Synthesis of 1,3-Dienes bearing both Electron-Donor and Acceptor Substituents

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Key Words 1,4-benzodioxin, allylic benzodioxinic alcohols, Claisen rearrangements, 2-alkylidene-1,4-benzodioxans, 1,3-dienes

Abstract Allylic benzodioxinic alcohols were prepared from 1,4-benzodioxin and then submitted to the orthoester Claisen rearrangement and Eschenmoser procedure leading to 3-substituted-2-alkylidene-1,4-benzodioxans Di-and trisubstituted 1,3-dienes bearing both electron-donor and acceptor substituents were obtained in good yields from these compounds

As part of our continuing studies on the chemistry of 1,4-benzodioxin and its synthetic applications we recently began to explore the reactivity of allylic benzodioxinic alcohols¹. Herein we report our new results in the sigmatropic rearrangements of these compounds.

It has already been shown that α -hydrogens of 1,4-benzodioxin can be directly lithiated via hydrogen metal interchange with alkyllithium reagents or lithium diisopropylamide and the resulting 2-lithiobenzodioxin species reacted on several electrophiles². Similarly, we prepared benzodioxinic alcohols 1 in fair to good yields (65-84 %) via the 2-lithiobenzodioxin and its addition to aldehydes and ketones.

The 2-hydroxymethyl-1,4-benzodioxin 1a (R = R' = H) was obtained in 80% yield by reduction of the 2-carbethoxy-1,4-benzodioxin⁴ with LAH in refluxing ether.

The allylic alcohols 1 submitted to the acid catalysed orthoester Claisen rearrangement⁵ (Scheme 1) or the related Eschenmoser procedure⁶ (Scheme 2) lead respectively to derivatives 2 and 3.





The orthoester Claisen rearrangement was realized at 150 °C with an excess of trimethylorthoacetate in the presence of a catalytic amount of propionic acid.

The results are summarized in Table 1^3 .

Substrate	R	R'	Time (h)	Yield (%) ^a
1a	н	Н	3	78
1b	CH ₃	Н	3	55
1c	CH ₃ (CH ₂) ₂	Н	6	60
1d	CH ₃ (CH ₂) ₆	Н	4	55
le	C ₆ H ₅ CH ₂	Н	4	16
lf	CH ₃	CH ₃	240	10
1g	-(CH ₂) ₅ -		140	4

Table 1

(a) Isolated yields based on the alcohol, after chromatography on silica gel.

The reaction proceeds in acceptable yields with primary and secondary alcohols (except 1e), but the yields dramatically fail in the case of tertiary alcohols.

Subsequently, following the Eschenmoser procedure, the allylic alcohols 1 were heated in refluxing o-xylene, in the presence of N_N -dimethylacetamide dimethylacetal (10 equivalents).

Scheme 2



The results are summarized in Table 2^3 .

Substrate	R	R'	Time (h)	Yield (%) ^a
1a	Н	Н	1	80
1b	CH ₃	Н	1	94
1c	CH ₃ (CH ₂) ₂	Н	1	73
1d	CH ₃ (CH ₂) ₆	Н	1.5	60
1e	С ₆ н ₅ Сн ₂	Н	1.5	84
lf	CH ₃	CH ₃	72	64
1g	-(CH ₂) ₅ -		96	53

Table 2

(a) Isolated yields after chromatography on silica gel.

Obviously, the Eschenmoser procedure provides better results than the orthoester Claisen rearrangement (higher yields, shorter reaction times) even in the case of tertiary alcohols.

The stereochemistry of the double bond for the derivatives **2b-e** and **3b-e** was determined with the assistance of ${}^{3}J_{CH}$ values between the vinylic protons and the sp₃ carbon of the heterocycle.

It has been firmly established in the literature⁷ that this coupling constant is larger in the E than in the Z form. We assumed that ${}^{3}J_{CH}$ values of more than 7 Hz or less than 5 Hz were sufficient proof of E or Z isomers, respectively. The coupling constant ${}^{3}J_{CH} = 4 \pm 0.5$ Hz was determined for the product 3b. We can therefore assign a Z-configuration, to the double bond.

We thought that derivatives 2 and 3 could constitute potential versatile intermediates both in heterocyclic and in aliphatic chemistry. Thus, from compounds 3, were prepared the di-and trisubstituted 1,3 dienes bearing both electron-donor and acceptor substituents, using the capacity of a phenoxyde ion as a leaving group in an elimination reaction under basic conditions.

After treatment of compounds 3 at 0 °C with t-BuOK then methylation with CH₃I, dienes 4 were isolated in good yields (Scheme 3).

Scheme 3



The results are summarized in the Table 3³

Compound	R	R'	Yield (%) ^a	mp (°C)
4 a	Н	Н	97	70
4b	CH ₃	Н	94	83
4c	CH ₃ (CH ₂) ₂	Н	64	011
4d	CH ₃ (CH ₂) ₆	Н	86	oil
4 e	C ₆ H ₅ CH ₂	Н	no reaction	-
4f	CH ₃	CH ₃	91	86
4g	-(CH ₂) ₅ -		97	oil

Table 3

(a) Isolated yields after chromatography on silica gel.

The stereochemistry of the double bond C_4 - C_5 for the dienes **4b-e** was confirmed to be Z according to Cabiddu *et al*⁷

In conclusion, we have shown that 3-substituted-2-alkylidene-1,4-benzodioxans are obtained by sigmatropic rearrangements of allylic benzodioxinic alcohols and easily converted in 1,3-dienes bearing both electron-donor and acceptor substituents. The use of these dienes in cycloaddition reactions is in progress in our laboratory.

Acknowledgements' the authors thank Dr P ROLLIN for helpful discussions.

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(Received in France 11 June 1991)