not precipitate. On these occasions, acidification of the water-soluble material gave an oil which did not crystallise. However, heating this oil, which must be a mixture of enols corresponding to the anions in the chart, *in vacuo*, caused the elimination of ethanol, and led on cooling to the crystalline keto-lactone (IX) in high yield. Ring-closure rather than decarbonylation of the intermediate ethoxalyl-ketone (XXI) finds an analogy in the change (XVI → XVII),[14]

[13] Rosenmund, Glet, and Pohl, *Arch. Pharm.*, 1954, **287**, 441.
[14] Kötz, Blendermann, and Meyer, *Ber.*, 1912, **45**, 3702.
[15] Ruzicka and Plattner, *Helv. Chim. Acta*, 1938, **21**, 1717.

although decarbonylation readily occurs on heating 2-ethoxalylcyclohexanone.[16,17] If the intermediate is the isomer (XXII), then the failure to decarbonylate is not unusual, as such αβ-unsaturated ketones are known to be thermally more stable.[17,18]

(XXI)   (XXII)
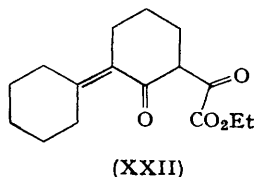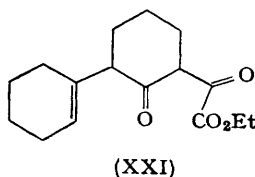
EXPERIMENTAL

Melting points were determined on a Kofler block. Ultraviolet spectra were measured with a Cary model 14 recording spectrophotometer, and, except where specified, were for ethanol solutions. Infrared spectra were recorded with Perkin-Elmer Infracord spectrophotometer models 127 and 137-G. Proton magnetic resonance spectra were recorded in deuterochloroform solutions by using a Varian A-60 spectrometer; the positions of the peaks were measured relative to tetramethylsilane as the internal reference. Thin-layer chromatography was conducted with silica gel as the adsorbant, chloroform–ethyl acetate (95:5) as the developing solvent, and iodine as the visualising agent; R_F values reported were only reproducible to ± 0·05. Microanalyses were performed by Dr. A. Bernhardt, Mulheim, Germany.

2-(1-Chlorocyclohexyl)cyclohexanone (I).—Dry hydrogen chloride was bubbled through cyclo-hexanone (40 g.) contained in a cooled (water) flask. After 15 hr. the gas flow was stopped and the crystalline 2-(1-chlorocyclohexyl)cyclohexanone (32 g., 71%) collected by filtration.

Liquid Ketone (A).—Compound (I) (20 g.) was well shaken with 2N-aqueous sodium hydroxide (100 ml.), the mixture allowed to stand for 2 hr., then extracted with ether (50 ml.). The ether extract was washed with water, dried, and the solvent was eliminated, leaving a red oil which was distilled. The liquid ketone (A) was obtained as an oil (15·3 g., 93%), b. p. 114—116°/3·5 mm.; $\lambda_{max.}$ 248 mμ (ε 830), at 254 mμ ε was 790; $\nu_{max.}$ (CHCl₃) 5·84s and 5·93m(sh) μ; $\nu_{max.}$ (liquid film) 5·84s, 5·93m(sh), and 6·16w μ; complex multiplet centred at τ 4·60 (0·8 protons), signals between τ 6·8 and 9·3 (17·2 protons).

Solid Ketone (B).—This was prepared from compound (I) in 88% yield using Reese's procedure.[7] Crystallised from methanol–water (4:1) it had m. p. 56—57° (lit.,[7] 57°); $\lambda_{max.}$ 254 mμ (ε 6800); $\nu_{max.}$ (CHCl₃) 5·93s μ, $\nu_{max.}$ (Nujol) 5·94 and 6·18m μ; signals between τ 6·8 and 9·1.

Condensation of Liquid Ketone (A) *and Diethyl Oxalate*.—(a) A solution of the liquid ketone (A) (8·9 g., 0·05 mole) and diethyl oxalate (7·3 g., 0·05 mole) in ether (10 ml.) was added to a stirred suspension of sodium powder (1·15 g., 0·05 mole) in ether (20 ml.) at such a rate that the temperature of the mixture did not exceed 20° (ice–water cooling), and stirring was continued until all the sodium had dissolved. The mixture was kept at room temperature overnight during which time a yellow solid separated which was collected by filtration and washed with ether. Dissolution of this solid in water followed by acidification of the resulting solution with 2N-hydro-chloric acid afforded a precipitate which was purified by crystallisation from methanol, giving the keto-lactone (IX) as bright yellow rods (6·2 g., 54%), m. p. 173—178° (lit.,[11] 182°); R_F 0·13; $\lambda_{max.}$ 232, 235 mμ (ε 6680, 23,800); $\lambda_{max.}$ (0·01N-sodium hydroxide in ethanol) 245, 352 mμ (ε 8640, 23,200); $\nu_{max.}$ (Nujol) 3·02s, 5·78s, 5·96m, and 6·22m μ; complex multiplet centred at τ 3·95 (1 proton), signals between τ 7·2 and 8·7 (15 protons) (Found: C, 72·2; H, 6·9; O, 20·4. Calc. for $C_{14}H_{16}O_3$: C, 72·4; H, 6·9; O, 20·7%).

(b) The above preparation was repeated, but the solid did not precipitate from the reaction medium. The mixture was shaken with ether (50 ml.) and water (50 ml.). The aqueous layer was acidified with 2N-hydrochloric acid and extracted with ether (4 × 100 ml.). The ether extract was washed with water, dried, and the solvent eliminated, leaving a viscous red oil (12·5 g.) which did not crystallise. This oil was heated at 180° (bath-temp.)/0·1 mm. for 1 hr., then allowed

¹⁶ Snyder, Brooks, and Shapiro, *Org. Synth.*, Coll. Vol. II, p. 531.
¹⁷ Mayer, *Chem. Ber.*, 1955, **88**, 1859.
¹⁸ Kuehne, *J. Amer. Chem. Soc.*, 1961, **83**, 1492.

to cool. The resulting solid was crystallised from methanol, giving compound (IX) (8·2 g., 71%), m. p. 173—178°.

Enol Acetate (X).—Compound (IX) (3·0 g.) in acetic anhydride (15 ml.) and pyridine (7·5 ml.) was heated on a steam-bath for 3 hr. The pyridine and excess of acetic anhydride were eliminated *in vacuo*, leaving a dark-red syrup (3·5 g.), which solidified on trituration with ether. This solid was crystallised three times from methanol, giving the *enol acetate* (X) as pale yellow prisms (2·3 g., 65%), m. p. 75·5—76°; R_F 0·70; $\lambda_{max.}$ 225, 328·5 mμ (ϵ 5650, 24,100); $\nu_{max.}$ (Nujol) 5·59s, 5·67s, 6·00w, and 6·21w μ; complex multiplet centred at τ 3·83 (1 proton), signals between τ 7·3 and 8·5 (17 protons, including a 3-proton singlet at τ 7·68) (Found: C, 70·0; H, 6·55; O, 23·5. $C_{16}H_{18}O_4$ requires C, 70·05; H, 6·6; O, 23·3%).

Hydrogenation of the Enol Acetate (X).—Compound (X) (1·50 g.) in ethanol (100 ml.) containing 12N-hydrochloric acid (10 drops), was hydrogenated at room temperature and 40 lb./sq. in. in the presence of Adams catalyst (0·75 g.). After 16 hr. the mixture was filtered through Celite 535, and the solvent was eliminated from the filtrate, leaving an oil (1·33 g.). This was taken up in ether (50 ml.), shaken with saturated sodium hydrogen carbonate (2 × 50 ml.), washed with water, dried, and freed of solvent, leaving a neutral oil (1·17 g.). Thin-layer chromatography showed the presence of a major constituent, R_F 0·81, two minor constituents, R_F 0·69 and 0·62, and two trace materials, R_F 0·54 and 0·19. The neutral oil (1·17 g.), dissolved in hexane (15 ml.), was applied to alumina (50 g.; Guilini, neutral, activity II). Hexane (500 ml.) eluted *ethyl 3-cyclohexylcyclohexylacetate* (XIII) as a sweet-smelling, mobile oil (669 mg.), R_F 0·81; tetranitromethane test negative; $\lambda_{max.}$ 256 mμ (ϵ 20), at 220 mμ ϵ was 137; $\nu_{max.}$ (liquid film) 5·75s μ; quartet ($J = 7$ c./sec.) centred at τ 5·87 (2 protons), signals between τ 7·6 and 9·5 [26 protons, including a 3-proton triplet ($J = 7$ c./sec.) centred at τ 8·75] (Found: C, 76·0; H, 11·1; O, 12·8. $C_{16}H_{28}O_2$ requires C, 76·1; H, 11·2; O, 12·7%). Benzene (200 ml.) eluted a solid (139 mg.), m. p. 60—80°, R_F 0·69, which was crystallised four times from pentane, giving 3-cyclohexyl-2-hydroxy-cyclohexylacetic acid lactone (XIV) as plates (29 mg.), m. p. 90—91° (lit.,[13] 94°); R_F 0·69; tetranitromethane test negative; $\lambda_{max.}$ 258 mμ (ϵ 35), at 220 mμ ϵ was 70; $\nu_{max.}$ (Nujol) 5·68s μ (in the range 2·5—15 μ the spectrum was identical with that of the material, m. p. 60—80°); complex multiplet centred at τ 5·43 [1 proton, (C_2=CHO–)], signals between τ 7·1 and 9·5 (21 protons) (Found: C, 75·85; H, 10·15; O, 14·1. Calc. for $C_{14}H_{22}O_2$: C, 75·6; H, 10·0; O, 14·4%). More benzene (100 ml.) and ether (50 ml.) eluted *ethyl 3-cyclohexyl-2-hydroxycyclohexylacetate* (XV) as a sweet-smelling, mobile oil (59 mg.), R_F 0·62; tetranitromethane test negative; $\lambda_{max.}$ 259 mμ (ϵ 227), at 220 mμ ϵ was 586; $\nu_{max.}$ (liquid film) 5·77s μ; quartet ($J = 7$ c./sec.) centred at τ 5·75 (2 protons), complex multiplet centred at τ 6·00 [1 proton (C_2=CHO–)], broad signal centred at τ 7·3 (1 proton) disappearing on deuteration (D_2O layer above $CHCl_3$ solution), signals between τ 7·9 and 9·5 [24 protons, including a 3-proton triplet ($J = 7$ c./sec.) centred at τ 8·71] (Found: C, 71·9; H, 10·3; O, 17·5. $C_{16}H_{28}O_3$ requires C, 71·6; H, 10·5; O, 17·9%). More ether (150 ml.) eluted a mixture of (XV) and the materials with R_F 0·54 and 0·19 (49 mg.).

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