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LETTERS

CLAY-CATALYZED SOLVENTLESS ADDITION REACTIONS OF FURAN WITH α,β-UNSATURATED CARBONYL COMPOUNDS[†,1]

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Abstract.- The reaction of furan with α,β-unsaturated carbonyl dienophiles catalyzed by K10 montmorillonite in the absence of organic solvents produces the corresponding Diels-Alder adducts and, in the case of methyl vinyl ketone, Michael-type products, under much milder conditions than the conventional protocols. The results are consistent with acid catalysis on the clay surface. Acrylates gave lower yields and/or decomposition products. The reaction can be extended to alkynic substrates such as DMAD to afford cycloadducts in good yields. © 1998 Elsevier Science Ltd. All rights reserved.

Key Words.- Clays, Diels-Alder, furan, montmorillonite, solid state reactions.

Numerous methods for the assembly of oxygenated organic molecules involve addition reactions of furan templates, because the resulting structures are central to many biological, pharmaceutical, and polymer molecules.[2] Cycloadditions of furans, however, are usually performed under Lewis acid catalysis[3,4] or high pressures[5] to afford products in practical yields. Clay-catalyzed reactions have emerged as a useful alternative and recent examples demonstrate the breadth of chemistry and diversity in structures attainable by this methodology.[6] Although these surface-mediated reactions are usually conducted in organic solvents and often with metal-exchanged clays to increase the number of Lewis acid sites, it is unclear whether both conditions are necessary and, in fact alternative radical pathways have been proposed on the basis of EPR studies.[6b]

Recently, we have reported that cycloadditions of cyclopentadiene and 1,3-cyclohexadiene with numerous dienophiles can be successfully conducted at 0 °C either with K10 montmorillonite or alumina in complete absence of solvents.[7] *For environmental reasons this is a preferred reaction protocol.* Encouraged by these preliminary results, cycloaddition reactions of furans were also evaluated following the same experimental procedure. The reaction with methyl vinyl ketone (MVK) was chosen as a model case and results are depicted in Scheme 1 and Table 1. The product distribution is largely dependent on reaction conditions and mixtures of Diels-Alder cycloadducts and mono- and/or dialkylated Michael-type products are obtained. It is interesting to note that, after adsorption of reagents on the clay catalyst, this turned a dark pink color. Likewise, while the isolated Diels-Alder adducts (**1** or **2**) are stable enough in the absence of montmorillonite, they converted rapidly into **4** when adsorbed on the clay surface at 25 °C (400-MHz NMR, $CDCl_3$, 20 min).

[†] In respectful memory of the late Professor Sir Derek H. R. Barton

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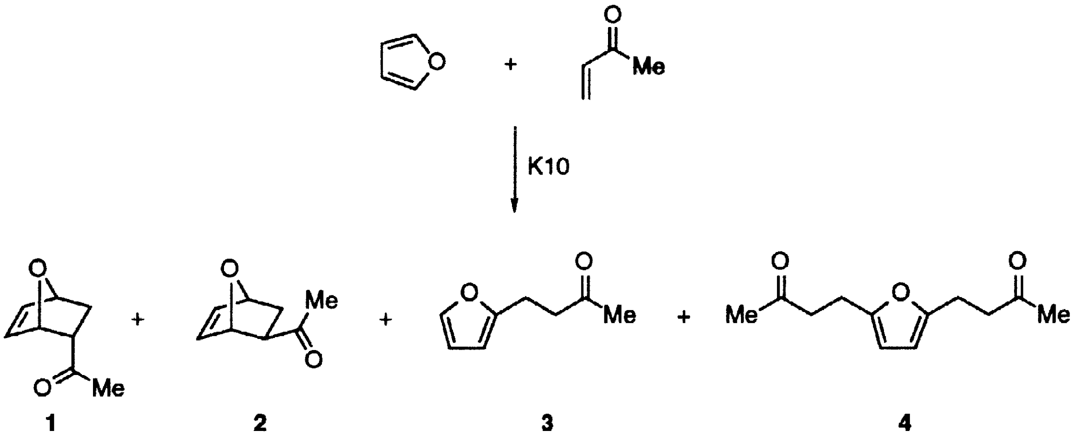


Scheme 1

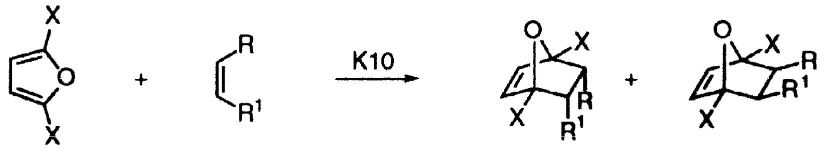
Table 1

Entry	Conditions	t	**1**	**2**	**3**	**4**[a]
1	0 °C	1h	1 (5)	3 (16)	2.5 (13)	3 (31)
2	25 °C	1h	-	-	3 (37)	2 (49)
3	- 50 °C → 25 °C	3h	7 (13)	10.5 (19)	2 (4)	1 (4)
4	- 50 °C → 0 °C	6h	9.4 (38)	8.2 (34)	-	1 (4)
5[b]	0 °C	3h	2.3 (14)	1 (6)	-	-
6	Microwaves, 150 w	1 min.	-	-	1 (11)	2.5 (57)
7	Microwaves, 150 w	5 min	-	-	-	1 (74)

[a]Ratio of products determined by ^{1}H-NMR (400 MHz). Values in parentheses refer to yields (%) of products. [b]Reaction catalyzed by Zn(II)-exchanged K10.

The formation of a 2,5-disubstituted furan (Table 1, entries 6, 7) represents a convenient methodology *en route* to bidirectional tetrahydrofuran-type compounds,[8,9] which can now be obtained under microwave irradiation in short reaction times.[10] Diels-Alder cycloadducts were prevalent at lower temperatures (entries 3, 4) and in the presence of Zn(II)–exchanged montmorillonite (entry 5).

Reactions with symmetrically-substituted cyclic dienophiles work equally well at 0 °C or under microwave irradiation (Scheme 2, Table 2). With the latter technique, lower yields are often obtained owing to the volatility of the products (entries 3, 4). As expected, the reaction with maleic anhydride affords preferentially the thermodynamically favored *exo* adduct (entries 3, 4, 7).[11] The protocol was also extended to 2,5-dimethylfuran (entries 5-8) which cannot give rise to alkylated adducts. The Diels-Alder adduct with MVK could be obtained with Zn(II)-exchanged K10 even at –50 °C (entry 8). In contrast, acrylic derivatives gave sluggish results under these conditions, although in the case of acrolein, the Diels-Alder cycloadduct (*endo*/*exo* = 1:1.5) could be isolated in 25% yield after 5h at –50 °C with Zn(II)–K10 montmorillonite.



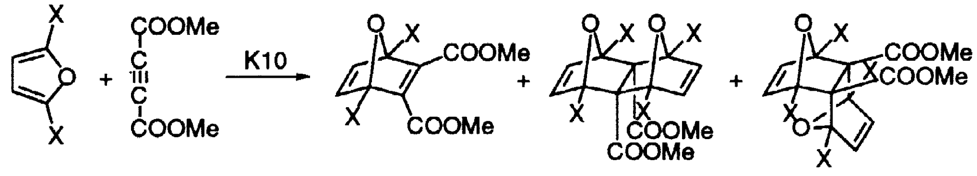
Scheme 2

Table 2

Entry	X	R	R^1	Conditions	t	Yield (%)	Endo/Exo[a]
1	H	–CO–NPh–CO–		0 °C	24 h	85	1.3/1
2	H	–CO–NPh–CO–		Microwaves, 150 w	15 min.	80	1.5/1
3	H	–CO–O–CO–		0 °C	3 h	36	1/3
4	H	–CO–O–CO–		Microwaves, 150 w	2 min.	16	1/3
5[b]	Me	–CO–NPh–CO–		0 °C	90 min.	77	2.3/1
6[c]	Me	–CO–NPh–CO–		Microwaves, 300 w	10 min.	100	2.3/1
7	Me	–CO–O–CO–		0 °C	45 min.	60	–/1
8[d]	Me	$COCH_3$	H	- 50 °C	7 h	52	2.5/1

[a]Determined by ^{1}H-NMR (400 MHz). [b]Substrates in an equimolar ratio. [c]Substrates in 2/1 ratio. [d]Zn(II)-exchanged K-10

The clay-catalyzed reaction has also been extended to alkynic substrates such as dimethyl acetylenedicarboxylate (DMAD),[12] to yield a mixture of the corresponding *endo* Diels-Alder monoadduct **5**, and remarkably, the *exo* and *endo* bisadducts **6** and **7** (Scheme 3, Table 3). Reactions were performed with Zn(II)-doped clay to improve yields in shorter reaction times.



5 **6** **7**

Scheme 3

Table 3

Entry	X	Conditions	t	**5**	**6**	**7**[a]
1[b]	H	K10–Zn(II), 25 °C	4 days	3	–	1
2[c]	H	K10–Zn(II), 25 °C	4 days	7.5	1	10
3[b]	Me	K10–Zn(II), 25 °C	20 h	1	–	–

[a]Determined by ^{1}H-NMR (400 MHz). [b]Substrates in an equimolar ratio. [c]Substrates in 4/1 ratio.

To sum up, the strategy described above meets the requirements for a "benign by design" process, and is also characterized by the technical ease of the reaction sequence, and the range of products obtainable. The experimental results will be rationalized with the aid of computational studies on simplified models to account for the role of acid catalysis, which will be reported elsewhere.

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