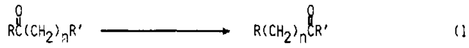
A New Method of 1,4-Transposition of a Carbonyl Group[1]

Summary: A new method of 1,4-transposition of a carbonyl group has been developed by using anodic regioselective γ-methoxylation of dienol acetates as a key step.

Sir: Synthesis of carbonyl compounds is undoubtedly an important process in organic synthesis, though the preparation of carbonyl compounds having the carbonyl group in a given position is often achievable with great difficulty. Thus, transposition of a carbonyl group from the original position to another position seems one of the effective methods to overcome such a difficulty.

A variety of methods[2,3] have been devised for the transposition of a carbonyl group to the neighboring position (1,2-transposition, $n = 1$, eq 1), whereas no effective methods have been found for the migration of the carbonyl group to further positions ($n > 2$).



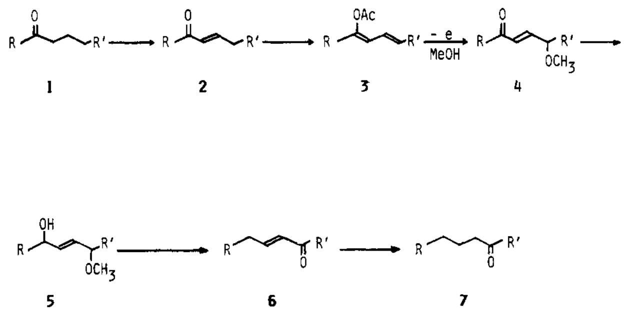
$$\overset{O}{\overset{\|}{RC}}(CH_2)_nR' \longrightarrow R(CH_2)_n\overset{O}{\overset{\|}{C}}R' \qquad (1)$$

It is shown in the present study that a novel method for carrying out the transposition of a carbonyl group to the γ-position (1,4-transposition, $n = 3$) is successfully achievable by using anodic oxidation of dienol acetates as a key reaction.

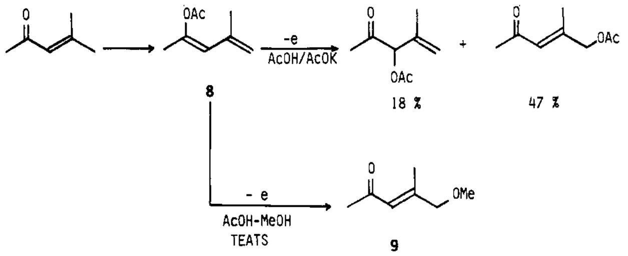
The whole reaction process is shown in Scheme I, in which the transformation of **2** and **6** is described in the present study.[4,5]

The anodic acetoxylation or methoxylation of carbonyl compounds at the α-position has been shown in the previous study,[6,7] whereas the anodic methoxylation of enones,

Scheme I



Scheme II



TEATS : tetraethylammonium p-toluenesulfonate

Scheme III

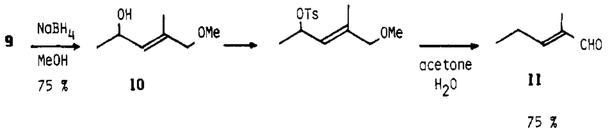
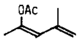
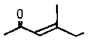
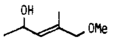
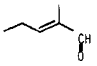
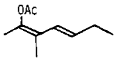
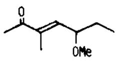
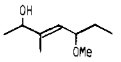
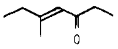
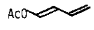
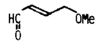
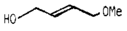
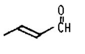
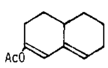
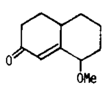
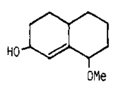
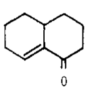
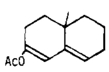
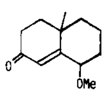
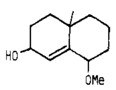
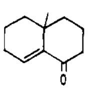
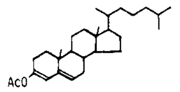
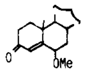
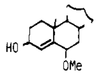
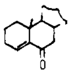


Table I. 1,4-Carbonyl Transposition

dienol acetate	γ-methoxy ketone	yield,[a,b] %	alcohol	yield,[a] %	product	yield,[a] %
 8	 9	81	 10	75	 11	76
		74		94		72
		76		85		68
		66		98		54
		64		92		50
		84		99		87[d]

[a] Isolated yields. [b] The yields were obtained at the stage when 2 F/mol of electricity was passed. [c] All products showed satisfactory results in spectroscopic analyses. [d] Solvolysis of the corresponding tosylate did not afford 4-cholesten-6-one in satisfactory yield,[12] while the treatment of the alcohol with trifluoromethanesulfonic anhydride and triethylamine in methylene chloride directly gave 4-cholesten-6-one in 87% yield.

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(1) Electroorganic Chemistry. 68.

(2) Shono, T.; Nishiguchi, I.; Nitta, M. *Chem. Lett.* **1976**, 1319.

(3) Trost, B. M.; Hiroi, K.; Kurozumi, S. *J. Am. Chem. Soc.* **1975**, *97*, 438 and references cited therein.

(4) The transformation of 1 to 2 has been well-known. For example: Sharpless, K. B.; Lauer, R. F.; Teranishi, Y. *J. Am. Chem. Soc.* **1973**, *95*, 6137. Trost, B. M.; Salzmann, T. N. *Ibid.* **1973**, *95*, 6840. Reich, H. J.; Reich, I. L.; Renger, J. M. *Ibid.* **1973**, *95*, 5813. Braude, E. A.; Evans, E. A. *J. Chem. Soc.* **1954**, 607.

(5) Reduction of 6 to 7 has been well exploited. For example: McQuillin, F. J.; Ord, W. O. *J. Chem. Soc.* **1959**, 2902, 3169. Brewster, J. H. *J. Am. Chem. Soc.* **1954**, *76*, 6361. Wilds, A. L.; Johnson, J. A., Jr.; Sutton, R. E. **1950**, *72*, 5524.

(6) Shono, T.; Matsumura, Y.; Nakagawa, Y. *J. Am. Chem. Soc.* **1974**, *96*, 3532.

(7) Shono, T.; Okawa, M.; Nishiguchi, I. *J. Chem. Soc.* **1975**, *97*, 6144.

0022-3263/83/1948-1939$01.50/0

especially its regioselectivity, is entirely unknown.

As shown in Scheme II, the anodic acetoxylation of 8 was not regioselective and gave a mixture of two positional isomers, while the anodic methoxylation[8] of 8 in methanol containing 10% acetic acid[10] gave 9 exclusively.

The reduction of 9 to an allylic alcohol (**10**) was easily accomplished with methanolic $NaBH_4$ in 75% yield. The transformation of 10 to the corresponding 1,4-transposed carbonyl compound 11 was studied under a variety of conditions, and it was found that the solvolysis of the *p*-toluenesulfonate of 10 in acetone containing 10% H_2O gave the desired product 11 in 75% yield[11] (Scheme III).

This method could be applied to a variety of carbonyl compounds as typical results are shown in Table I. The results found in this study would afford the first convenient method for the 1,4-transposition of a carbonyl group.[13]

Registry No. 8, 37562-76-8; 9, 5369-72-2; 10, 85565-77-1; 11, 623-36-9; $CH_3C(OAc)=C(CH_3)CH=CHCH_2CH_3$, 85565-78-2; $CH_3COC(CH_3)=CHCH(OMe)CH_2CH_3$, 85565-79-3; $CH_3CH(OH)C(CH_3)=CHCH(OMe)CH_2CH_3$, 85565-80-6; $CH_3CH_2C(CH_3)=CHCOCH_2CH_3$, 1447-26-3; $AcOCH=CHCH=CH_2$, 1515-76-0; $HCOCH=CHCH_2OMe$, 85565-81-7; $HOCH_2CH=CHCH_2OMe$, 26089-32-7; $CH_3CH=CHCOH$, 4170-30-3; 2-acetoxy-3,4,4a,5,6,7-hexahydronaphthalene, 85565-82-8; 4,4a,5,6,7,8-hexahydro-8-methoxy-2(3*H*)-naphthalenone, 85565-83-9; 2-hydroxy-8-methoxy-2,3,4,4a,5,6,7,8-octahydronaphthalene, 85565-84-0; 3,4,4a,5,6,7-hexahydro-1(2*H*)-naphthalenone, 24037-79-4; 2-acetoxy-4a-methyl-3,4,4a,5,6,7-hexahydronaphthalene, 72938-40-0; 8-methoxy-4a-methyl-4,4a,5,6,7,8-hexahydro-2-(3*H*)-naphthalenone, 85565-85-1; 2-hydroxy-8-methoxy-4a-methyl-2,3,4,4a,5,6,7,8-octahydronaphthalene, 85565-86-2; 3,4,4a,5,6,7-hexahydro-4a-methyl-1(2*H*)-naphthalenone, 54339-54-7; cholesta-3,5-dien-3-ol acetate, 2309-32-2; 6-methoxycholest-4-en-3-one, 85646-42-0; 6-methoxycholest-4-en-3-ol, 85646-43-1; cholest-4-en-6-one, 13095-36-8.

Tatsuya Shono,* Shigenori Kashimura

Department of Synthetic Chemistry
Faculty of Engineering, Kyoto University, Yoshida
Sakyo, Kyoto 606, Japan

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[8] The anodic oxidation of dienol acetate 8 synthesized by a known method[9] was carried out as follows: Into a 50-mL undivided cell equipped with carbon rod electrodes and a dropping funnel was put a solution of methanol (30 mL) containing 10% acetic acid and TEATS (10 mmol). A solution of 8 in 5 mL of methanol was added dropwise to the cell over the period of the reaction. After 2 F/mol of electricity was passed, usual workup gave 9 in 81% yield: bp 65–70 °C (25 mmHg).

[9] Romo, J.; Rosenkranz, G.; Dyerassi, C.; Sondheimer, F. *J. Org. Chem.* **1954**, *19*, 1509.

[10] The anodic methoxylation of 8 in methanol containing TEATS gave only tarry materials.

[11] The transformation of 10 to 11 was carried out according to the following method. *p*-Toluenesulfonyl chloride (22 mmol) was added to the ice-cold solution of 10 (20 mmol) in CH_2Cl_2 (20 mL) containing triethylamine (22 mmol). After being stirred for 1 h, the reaction mixture was poured into a saturated aqueous solution (50 mL) of $NaHCO_3$ and extracted with ether. The crude tosylate was isolated by evaporation and subjected to reflux for 1 h in acetone containing 10% H_2O. The product 11 was extracted with ether and purified by distillation: bp 56–60 °C (50 mmHg).

[12] Isolated yield of 4-cholesten-6-one was 17% when the tosylate was refluxed in acetone containing 10% H_2O.

[13] We are grateful to Dr. I. Nishiguchi and Y. Sugihara for their collaboration.