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A NOVEL TRANSANNULAR REACTION OF 2,4,6-CYCLOOCTATRIEN-1-ONE

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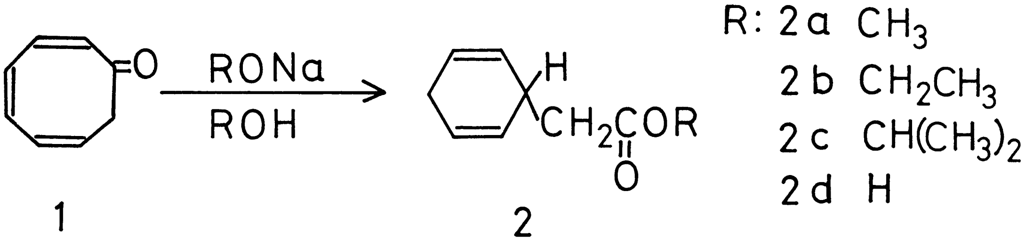
Esters of 2,5-cyclohexadienylacetic acid were formed in the reaction of 2,4,6-cyclooctatrien-1-one with alkoxides in alcohols. A ring contraction concerted with a transannular hydrogen transfer to C(4) position from an intermediate hemiacetal was proposed as a plausible pathway on the basis of deuterium distribution in the product.

There are several publications concerning the isomerizations of 2,4,6-cyclooctatrien-1-one (**1**)1), ring cleavage2) and ring contraction3,4), in the reaction with some nucleophilic reagents. In this communication, we wish to report a new transannular reaction of **1** with alkoxides in alcohols to the corresponding esters of 2,5-cyclohexadienylacetic acid (**2**), (Eq. 1).



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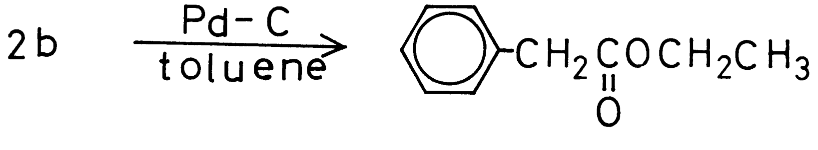


(2)

In a typical experiment 2.4 g. (20 mmol) of **1** was added to a solution of sodium ethoxide in ethanol (0.6 g., 25 mg-atom of sodium in 100 ml anhydrous ethanol) and the mixture was refluxed for 30 min under nitrogen. After the reaction mixture was worked up in usual manner, the principal product was separated and purified from an ethereal concentrate by preparative gaschromatography.

The structure of the product (**2b**) was established by the following spectral data and dehydrogenation on Pd-carbon in refluxing toluene to give ethyl phenylacetate, (Eq. 2).

IR: ν c=o 1735 cm^{-1}, ν c=c 1660 cm^{-1}, UV: λ max 250 nm (ε max 240),
Mass: M$^+$ 166 (calcd for $C_{10}H_{14}O_2$; 166), NMR: δ, ppm; 1.25 (t, 3H),
2.26 (d, 2H), 2.61 (m, 2H), 3.00 (m, 1H), 4.10 (q, 2H), 5.61 (m, 4H).

The results of the similar reaction of **1** with other combinations of sodium alkoxide and alcohol were listed in Table 1, where the progress of the reaction was followed by IR measurement of the reaction mixture for the remaining ketone (ν c=o 1660 cm^{-1}.). Large difference in absorbances at the band between the product and the ketone (ca. 1 : 50) allowed the use of the present technique. The reaction of **1** with aqueous sodium hydroxide also afforded the parent acid (**2d**), but proceeded at much slower rate. Table 1 shows that the rate of reaction appears to be related to the bulkiness of alcohols and the basicity of alkoxides.

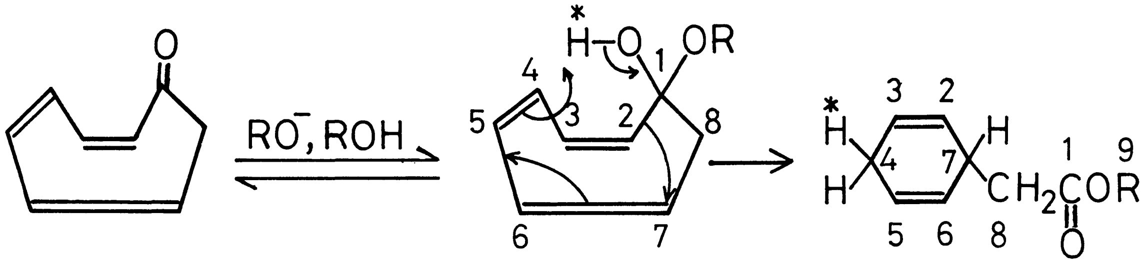
Table 1. Effect of Base and Alcoholic Solvent

Ketone mmol	Base concn.,	M	Solvent	Temp. °C	Time*1 min	Yield*2 %
16.7	$NaOCH_3$,	0.20	CH_3OH	reflux	50	17
20.0	$NaOC_2H_5$,	0.25	C_2H_5OH	reflux	30	24
16.7	$NaOC_3H_7$-i,	0.22	i-C_3H_7OH	68	90	22
14.0	$NaOC_4H_9$-t,	0.20	t-C_4H_9OH	reflux	450	-*3
8.0	$NaOC_6H_5$,	0.14	C_6H_5OH THF	63	360	-*3

*1 The time required for disappearance of the strong C=O absorption of the ketone except for *3.

*2 Yields for the products isolated by distillation.

*3 Most of the starting material was recovered unchanged.



(3)

1 3 2

The examination of Dreiding model of the possible hemiacetal intermediate (**3**) showed that C(4) carbon and the hemiacetal hydrogen are disposed at such a close distance as 0.96 Å. The proximity and a relatively strong acidity of the hydroxyl hydrogen in **3** imply that transannular proton transfer could occur easily and the reaction would proceed via the pathway shown above, (Eq. 3). To make sure the proposed scheme, deuterium insertion study was carried out in methanol-d_1 with sodium methoxide. The deuterium distribution in the product (A in Table 2) was determined by NMR spectra taking the ester methyl group as a reference. The incorporation of deuterium into all carbon atoms except for the reference position is attributable to the base-catalyzed exchange in both the starting ketone5) and product itself (B in Table 2).

Table 2. Deuterium Distribution in the Product

Position and No. of H(n)	7 (1)	2,3,5,6 (4)	4 (2)	8 (2)	9 (3)
(A) In the reaction					
H, found	0.55	2.68	0.85	0.30	3.0
D, calcd	0.45	1.32	1.15	1.70	0.0
D content, %	45.0	33.0	57.5	85.0	0
(B) Exchange in the product*1					
H, found	0.91	3.69	1.99	0.68	3.0
D, calcd	0.09	0.31	0.01	1.32	0.0
D content, %	9.0	8.0	0.5	66.0	0
(C) Corrected vales for the exchange in the product (A-B)					
D content, %	36.0	25.0	57.0	19.0	0

*1 A mixture of 2a (16.7 mmol) and $NaOCH_3$ (10.0 mmol) in 25 ml MeOD was refluxed for 50 min under nitrogen.

Roberts et al.[5)] have briefly described that deuterium exchange was observed at positions of C(2), C(4), C(6), and C(8) in the treatment of **1** with sodium deuteroxide in refluxing deuterium oxide-dioxane mixture, but not referred to the extent of the exchange in each position. NMR measurement of the ketone recovered in the middle of the present reaction did not afford successful result for estimating the relative exchange ratio, because of the complex nature of the coupling among eight protons (or deuterium).

Although there remains an ambiguity in the esimation for the exchange in the starting ketone, deuterium content over 50 % occurred at C(4) position could be assumed to be in good accord with the proposed scheme.

Further studies about the behavior of **1** toward a variety of nucleophiles ar in progress.

References

1) A.C.Cope and B.D.Tiffany, J.Amer. Chem. Soc., 73, 4158 (1950).
2) M.Kröner, Chem. Ber., 100, 3172 (1967).
3) M.Kröner, Chem. Ber., 100, 3162 (1967).
4) A.H.Khuthier and J.C.Robertson, J. Org. Chem., 35, 3760 (1970).
5) C.Ganter, S.M.Pokras, and J.D.Roberts, J. Amer. Chem. Soc., 88, 4235 (1966).

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