Hetero-Diels–Alder Reactions of 2-Methylene-1,3-dicarbonyl Compounds with Alkyl Vinyl Ethers

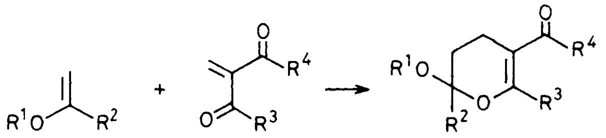
Masashige Yamauchi,* Sadamu Katayama, Osamu Baba, and Toshio Watanabe

Faculty of Pharmaceutical Sciences, Josai University Keyakidai, Sakado, Saitama 350-02, Japan

2-Methylene-1,3-dicarbonyl compounds reacted with alkyl vinyl ethers in benzene to give hetero-Diels–Alder reaction products, 3,4-dihydro-2*H*-pyrans, regioselectively and/or chemoselectively.

Hetero-Diels–Alder reactions of α,β-unsaturated carbonyl compounds as heterodienes are well known and require severe experimental conditions.[1] The introduction of electron-withdrawing groups at the α-position of the α,β-unsaturated carbonyl compounds would be expected to lower the LUMO energy level, and therefore increase the reactivity of such a heterodiene[2] in the inverse Diels–Alder reaction.[3] Some examples of this have been reported.[4–8] Recently we reported the synthesis of the 2-methylene-1,3-dicarbonyl compounds (**1**).[9] We report herein the regioselective and/or chemoselective Diels–Alder reaction of (**1**) with alkyl vinyl ethers.

Compounds (**1**) were mixed with alkyl vinyl ethers in benzene at ambient temperature for 3 h [equation (1)]. Evaporation gave viscous oils, from which the 3,4-dihydro-2*H*-pyrans (**2**) were obtained as a single cycloaddition product in almost quantitative yields after medium pressure chromatography or preparative centrifugal t.l.c. (Table 1). In the ^{1}H n.m.r. spectra, the small coupling constants ($J < 3$ Hz) between the anomeric protons in (**2**) (R^2 = H) and the pair of double quartets (the AB part of an ABX_3 system) of the methylene proton in the ethoxy-group in (**2**) (R^1 = Et) with restricted rotation around the C–O bond indicate that the R^2 and OR^1 groups occupy quasi-equatorial and quasi-axial positions as depicted in (**3**).



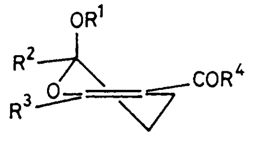
(**1**) (**2**) (1)

The absorption due to the conjugated ester group at *ca.* 1700 cm^{-1} in the i.r. spectra of (**2**) (R^3 = Ph; R^4 = OEt) suggests that chemoselective cycloaddition was achieved at the ketone carbonyl group. Further, the $LiAlH_4$ reduction of (**2h**) gave (**4**) in which the singlet n.m.r. resonance due to the methylene proton of the hydroxymethyl group appeared at δ 4.1. In some of the cycloadditions the carbonyl group in the heterodiene could arise from either a benzoyl or an acetyl group. To clarify this, the pyran (**2f**) was reduced ($LiAlH_4$) to (**5**) whose benzylic proton appeared as a singlet at δ 5.4 in the ^{1}H n.m.r. spectrum. This and the triplet (*J ca.* 2 Hz) due to the C-6 methyl groups in the ^{1}H n.m.r. spectrum of (**2a, f**)[10] showed that the carbonyl of the heterodiene was derived from the acetyl group.

Table 1. Yields of 3,4-dihydro-2*H*-pyrans (2).

Compound	R^1	R^2	R^3	R^4	Yield (%)[a] of (**2**)
a	Me	H	Me	Ph	96
b	Me	H	Ph	Ph	98
c	Me	H	Ph	OEt	98
d	Me	Me	Ph	Ph	97
e	Me	Me	Ph	OEt	98
f	Et	H	Me	Ph	97
g	Et	H	Ph	Ph	98
h	Et	H	Ph	OEt	99

[a] Yields refer to pure isolated compounds.



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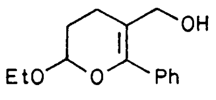

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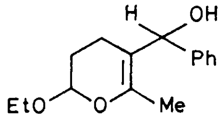

(5)

This regioselective and/or chemoselective preparation of dihydro-2*H*-pyrans under mild conditions could be used in the synthesis of carbohydrates and natural products.

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