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NOVEL NAZAROV-TYPE CYCLIZATION OF TETRAHYDRO-4-OXOPYRAN-3-CARBOXYLIC ESTERS BY THE USE OF Me_3SiCl-NaI REAGENT

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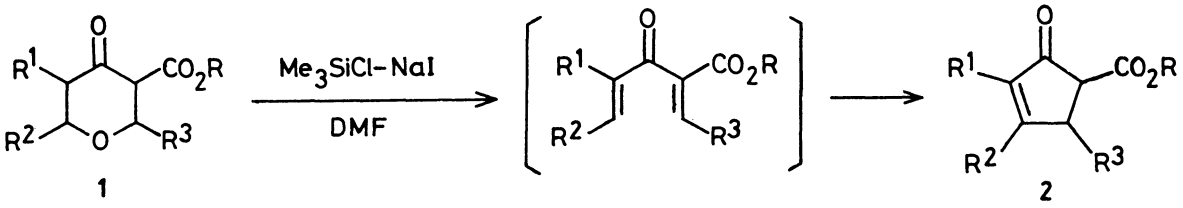
Treatment of 2,5,6-tri-substituted tetrahydro-4-oxopyran-3-carboxylic esters with Me_3SiCl-NaI reagent in DMF at 120 °C gave cyclopentenone derivatives *via* the Nazarov-type cyclization subsequent to possible dehydration.

The Nazarov cyclization is well known as one of the most useful methods for the preparation of cyclopentenone derivatives, which have played an important role in natural product synthesis.[1] However, it often sustains limited utility by the reasons of the difficulty in preparing starting divinyl ketones and their synthetic equivalents, especially those having additional functionality such as alkoxycarbonyl moiety. The appropriate reaction is usually catalyzed by mineral acids or Lewis acids. Consequently, the variation of the starting materials is further restricted. The proper functionalization of divinyl ketones and the use of mild reaction condition would, therefore, help to extend the applicability of the Nazarov cyclization to more complex system.

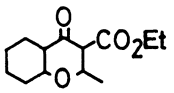
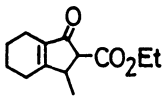
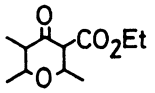
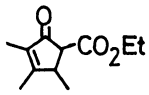
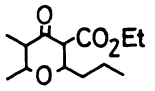
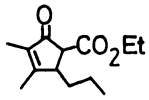
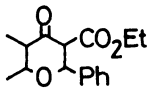
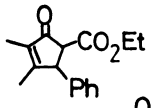
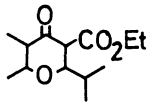
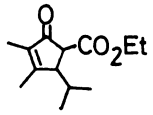
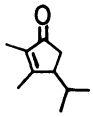
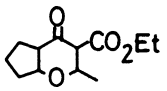
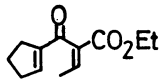
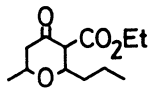
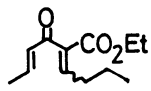
We found that 2,5,6-tri-substituted tetrahydro-4-oxopyran-3-carboxylic esters (**1**) were successfully converted into the corresponding 3,4,5-tri-substituted 2-oxo-3-cyclopentene-1-carboxylic esters (**2**) by the action of Me_3SiCl-NaI reagent in DMF, in good to moderate yields (Table 1). The starting materials are readily available [2] and the reaction can be carried out in neutral condition.



1 2

The typical procedure is as follows: To a mixture of ethyl perhydro-2-methyl-4-oxo-1-benzopyran-3-carboxylate (**1a**) [2c] (60 mg, 0.25 mmol) and NaI (375 mg, 2.5 mmol) in DMF (1 mL), was added Me_3SiCl (0.32 mL, 2.5 mmol) with stirring at 120 °C. After being stirred for 5 h, the mixture was diluted with water, washed with aqueous $Na_2S_2O_3$ to remove liberated iodine. The organic layer was treated in a usual manner to give 41 mg of 2-(ethoxycarbonyl)-3-methyl-4,5,6,7-tetrahydroindan-1-one (**2a**) [3] in 77% yield, after purification by TLC (hexane-acetone 3:1).

Table 1. Synthesis of 3,4,5-tri-substituted 2-oxo-3-cyclopentene-1-carboxylic esters

Tetrahydro-4-oxopyran[a]		Reaction time /h	Product(s)[a]		Yield/%[b]
	**1a**[c]	5		**2a**[d]	77
	**1b**	6		**2b**	59
	**1c**	7		**2c**	68
	**1d**	10		**2d**	64
	**1e**	10	 **2e** 	**3**[e]	76[f]
	**1f**	3		**2f**[d]	55
	**1g**	2		**2g**[g]	53

a) The structures of these compounds were identified by IR, ^{1}H NMR, and ^{13}C NMR (**2a-g** and **3**) spectra. New compounds **1b-g**, **2b-e**, and **2g** showed satisfactory analytical data. b) Isolated yields by preparative TLC. c) See referance 2c. d) Identified by comparison of the spectral data. See reference 3. e) O. P. Vig and M. S. Bhatia, Riechst. Aromen. Körperpflegem., 25, 228 (1975); Chem. Abstr., 84, 16814p (1976). f) A mixture of **2e** (32% yield) and **3** (44% yield). g) Geometry of butylidene group is not ascertained.

As summarized in Table 1, the present reaction can be applied to various tetrahydro-4-oxopyran-3-carboxylic esters. Compounds **1f** and **1g** afforded divinyl ketones **2f** and **2g** as primary products but failed to be cyclized to cyclopentenone derivatives even in a prolonged reaction.

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References

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2) a) B. Chantegrel, A.-I. Nadi, and S. Gelin, Synthesis, 1983, 948; b) C. Eskenazi and P. Maitte, Bull. Soc. Chim. Fr., 1976, 995; c) D. A. A. Kidd, P. A. Robins, and J. Walker, J. Chem. Soc., 1953, 3244.
3) Me_3SiI-induced Nazarov cyclization of the corresponding divinyl ketone precursor has been reported (yield 48%): J. P. Marino and R. J. Linderman, J. Org. Chem., 46, 3696 (1981).

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