



EFFECT OF TETHER POSITION ON THE INTRAMOLECULAR REACTION BETWEEN RHODIUM STABILIZED CARBENOIDS AND FURANS

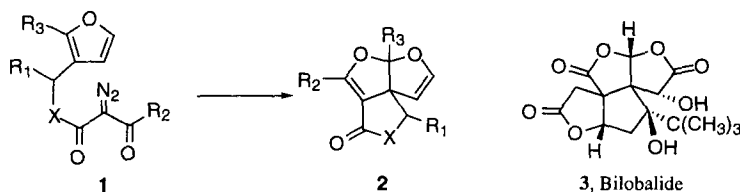
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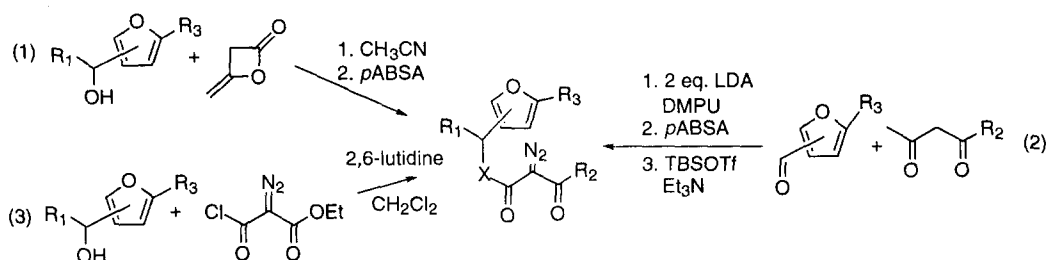
Abstract: The product distribution from the intramolecular reaction between carbenoids and furans is strongly influenced by the position of the linking tether on the furan. © 1997 Elsevier Science Ltd.

The reaction between furans and carbenoids derived from diazoacetates or diazoketones is an established process for the formation of highly functionalized dienes.¹ For some time we have been interested in the reaction of more elaborate carbenoids with furans, in which the additional functionality on the carbenoid enables alternate reaction pathways to occur.² Most notable so far has been the reaction between vinylcarbenoids and furans. This results in a general method for the synthesis of highly functionalized oxabicyclo[3.2.1]octanes by means of a tandem cyclopropanation Cope rearrangement.² In this paper we report that a keto functionality is also capable of interfering with the typical reaction pathways that occur in the intramolecular reactions between carbenoids and furans.³ This leads to the formation of the tricyclic products **2**, which are potentially useful as advanced intermediates for the synthesis of bilobalide (**3**) and the more complex ginkgolides.⁴⁻⁶



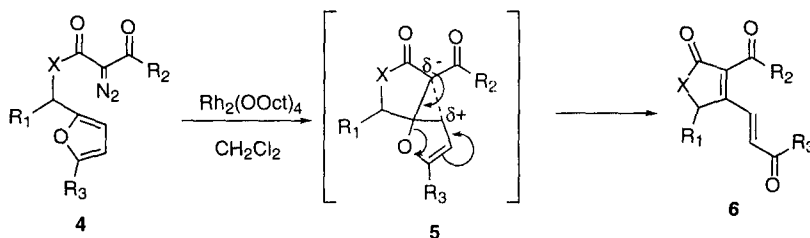
In order to evaluate the role that a second carbonyl group may have on the chemistry of the furan/carbenoid system, a series of 2- and 3-substituted furan derivatives were prepared as illustrated in Scheme 1. Simple diazoacetoacetate derivatives were readily prepared from the furan alcohols by reaction with diketene and *p*-ABSA (eq 1).⁷ More elaborate diazoacetoacetone and diazoacetoacetate derivatives were prepared by reaction of the furaldehyde with the dianion of the appropriate dicarbonyl, followed by diazo transfer with *p*-ABSA and alcohol protection with TBSOTf (eq 2).² Diazomalonates were prepared by reaction of the furan alcohols with ethyl 2-diazomalonyl chloride (eq 3).⁸

Scheme 1



The outcome of the intramolecular reactions between the carbenoids and the furans is strongly influenced by the position of the linker on the furan. In the case of rhodium(II) octanoate catalyzed decomposition of the 2-substituted furans **4**, the products were the highly functionalized dienes **6**. Reasonable intermediates for the formation of these products would be the zwitterionic structures **5**.^{1f} Even though these transformations represent standard furan/carbenoid chemistry, the products are illustrative of the structural complexity that can be introduced into the resulting dienes. The cyclopentenones **6b** and **6e** are particularly interesting systems, as they contain much of the functionality that would be required for the synthesis of prostaglandin derivatives.⁸

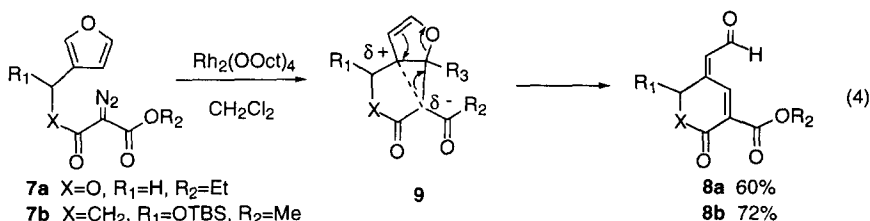
Scheme 2



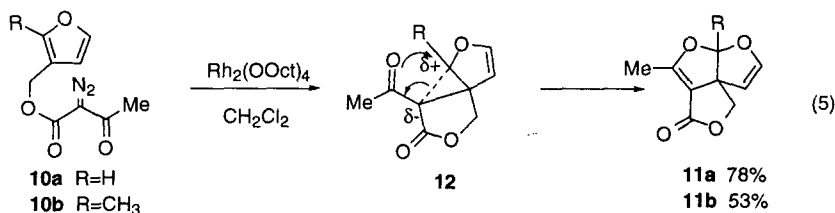
	X	R ₁	R ₂	R ₃	Yield ^a
a	O	H	OEt	H	75
b	CH ₂	OTBS	OMe	H	75
c	O	H	Me	H	64
d	O	H	Me	Me	52
e	CH ₂	OTBS	Me	H	63

^a Determined by ¹H NMR using an internal standard (1,4-dimethoxybenzene)

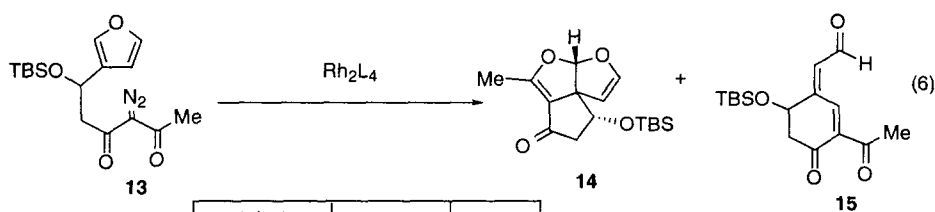
In contrast to the results for the 2-substituted furans, the chemistry of the 3-substituted furans is very dependent on the structure of the carbenoid (eq 4). In the case of rhodium(II) octanoate catalyzed decomposition of the ester derivatives **7a** and **7b**, the only products that were observed in the crude reaction mixtures were the dienals **8a** and **8b**. These are the expected products from the zwitterionic structures **9**, which may be formed directly in the interaction of the carbenoids with the furan or by ring-opening of unstable furanocyclopropanes.



When a keto functionality instead of an ester is present at the terminus of the carbenoid, an alternative reaction pathway becomes available (eq 5). Decomposition of the diazoacetates **10a** and **10b** resulted in the direct construction of the tricyclic systems **11a** and **11b**.¹⁰ These products are presumably formed from the zwitterionic structures **12**. The formation of [3 + 2] annulation products have been reported in intermolecular reactions of diazodimedone with furans,³ but the examples here represent the first intramolecular [3 + 2] annulations between ketocarbenoids and furans.



In the case of **13**, containing a carbocyclic tether, both the [3 + 2] annulation product **14**¹⁰ and the diene **15** are formed (eq 6). The combined yield of **14** and **15** is high (92% yield for Rh₂(OOct)₄ in CH₂Cl₂) while the ratio of **14** and **15** is dependent on the solvent and the size of the catalyst. The use of hexanes instead of dichloromethane as solvent increases the amount of **14** formed. The catalyst has a major effect on product distribution, but this effect is due to steric rather than electronic factors. Small catalysts such as Rh₂(OAc)₄ and Rh₂(TFA)₄ result in the lowest ratios of **15/14** while the largest catalyst, Rh₂(OPiv)₄, gives the highest ratio of **15/14**. A particularly attractive feature of this chemistry is that the [3 + 2] annulation product **14** is formed with full control of relative stereochemistry.



catalyst	solvent	14/15
Rh ₂ (OOct) ₄	Hex	1:2
Rh ₂ (OOct) ₄	CH ₂ Cl ₂	1:4
Rh ₂ (TFA) ₄	Hex	1:2
Rh ₂ (OAc) ₄	CH ₂ Cl ₂	1:3
Rh ₂ (OPiv) ₄	CH ₂ Cl ₂	1:9

In conclusion, the effect of the second carbonyl group on the chemistry of the furan/carbenoid system depends on the tether position and the nucleophilicity of the carbonyl. The 2-substituted furans result in the formation of highly functionalized dienes, while the 3-substituted furans result in the formation of either [3 + 2] annulation products or dienes.

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10. ¹H NMR (300 MHz, CDCl₃) data: **11a**: δ 6.55 (s, 1 H), 6.52 (d, 1 H, *J* = 2.7 Hz), 5.45 (d, 1 H, *J* = 2.7 Hz), 4.36 (d, 1 H, *J* = 9.3 Hz), 4.31 (d, 1 H, *J* = 9.3 Hz), 2.14 (s, 3 H); **11b**: 6.51 (d, 1 H, *J* = 2.8 Hz), 5.42 (d, 1 H, *J* = 2.8 Hz), 4.27 (d, 1 H, *J* = 9.5 Hz), 4.22 (d, 1 H, *J* = 9.5 Hz), 2.12 (s, 3 H), 1.62 (s, 3 H); **14**: 6.51 (d, 1 H, *J* = 2.9 Hz), 6.45 (s, 1 H), 5.43 (d, 1 H, *J* = 2.9 Hz), 4.42 (dd, 1 H, *J* = 7.0, 10.0 Hz), 2.87 (dd, 1 H, *J* = 7.0, 17.2 Hz), 2.73 (dd, 1 H, *J* = 10.0, 17.2 Hz), 2.16 (s, 3 H), 0.85 (s, 9 H), 0.02 (s, 3 H), 0.01 (s, 3 H).

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