Reaction of Cyclopent-2-en-1-one Ethylene Acetal with Dienophiles *via* its Ring-opened Enol Ether Form. Single Step Synthesis of Norbornan-2-one Ethylene Acetals

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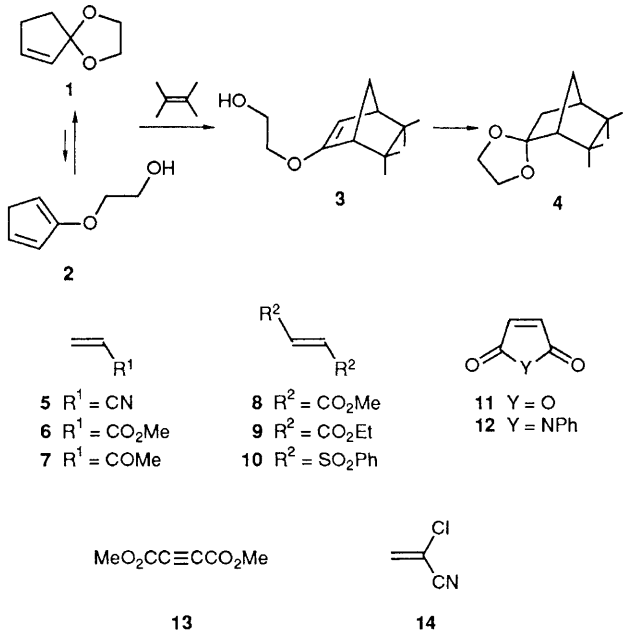
Cyclopent-2-en-1-one ethylene acetal undergoes Diels–Alder reaction with a variety of dienophiles *via* its ring-opened enol ether, 2-(2-hydroxyethoxy)cyclopenta-1,3-diene, under neutral conditions to give norbornan-2-one ethylene acetals.

Oxygenated 1,3-dienes are of increasing importance as building blocks for the synthesis of highly functionalized ring systems.[1] Despite the known propensity of cyclic acetals to isomerize to ring-opened enol ether forms in a reversible manner, the equilibration has so far been little exploited except for bromination,[2] probably because in general the equilibrium does not favour the ring-opened form. In this communication we report that cyclopent-2-en-1-one ethylene acetal **1** undergoes Diels–Alder reactions with a variety of dienophiles *via* the opened form **2** under mild, neutral conditions directly to give norbornan-2-one ethylene acetals **4**.

The cycloaddition of dienophiles to **1** is simple and heating of them in acetonitrile at *ca.* 70 °C followed by usual work-up produced **4** in good to excellent yield. The results are summarized in Table 1. Stereochemical assignment of the adducts was primarily based on their 500 MHz ^{1}H NMR spectra.† Reaction times may be shortened by use of higher concentrations and/or higher temperatures.

The formation of norbornan-2-one ethylene acetals from **1** and dienophiles seems to be accounted for only in terms of the Diels–Alder addition of dienophiles to **2** which is in equilibrium with **1** and recyclization of resultant hydroxyethyl enol ethers **3**.‡ The observed high regio- and endo-selectivities are also in accord with the intermediacy of **2**.[3] No regioisomers of



† The stereoisomeric pairs produced in the reactions of **1** with **8**–**10** and **14** were not separated from each other and were analysed as a mixture. The minor product obtained in the reaction of **12** was not isolated in a pure form, but exhibited a GLC–mass spectrum almost superimposable on that of **23a** and was tentatively assigned as **23b**. Structural assignment to **18b** is also tentative. The other products were isolated and gave satisfactory elemental analyses and spectroscopic data.

‡ Attempts to detect **2** and **3** by ^{1}H NMR spectroscopy have so far been unsuccessful. The concentration of **2** at equilibrium with **1** and that of the transient **3** would be too low for them to be observed by ^{1}H NMR spectroscopy.

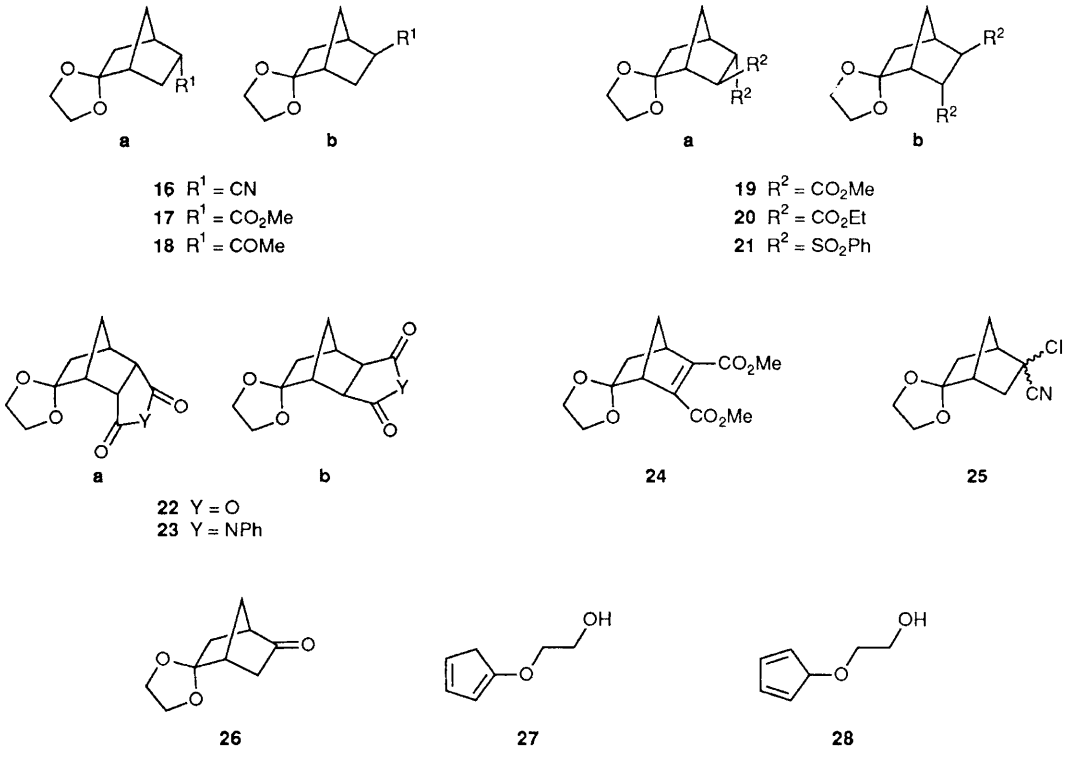


Table 1 Reactions of **1** with dienophiles in acetonitrile

[**1**]/ mol l^{-1}	Dienophile (c/mol l^{-1})	T/°C	Time	Products (% Yield;[a] **a** : **b**[b])
0.33	**5** (1.00)[c]	70	3 w	**16** (81;[d] 63 : 37)
0.33	**6** (1.00)[c]	70	3 w	**17** (73;[e] 95 : 5)
0.50	**7** (1.50)[c]	70	6 w	**18** (100; 91 : 9)
0.66	**8** (0.66)	70	9 d	**19** (93; 58 : 42)
0.66	**9** (0.66)	70	17 d	**20** (93; 60 : 40)
0.14	**10** (0.11)	80	3 h	**21** (77;[f] 88 : 12)
0.33	**11** (0.37)	50	2 h	**22** (62;[g] 93 : 7)
0.40	**12** (0.37)	70	9 d	**23** (84;[f] 96 : 4)
0.33	**13** (2.20)	70	2 d	**24** (94; —)
0.40	**14** (1.20)[h]	70	20 h	**25** (80;[i])

[a] Isolated yield based on amount of **1** used. Conversion of **1** was almost complete unless otherwise indicated. [b] Determined by 500 MHz ^{1}H NMR and/or GLC. [c] Hydroquinone was added as an inhibitor. [d] Conversion of **1** was 65%. [e] Conversion of **1** was 60%. [f] Based on amount of dienophile used. [g] GLC yield. [h] 2,6-Dimethylpyridine (0.06 mol l^{-1}) was added. [i] A mixture of two stereoisomers in a ratio of 83 : 17.

16–18 and **25** were detected. It is noteworthy that the reaction was not complicated by the addition of dienophiles to **27** and **28** which could be generated by 1,4-elimination in **1** and 1,5-hydrogen migration in **2** prior to its reaction with dienophiles,[4] respectively. Acetonitrile was the solvent of choice; other solvents such as chloroform, 1,4-dioxane or toluene resulted in lower yields of adducts or in slower reactions. The addition of various Brønsted or Lewis acids to the reaction mixture in attempts to facilitate the interconversion of **1** and **2** and to activate the dienophiles proved to be rather detrimental to the formation of adducts, probably because the acids induced the decomposition of **1** rather than its isomerization to **2**. The observation that 2,6-dimethylpyridine as an additive greatly improved the yield of **25** from 10% in the absence of the base to 80% also suggests that acidic impurities liberated from **14** and/or **25** would efficiently destroy **1**. Somewhat less satisfactory yields of adducts in the reaction of **1** with **11** might result from the undesirable side reaction of the latter with the hydroxy group in **2**.

The adduct **25** was readily hydrolysed in alkaline solution[5] to give **26** in 59% yield. The selective formation of the singly protected **26** in two steps from **1** in 47% overall yield demonstrates the potential usefulness of the present method as a synthetic reaction.[6]

M. O. thanks the Ministry of Education, Science and Culture, Japan, for a Grant-in-Aid for the Encouragement of Young Scientists.

Received, 10th August 1990; Com. 0/03683H

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