J. Chem. Soc. (C), 1968

Aliphatic Friedel-Crafts Reactions. Part VII.¹ Preparation of $\alpha\beta$ - and $\beta\gamma$ -Unsaturated Ketones from Substituted Cyclohexenes

By J. K. Groves and N. Jones,* Chemistry and Metallurgy Department, Lanchester College of Technology, Priory Street, Coventry

The yield of $\beta\gamma$ -unsaturated ketone obtained by acylation of 1-methylcyclohexene under various conditions is reported. A series of 1-acyl-2-alkylcyclohexenes has been prepared by base-catalysed isomerisation of some initial acylation products.

We have described the preparation of $\beta\gamma$ -unsaturated ketones (I) by the zinc chloride-catalysted acetylation of 1-alkylcyclohexenes.¹ Good yields of 6-acyl-1-methylcyclohexenes are also obtained from isobutyric and propionic anhydrides when extended reaction times are employed. The effect of different catalysts upon the interaction of acetic anhydride and 1-methylcyclohexene has been investigated, the product in each case being 6-acetyl-1-methylcyclohexene (Table 1).

TABLE 1

Acylation of 1-methylcyclohexene

| Acylating | | | | Time | Yield |
|-------------------------------------|-------------------|-----------------|-------------|-----------|-----------|
| agent | Catalyst | Solvent | Temp. | (hr.) | (%) |
| (Pr ⁱ CO) ₉ O | ZnCl, | | 2 0° | 40 | 66 |
| (EtCO) ₂ O | ZnCl ₂ | | 5 | 20 | 53 |
| Ac ₂ O | $ZnCl_2$ | | 2 | 12 | 79 |
| Ac ₂ O | SnCl₄ | CS ₂ | 5 | 6 | 48 |
| Ac ₂ O | AlCla | CH,Cl, | -5 | 0.75 | 38 |
| Ac ₂ O | BF_3 | Et,Ō | 5 | 12 | 48 |

The effect of sodium methoxide upon the acylation products described in both this and the preceding paper shows that, in general, partial conversion to the $\alpha\beta$ -unsaturated ketone (II) occurs.

The ketones shown in Table 2 were isolated either by

 Part VI, J. K. Groves and N. Jones, J. Chem. Soc. (C), 1968, 2215.
 E. A. Braude and C. J. Timmons, J. Chem. Soc., 1955, 3766. preparative g.l.c. or by regeneration from purified semicarbazones.



The proportion of $\alpha\beta$ -unsaturated ketone present after treatment of the acylation product with base was observed to decrease as the size of the acyl or alkyl substituent increased. This imposes a limitation on the method for preparing $\alpha\beta$ -unsaturated ketones and with 6-acetyl-1-isopropylcyclohexene no detectable amount of conjugated ketone is formed. This observation is consistent with the reported ² dehydrochlorination of 1-chloro-1-methyl-2-pivaloylcyclohexane with alcoholic potassium hydroxide to give 1-methyl-6-pivaloylcyclohexene only.

The u.v. extinction coefficients of the pure conjugated ketones (II) were also found to decrease with increasing size of acyl and alkyl substituents. Such reduction in absorption intensity is a consequence of either non-planarity of the chromophore³ or the adoption of an enforced *s*-*cis* conformation.⁴ In either case a reduction

³ W. F. Forbes, in 'Steric Effects in Conjugated Systems,' Butterworths, London, 1958.

⁴ R. L. Erskine and E. S. Waight, J. Chem. Soc., 1960, 3425.

N 18·8

16.7

(%)

| | | | TABLE 2 | 2 | | |
|--|--|--|---------|---|---|--|
| | | | _ | | - | |

1-Acyl-2-alkylcyclohexenes and semicarbazones

| | Ketone | | | | | Semicarbazone | | | | | | |
|-----------------------------|-------------------------------|--------------|----------------|--|---|----------------|------|-----|------|----------------------|--------------|------------|
| | Found (%) | | | Calc. (%) | | Found (%) | | | | Calc. | | |
| R1 | \mathbb{R}^2 | ĉ | Н | Formula | c | H | c | н | N | Formula | C | н |
| Me Me | Et Pr ⁿ | 78.6 79.2 | $10.5 \\ 10.8$ | С ₁₀ Н ₁₆ О С ₁₁ Н ₁₈ О | $\begin{array}{c} 78 \cdot 9 \\ 79 \cdot 5 \end{array}$ | $10.5 \\ 10.8$ | 64·7 | 9·5 | 18·8 | $C_{12}H_{21}N_{3}O$ | 64·6 66.9 | 9·4 9.9 |
| Me Et Pr ⁱ | Pent ⁿ Me Me | 78∙9 79∙6 | 10·5 10·8 | C ₁₀ H ₁₆ O C ₁₁ H ₁₈ O | 78·9 79·5 | $10.5 \\ 10.8$ | 62·9 | 9·2 | 10.9 | $C_{11}H_{19}N_{3}O$ | 63·2 | 9·1 |

in the stability of the conjugated ketone relative to its $\beta\gamma$ -unsaturated isomer is to be expected.

The i.r. and u.v. absorption data for the conjugated ketones are summarized in Table 3. Also shown

Spectral data for 1-acyl-2-alkylcyclohexenes

| R1 | R² | v(C=O) (cm. ⁻¹) | v(C=C) (cm. ⁻¹) | $\lambda_{max.}$ (m μ) | ε | ε _{app} |
|-----------------|-------------------|--------------------------------|--------------------------------|-----------------------------|------|------------------|
| Me | Me | 1683 | 1617 | 248 | 6500 | 4290 |
| Me | Et | 1682 | 1613 | 248 | 5800 | 3200 |
| Me | Pr ⁿ | 1682 | 1613 | 248 | 5150 | |
| Me | Bun | 1683 | 1613 | 248 | 4050 | |
| Me | Pent ⁿ | 1682 | 1613 | 248 | 3850 | |
| Et | Me | 1685 | 1620 | 247 | 5000 | 2270 |
| Pr ⁱ | Me | 1686 | ca. 1633* | 247 | 4000 | 1170 |
| | | * Ve | ry broad ba | ind. | | |

are typical values of extinction coefficients (ε_{app}) for equilibrium mixtures of the ketones (I) and (II) obtained by treatment of the pure $\alpha\beta$ -unsaturated ketone (II) with sodium methoxide.

EXPERIMENTAL

Spectroscopic Measurements.—N.m.r. spectra were determined for 5—10% solutions in carbon tetrachloride using a 60 Mc. Perkin-Elmer R10 spectrometer. Liquid films were used for i.r. spectra and u.v. absorptions were determined for methanol solutions.

Analytical Gas Chromatography.—Product purities were confirmed by g.l.c. on a Pye Panchromatograph fitted with a 9 ft. 10% silicone gum (SE 30) column at 150° and/or a Perkin-Elmer F11 chromatograph with a 2 m. 20% Apiezon (DE301) column at 220°.

Zinc Chloride-catalysed Acylations.—The general method was as described in Part VI employing the reaction times and temperatures indicated below.

1-Methylcyclohexene and Isobutyric Anhydride.—Reaction at 20° for 40 hr. afforded 6-isobutyryl-1-methylcyclohexene (11.0 g.), b.p. 50°/1 mm., n_p^{25} 1.4642, ν_{max} 1702s (C=O str.) and 1660w cm.⁻¹ (C=C str.) (Found: C, 79.3; H, 10.7. C₁₁H₁₈O requires C, 79.5; H, 10.8%). The ketone formed a semicarbazone (from MeOH), m.p. 185—186°.

1-Methylcyclohexene and Propionic Anhydride.—Reaction at 5° for 20 hr. afforded a liquid (8.0 g.), b.p. 54—55°/ 2 mm., which readily formed a semicarbazone, m.p. 182— 183° (Found: C, 62.9; H, 9.3. $C_{11}H_{19}N_3O$ requires C, 63.1; H, 9.1%). Steam distillation from phthalic anhydride afforded 1-methyl-6-propionylcyclohexene, n_D^{22} 1.4700, v_{max} 1705s and 1660w cm.⁻¹ (unspecified assignments here and below are as in the preceding paragraph).

1-Isopropylcyclohexene and Acetic Anhydride.—Reaction at 5° for 12 hr. afforded a product (9.6 g.), b.p. $90-94^{\circ}/$ 7 mm., containing 6-acetyl-1-isopropylcyclohexene together with a second ketone (probably 1-acetyl-2-isopropylidenecyclohexane¹) in a ratio of ca. 3:1. The former compound was isolated by preparative g.l.c. (conditions as described below), v_{max} . 1705s and 1660w cm.⁻¹ (Found: C, 79.5; H, 10.8. C₁₁H₁₈O requires C, 79.5; H, 10.8%). N.m.r. bands at τ 4.62 (m, C=C-H), 7.95 (s, COMe), and 9.04 (d, CHMe₂, J 8 c./sec.).

The Interaction of 1-Methylcyclohexene and Acetic Anhydride.—(a) Aluminium chloride. Acetic anhydride (0.052 mole) was added to a suspension of finely powdered aluminium chloride (0.055 mole) in methylene chloride (50 ml.). The resulting solution was filtered through a glass-wool plug, and cooled to -5° ; 1-methylcyclohexene was added during 15 min. The solution was maintained at -5° for a further 30 min. and then poured into ice-water. The organic layer was washed with sodium hydrogen carbonate solution and water, dried (MgSO₄), solvent removed, and the liquid distilled. The fraction b.p. $46-50^{\circ}/5$ mm. contained polymeric material (g.l.c., i.r.) from which pure 6-acetyl-1-methylcyclohexene (2.6 g.) was separated by chromatography on alumina (activity I) using diethyl ether as eluant.

(b) Stannic chloride. The alkene (0.050 mole) was added slowly to a solution of acetic anhydride (0.052 mole) and stannic chloride (0.052 mole) in carbon disulphide (50 ml.)and the solution maintained at 5° for 6 hr. 6-Acetyl-1-methylcyclohexene (3.3 g.) was isolated as described above.

(c) Boron trifluoride-diethyl ether. The alkene (0.10 mole) was added slowly to a solution of acetic anhydride (0.11 mole) and boron trifluoride-diethyl ether (0.11 mole) in ether (10 ml.) and the mixture was maintained at 5° for 12 hr. Decomposition of the reaction mixture and subsequent distillation afforded unchanged alkene (0.025 mole) and crude 6-acetyl-1-methylcyclohexene (7.3 g.) shown by g.l.c. to contain *ca.* 10% polymeric material.

Base-catalysed Formation of 1-Acyl-2-alkylcyclohexenes.— The products (3.0 g.) obtained from the zinc chloridecatalysed acylations described in this and the preceding paper were treated with sodium methoxide [sodium (1 g.) methanol (30 ml.)] at room temperature for 24 hr. Each resulting solution was neutralised with N-hydrochloric acid and extracted with ether (2×25 ml.). The extract was washed with water and dried (MgSO₄); solvent was removed to give a ketone mixture from which the $\alpha\beta$ -unsaturated isomer was isolated by method (i) or (ii).

(i) The mixture was treated with sodium acetatesemicarbazide hydrochloride to afford a mixture of semicarbazones. Fractional crystallisation from methanol afforded the pure semicarbazone of the $\alpha\beta$ -unsaturated isomer and steam distillation of the derivative with twice its own weight of phthalic anhydride gave the pure (g.l.c.) conjugated ketone. (ii) Preparative g.l.c. was carried out on a Wilkens Autoprep A700 chromatograph fitted with a 20 ft. column containing 10% diethylene glycol adipate cross-linked with pentaerythritol (L.A.C.) operating at 170°. Repeated injection of 100 μ l. quantities of the mixture afforded a pure sample of the conjugated ketone.

1-Acetyl-2-methylcyclohexene was isolated by method (i), n_p^{25} 1·4870 (lit.,⁵ 1·4872); n.m.r. bands at τ 7·91 (s, COMe) and 8·20 (s, C:CMe). Semicarbazone, m.p. 226–227° (lit.,⁵ 226–227°).

1-Acetyl-2-ethycyclohexene was isolated by method (ii), $n_{\rm D}^{25}$ 1.4860; n.m.r. bands at τ 7.90 (s, COMe) and 9.00 (t, Et, J 8 c./sec.).

1-Acetyl-2-n-propylcyclohexene was isolated by method (ii), $n_{\rm p}^{22}$ 1.4808, semicarbazone, m.p. 170–171°.

1-Acetyl-2-n-butylcyclohexene was isolated by method (ii), $n_{\rm p}^{22}$ 1.4761 (lit., ⁶ 1.4760).

1-Acetyl-2-n-pentylcyclohexene was isolated by method (i), semicarbazone, m.p. 164—165°.

1-Methyl-2-propionylcyclohexene was isolated by method

⁵ R. B. Turner and D. M. Voitle, J. Amer. Chem. Soc., 1951, 78, 1403.

(i), $n_{\rm p}^{22}$ 1·4815 (lit.,⁷ 1·4820), semicarbazone, m.p. 196–197° (lit.,⁷ 212°).

1-Isobutyryl-2-methylcyclohexene was isolated by method (ii).

Treatment of 6-acetyl-1-isopropylcyclohexene with base under the conditions specified above resulted in the recovery of unchanged ketone (g.l.c., i.r.).

Treatment of 1-Acyl-2-alkylcyclohexenes with Base.— Samples of the pure $\alpha\beta$ -unsaturated ketones were treated with sodium methoxide solution as described above. Each product was shown to be a mixture of ketones (1) and (II) (i.r., g.l.c.). Apparent extinction coefficients (ε_{app}) for these mixtures are shown in Table 3.

We are indebted to the S.R.C. for a grant to purchase equipment and to the University of Warwick for the use of a Wilkens A700 chromatograph and the determination of n.m.r. spectra.

[8/1031 Received, July 22nd, 1968]

⁶ E. A. Braude, E. R. H. Jones, H. P. Koch, R. W. Richardson, F. Sondheimer, and J. B. Toogood, *J. Chem. Soc.*, 1949, 1890.

⁷ J. Colonge and E. Duroux, Bull. Soc. chim. France, 1940, 7, 459.