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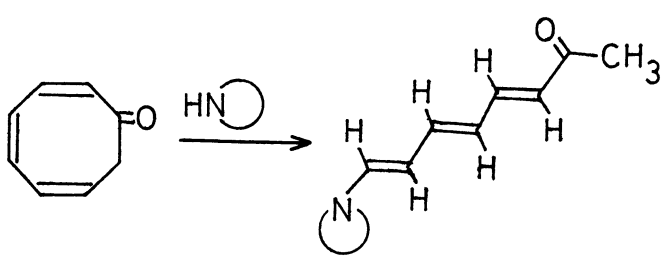
A NOVEL RING CLEAVAGE OF 2,4,6-CYCLOOCTATRIEN-1-ONE

Masashi OGAWA and Tsutomu MATSUDA

Department of Organic Synthesis, Faculty of Engineering,
Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812

Piperidine reacts with 2,4,6-cyclooctatrien-1-one(1) to give 8-piperidino-3,5,7-octatrien-2-one and acetophenone. When pyrrolidine and morpholine were used the corresponding 8-amino ketones were produced. Deuterium insertion study of 1 with N-deuteriopiperidine suggests that in DMSO the ring cleavage proceeds by initial addition of piperidine at the C(7) and C(2) carbons (2,7-addition) followed by subsequent fission of C(7)-C(8) bond of 1.

Both ring contraction[1,2] and ring cleavage[3] of 2,4,6-cyclooctatrien-1-one(1) have been known in the reactions with some nucleophilic reagents. Previously we reported a transannular ring contraction of 1 with alkoxide in alcoholic media to give 2,5-cyclohexadienylacetic acid esters.[4] In this communication, we present another type of the ring transformation of 1 to 8-amino-3,5,7-octatrien-2-one(2) in the reaction with secondary amines.



1 2

		m.p. °C
2a	HN⟨⟩	98.5-99.5
2b	HN⟨⟩	84.0-85.0
2c	HN⟨O⟩	90.5-92.5

A solution of 1 (4 mmol) in 4 ml of piperidine was heated at 80-85°C for 100 min under nitrogen atmosphere. Most of piperidine was removed from the reaction mixture under vacuum at room temperature. Ether (40 ml) was added to the residue and the mixture was washed with water and dried. A precipitate formed on concentration of the ethereal solution was recrystallized from ether to give reddish-orange crystals, mp 98.5-99.5°C, 190 mg (18%). Distillation of the mother liquid afforded acetophenone, 260 mg (55%). When the reaction was carried out in a mixture of piperidine (5 mmol) and DMSO (15 ml) at 50-55°C, only 2a was obtained in a 90% yield. Tetrahydrofuran as a solvent was inadequate since the reaction became sluggish even under refluxing for 6 hr.

The structure of 2a was established on the basis of the following spectral data as well as elementary analyses. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82%. Found: C, 75.85; H, 9.32; N, 6.83%.

UV(MeOH): λ_{max}, nm(ε); 260(3900), 283sh(3200), 298sh(2500), 438(47000). MS: 205(M^+), 162(M^+-COCH_3), 121($M^+-NC_5H_{10}$), 102.5(M^{2+}), 105, 77, 43. NMR(CCl_4, TMS): δ 1.60(m, 6H), 2.11(s, 3H), 3.11(m, 4H), 5.17(dd, 1H, J=13, 11 Hz), 5.81 (d, 1H, J=15 Hz), 5.86(dd, 1H, J=14, 11 Hz), 6.35(d, 1H, J=13 Hz), 6.52(dd, 1H, J=14, 11 Hz), 7.06(dd, 1H, J=15, 11 Hz). TLC: one spot.
Hydrogenation of 2a in ethanol over Pd-$BaCO_3$ resulted in the absorption of three molar equivalents of hydrogen to give 8-piperidinooctan-2-one, which was confirmed by comparison with an authentic specimen prepared by the reaction of 8-piperidinoheptanenitrile with methylmagnesium iodide.

Pyrrolidine and morpholine afforded similar crystalline products, 2b and 2c, in 25 and 48% yields together with acetophenone, respectively, and nearly quantitative yields of the products were obtained in the reactions in DMSO. An oily product obtained with diethylamine could not be purified because of its facile conversion to tarry material. The crystalline products, 2a, 2b, and 2c, showed one spot in TLC analyses and did not change in the treatment with iodine in benzene. Thus, they are considered to be all-trans isomers on the basis of the coupling constants as mentioned above.

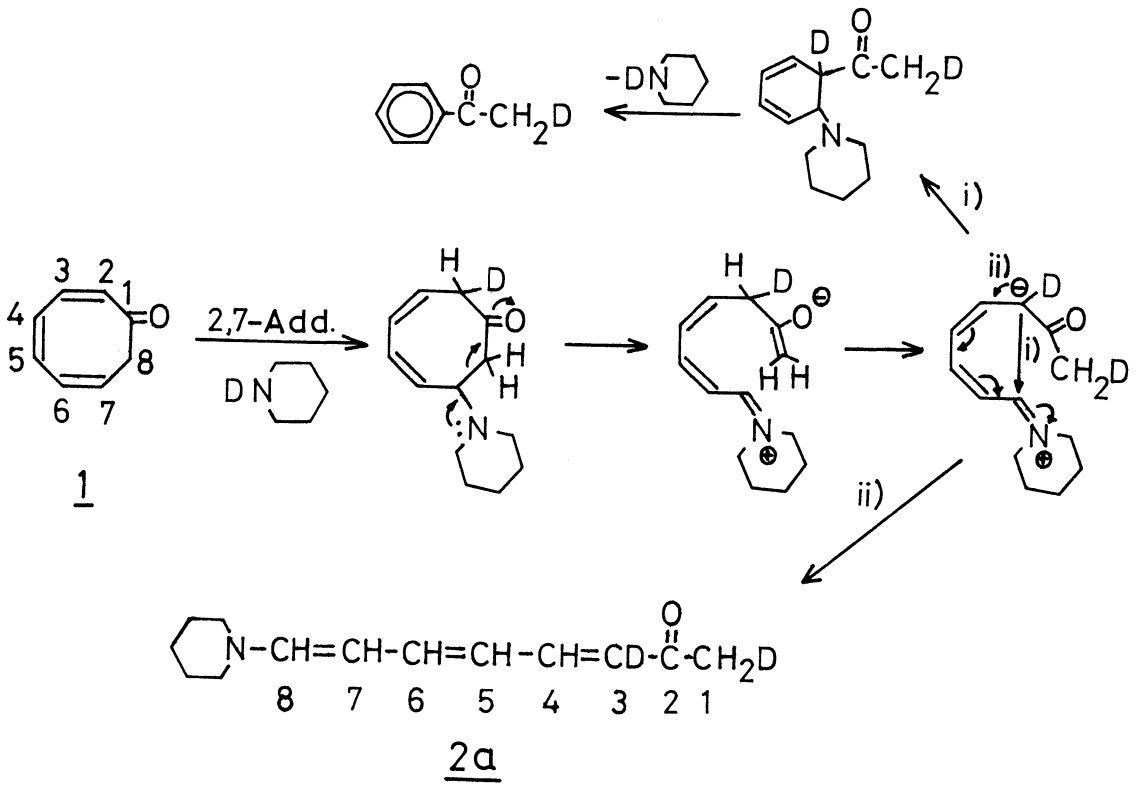
Deuterium insertion to 2a in the reaction of 1 with N-deuteriopiperidine was examined in order to determine the mode of addition of the amine and the position of the bond cleaved in 1. It is to be noted that hydrogen atoms at C(8) in 1 have been found to be very resistant to deuterium exchange even in the treatment

of 1 with sodium deuteroxide in deuterium oxide - dioxane mixture,[5] but the exchange of the hydrogen atoms in 2a is expected to occur especially at those in methyl group under the present reaction conditions. The results obtained under two conditions (neat and in DMSO) are listed in Table 1, along with the deuterium exchange in 2a under the same conditions (shown in parentheses). Deuterium insertion in acetophenone was found to occur at the methyl group (37%), but was observed to a limited extent at the ring hydrogens (0% at ortho, 7% at meta and para).

Table 1. Deuterium Contents in the Product 2a

Position and No. of H(n)	1(3)	3(1)	4(1)	5(1)	6,8(2)	7(1)
in DMSO,%	27.7 (8.0)	41.0 (0)	3.0 (-)*	3.0 (0)	5.5 (10.0)	12.0 (0)
neat,%	50.7 (52.3)	48.0 (14.0)	9.0 (8.0)	4.0 (0)	3.6 (0)	3.0 (11.0)

*A trace of $CHCl_3$ (δ 7.23) in $CDCl_3$ disturbed an exact estimation of the D content at the position (dd centered at δ 7.06).



On the basis of the results in Table 1, and the structure of 2a, the reaction of 1 in DMSO is considered to proceed principally by a pathway involving initial attack of piperidine to 1 in a 2,7-manner, subsequent cleavage of C(7) - C(8) bond, and internal electron transfer (route ii) to lead to 2a, as shown in the scheme depicted above. However, in the reaction in excess piperidine (neat) one can not differenciate between the 2,7-addition and 2,3-addition accompanied by C(2) - C(3) bond fission, because of nearly equal degree of deuterium insertion (or exchange) at C(1) and C(3) of 2a. Acetophenone is presumed to be produced after the cleavage of the ring and via recyclization to form a cyclohexadienyl intermediate (route i). A facile double bond forming elimination of piperidine (or related secondary amine) from β-piperidinoketone[6] is a frequently observed process in enamine chemistry.

It would be worthy to mention that the cleavage of 1 takes place by the action of such a weak nucleophile as secondary amine under rather mild condition, and the mode of the ring cleavage is sharply contrast with the proposed route[3] consisting of 1,2-addition and C(1) - C(8) bond fission in the reactions of 1 with lithium aluminum hydride,[3] Grignard reagents,[3,7] and triethylaluminum.[7]

References

1) M. Kröner, Chem. Ber., 100, 3162(1967).
2) A. H. Khuthier and J. C. Robertson, J. Org. Chem., 35, 3760(1970).
3) M. Kröner, Chem. Ber., 100, 3172(1967).
4) M. Ogawa, M. Takagi, and T. Matsuda, Chem. Lett., 527(1972).
5) C. Ganter, S. M. Pokras, and J. D. Roberts, J. Amer. Chem. Soc., 88, 4235 (1966).
6) G. Stock, A. Brizzolara, H. Landesman, J. Smuszkovicz, and R. Terrell, J. Amer. Chem. Soc., 85, 207(1963).
7) M. Ogawa, M. Takagi, and T. Matsuda, Tetrahedron, 29, 3813(1973).

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