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1,2-CARBONYL TRANSPOSITION IN SOME KETONES[1)]

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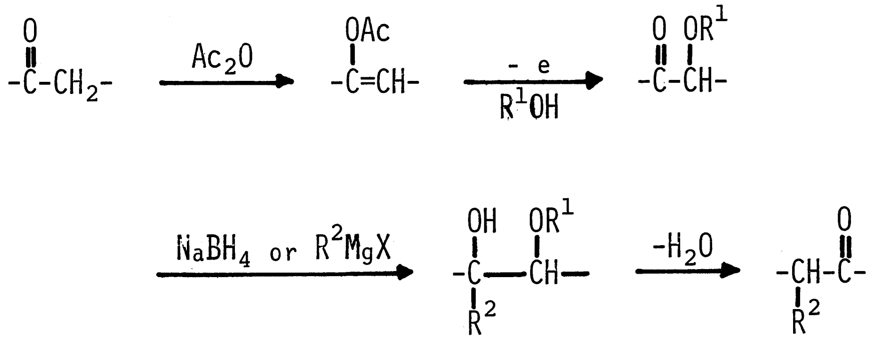
The electrochemical method of the introduction of α-acetoxy or α-methoxy group on a ketone was applied to accomplish the 1,2-carbonyl transposition in ketones. The acid-catalyzed reaction of β-acetoxy or β-methoxy alcohols prepared by the reduction or Grignard reaction of the α-acetoxy or α-methoxy ketones gave the 1,2-carbonyl transposed ketones.

Relocation of the carbonyl group in ketones may be an important problem[2)] in organic syntheses and a powerful clue in the transformation of the readily available ketones to those inaccessible by the hitherto known methods.
Our recent study[3,4)] on the α-acetoxylation of ketones by the anodic oxidation of enol acetates strongly suggested the potentiality of the α-substituted ketones as the key compound in the 1,2-transposition of the carbonyl group. The overall process is shown in equation 1.[5)]



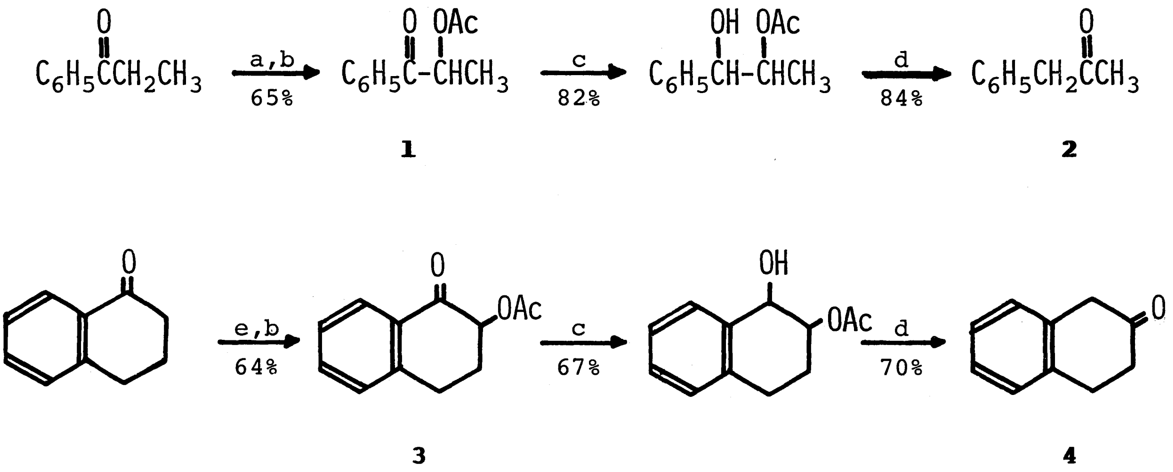
.....(1)

$R^1 = COCH_3$, $R^2 = H$

$R^1 = CH_3$, R^2 = alkyl or aryl

The α-acetoxy ketones **1** and **3** obtained from the anodic oxidation[4)] of the corresponding enol acetates[6)] in acetic acid containing triethylamine as a supporting electrolyte were smoothly reduced to the alcohols with sodium borohydride in diglyme. Subsequent acid-catalyzed dehydration of the vicinal acetoxy alcohols gave the ketones **2** and **4** as the sole products (Scheme I).

Scheme I. Simple Carbonyl Transposition



a: A mixture of the ketone(0.10 mole), p-TsOH(0.50 g) and Ac_2O(100 ml) was refluxed with continuous removal of AcOH.

b: Anodic oxidation was carried out according to the previous report.[4)]

c: The acetoxy ketone **1** or **3**(0.03 mole) was treated with $NaBH_4$(0.02 mole) in diglyme(30 ml) at room temperature for 10 hr.

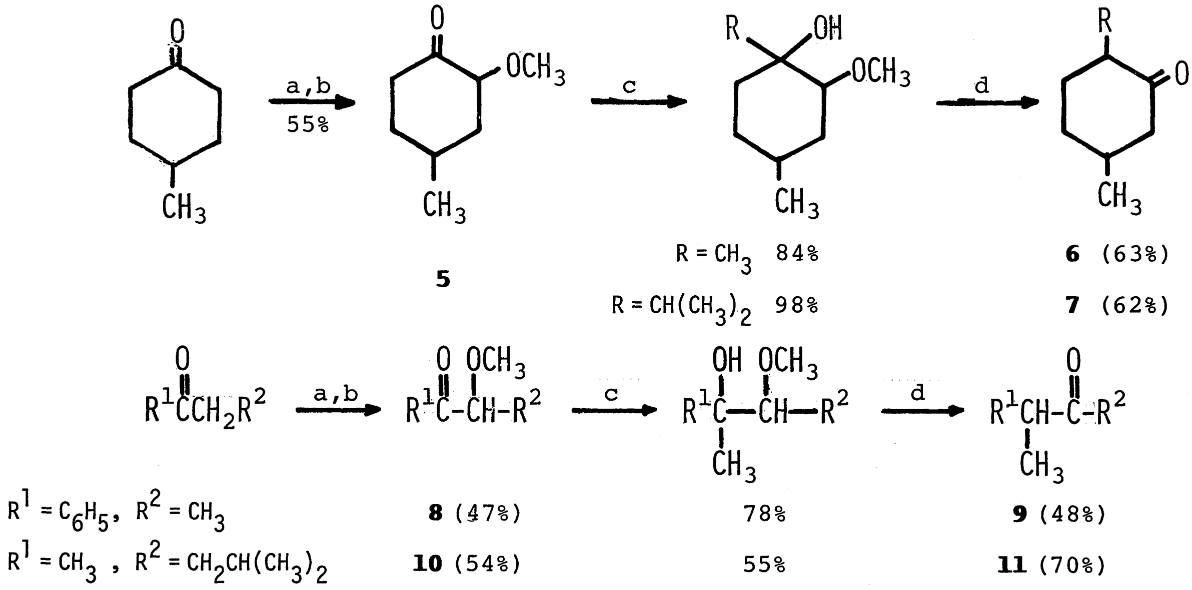
d: The acetoxy alcohol(0.01 mole) was added dropwise to $KHSO_4$(2.0 g) at 150-160°C under reduced pressure(25-30 mmHg).

e: A mixture of the ketone(0.10 mole), p-TsOH(0.50 g) and isopropenyl acetate(100 ml) was refluxed with continuous removal of acetone.

The use of absolute methanol-tetraethylammonium p-toluenesulfonate as the solvent-supporting electrolyte system in the anodic oxidation of enol acetates brought about the formation of α-methoxy ketones in moderate yields.[7)] The reaction of the α-methoxy ketones with a Grignard reagent followed by the dehydration resulted in the alkylative 1,2-carbonyl transposition (Scheme II).

The treatment of the alcohol, prepared from the Grignard reaction of α-methoxy ketone **5**[8)] with 20% sulfuric acid at reflux temperature for 2-3 hr gave 2,5-dimethyl(or 2-isopropyl-5-methyl)cyclohexanone, **6** (or **7**[9)]). The similar procedure brought about the smooth transformation of **8** or **10**[10)] to **9** or **11**, respectively.

Scheme II. Alkylative Carbonyl Transposition



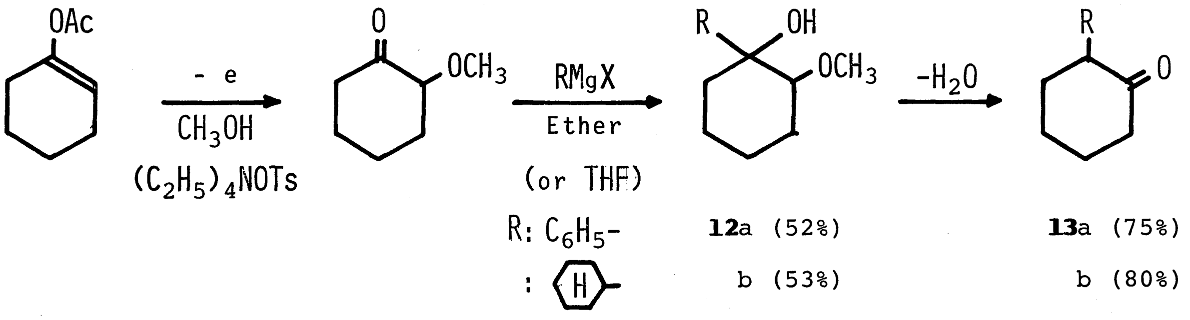
a: A mixture of the ketone(0.10 mole), p-TsOH(0.50 g) and Ac_2O(100 ml) was refluxed with continuous removal of AcOH.

b: Anodic oxidation of the enol acetate(0.05 mole) was carried out in CH_3OH(150 ml) using $(C_2H_5)_4NOTs$(1.0 g) as a supporting electrolyte at room temperature.

c: The methoxy ketone **8** or **10** (0.03 mole) was treated with CH_3MgI or $(CH_3)_2CHMgBr$(0.06 mole) in ether(100 ml) at 10-15°C for 5 hr.

d: The methoxy alcohol(0.01 mole) was refluxed in 20% H_2SO_4(30 ml) during 2-3 hr for **6** and **7**, 3 days for **9** and a day for **11**.

The employment of phenyl- or cyclohexyl-magnesium bromide as a Grignard reagent in this alkylative transposition readily gave the corresponding α-substituted cyclohexanone which may be difficultly prepared by the usual methods.[11,12]



The facile 1,2-transposition of a carbonyl group and the introduction of an alkyl or aryl group on the position of the original carbonyl group may provide us with an interesting tool in organic syntheses.

References and Notes

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3) T. Shono, Y. Matsumura, and Y. Nakagawa, J. Am. Chem. Soc., 96, 3532 (1974).
4) T. Shono, M. Okawa, and I. Nishiguchi, ibid., 97, 6144 (1975).
5) The compounds **1-4**, **6**, **8**, **9**, **11**, and **13** were characterized through the comparison of their spectroscopic and gas chromatographic behaviors with those of authentic samples. Bp[°C/mmHg]: **1**[120-123/5 (lit.,[13] 120-126/5)], **2**[62-63/3 (lit.,[14] 122-125/50)], **3**[150/5, mp 72-74°C (lit.,[15] mp 73-75°C)], **4**[125-128/5 (lit.,[16] 114-116/4.5)], **6**[93-94/30 (lit.,[17] 182-184/720)], **8**[70-72/2 (lit.,[18] 89-95/4)], **9**[70-73/8 (lit.,[19] 100-106/18)], **11**[62-63/28 (lit.,[20] 75/50)], **13**a[119-120/2 (lit.,[11a] 86-95/0.3)], **13**b[127/4 (lit.,[12b] 98-100/2)].
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   b) H. O. House, M. Gall, and H. D. Olinstead, J. Org. Chem., 36, 2361 (1971).
7) The electrolysis was carried out in an undivided cell using carbon rod electrodes with stirring until 2-3F/mole of electricity was passed.
8) **5**: bp 90°/25mm; nmr ($\mathrm{CCl_4}$, δ-ppm), 3.33(t., 1H, -O-CH<), 3.20(s., 3H, $\mathrm{-OCH_3}$), 0.95(d., 3H, $\mathrm{-CH_3}$), 0.98-2.46(m., 7H, $\mathrm{-CH_2-}$ and -CH<); ir (neat, $\mathrm{cm^{-1}}$), 1710(>C=O), 1100(>CH-O-$\mathrm{CH_3}$).
9) **7**: bp 100°/30mm; nmr ($\mathrm{CCl_4}$, δ-ppm), 0.75-1.05(m., 9H, $\mathrm{-CH_3}$), 1.20-2.44(m., 9H, $\mathrm{-CH_2-}$ and -CH<); ir (neat, $\mathrm{cm^{-1}}$), 1700(>C=O).
10) **10**: bp 70°/25mm; nmr ($\mathrm{CCl_4}$, δ-ppm), 3.41(m., 1H, -CH<), 3.30(s., 3H, $\mathrm{-OCH_3}$), 2.05(s., 3H, $\mathrm{-COCH_3}$), 0.92(d., 6H, $\mathrm{-CH(CH_3)_2}$), 1.20-1.61(m., 3H, $\mathrm{-CH_2-}$, and -CH<); ir (neat, $\mathrm{cm^{-1}}$), 1720(>C=O), 1100($\mathrm{-OCH_3}$).
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