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2-NITROFURANS AS DIENOPHILES IN DIELS-ALDER REACTIONS

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Abstract. *a*-nitrofurans derivatives are studied in Diels-Alder reactions under thermal conditions. In contrast to *a*-acylfurans, they showed to be efficient dienophiles.

Keywords: *nitrofurans, dienophiles, Diels-Alder*

Introduction

Despite furans is well known as diene component in Diels-Alder (DA) reactions only a few examples can be found where furans act as dienophile in DA reactions with normal electron demand, e.g. *b*-acylated furans have shown to be excellent dienophiles on interaction with isoprene.^{1,2} It has also been reported that furans react with diene partners such masked *o*-benzoquinones through DA reactions with inverse electron demand.³

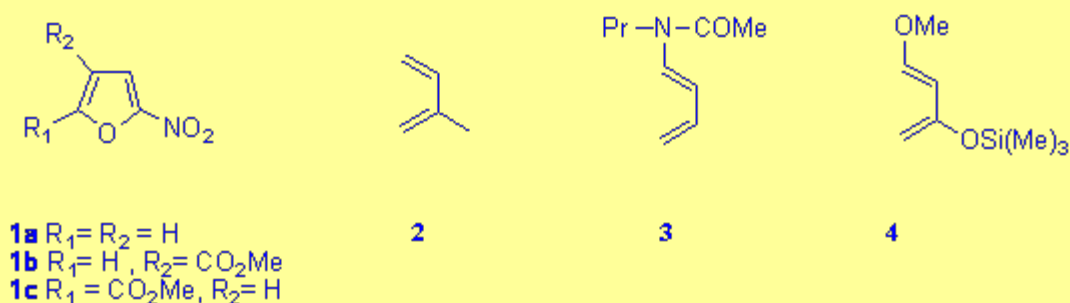
We have reported studies on the dienophilic character of other aromatic systems like substituted indoles,⁴ naphthalenes⁵ and thiophenes⁶ in DA reactions with normal electron demand. Since we want to know if a strong electron withdrawing group induces reactivity in a less-favorable *a*-position, we would like to explore in this work the behavior of 2-nitrofurans in reactions with dienes under thermal conditions.

Results and Discussion

This research was carried out using 2-nitrofuran (**1a**), 2-nitrofuran-4-carboxylic methyl ester (**1b**) and 2-nitrofuran-5-carboxylic methyl ester (**1c**) as dienophiles.

Isoprene (**2**), 1-*N*-acetyl-*N*-propyl-1,3-butadiene (**3**) and 1-methoxy-3-trimethylsilyloxy-1,3-butadiene

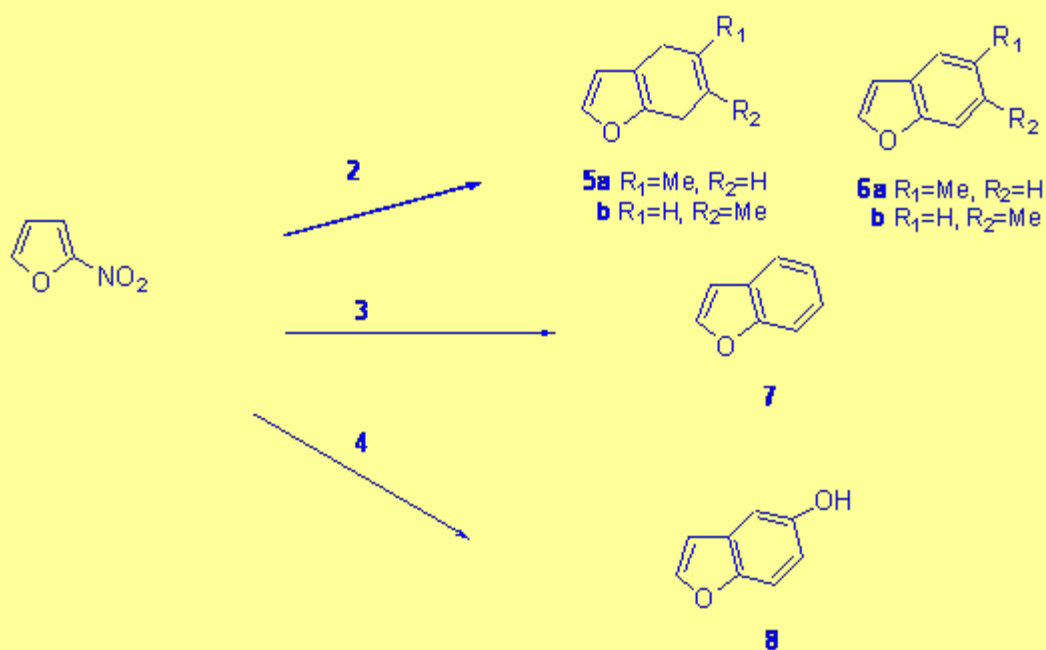
(Danishefsky's diene) (**4**) were chosen as the diene partners (Scheme 1).



Scheme 1

When **1a** reacted with the above mentioned dienes in different reaction conditions, showed its dienophilic character taking part in DA cycloaddition. When **1a** react with isoprene gave a mixture of dihydrobenzofurans **5a**, **5b** (with thermal extrusion of nitrous acid accompanying the DA reaction) and benzofurans **6a**, **6b**; with 1- *N*-acetyl-*N*-propyl-1,3-butadiene afforded the benzofuran **7** and with Danishefsky's diene was obtained 5-hydroxy-benzofuran **8** (Scheme 2).

In contrast to the 2-acylated furans that react on the non-substituted side giving poor yields,¹ 2-nitrofurans proved to be an efficient dienophiles with the cycloaddition taking place on the nitrated bond.



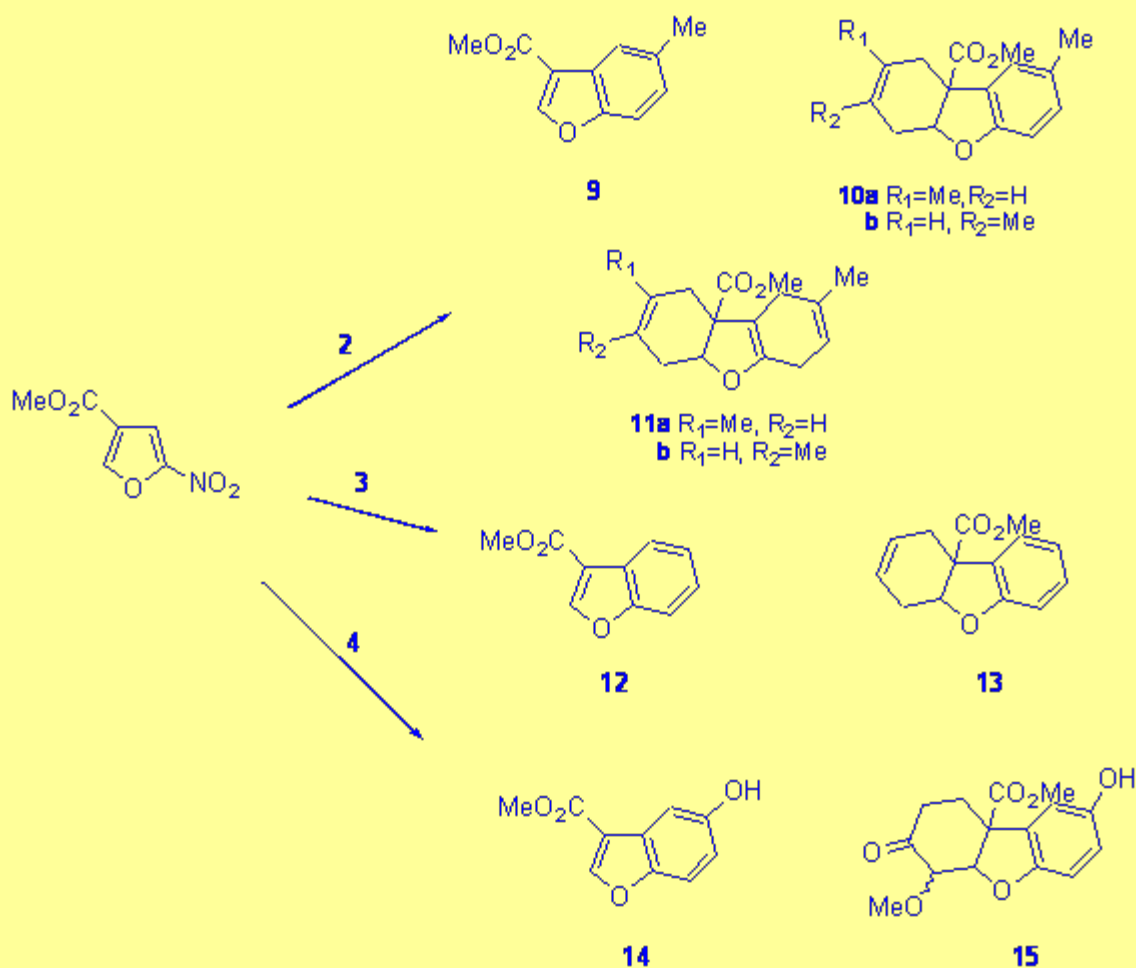
Scheme 2

Dienophile	Diene	D:D	T(°C)	Time	Product	Yield ^a
1a	2	12:1	200	72 h	5a,5b,6a,6b	60%
		12:1	150	72 h	5a,5b,6a,6b	50%
	3	3:1	140	72 h	7	50%

		3:1	120	72 h	7	45%
	4	2:1	140	72 h	8	65%
		2:1	120	72 h	8	60%

^a based on consumed nitrofuran

When 2-nitrofuran held an additional electron withdrawing substitution at 4 or 5 position, the reaction followed the DA normal way but showed a strongly trend to double addition thus exposure of **1b** to the diene **2** led to mixture of cycloadducts **9** and a mixture of tricycles **10** and **11** with good yields. When this dienophile react with the diene **3** afforded the bicycle **12** and cycloadduct **13**. Treatment with **4** gave **14** and **15** respectively (Scheme 3).



Scheme 3

Dienophile	Diene	D:D	T(°C)	Time	Product	Yield ^a
1b	2	12:1	200	72 h	9,10a,10b,11a,11b	80%
	2	12:1	150	72 h	9,10a,10b,11a,11b	70%
	3	3:1	140	72 h	12, 13	65%

	◆◆	◆ 3:1	120	72 h	12, 13	◆◆◆◆◆ 65%
◆	◆◆ 4	◆ 2:1	140	72 h	14, 15	◆◆◆◆◆ 70%
	◆◆	◆ 2:1	120	72 h	14, 15	◆◆◆◆◆ 60%

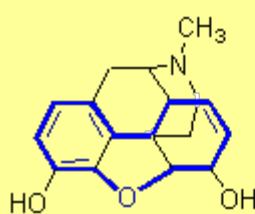
^a based on consumed nitrofurans

On the other hand reaction of **1c** with different dienes gave the expected products but with poor yields probably due to the special combination of the substituent.

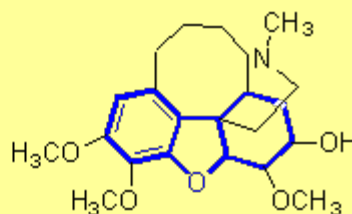
Conclusion

In summary, it has been demonstrated that 2-nitrofurans react ◆ efficiently with the above mentioned dienes in normal electron demand Diels-Alder reactions, with ◆ the ◆ nitro group inducing side selectivity. This substituent is easily extruded under thermal condition, giving nitroderivatives of high interest as intermediary in the synthesis of some alkaloid families like Morphine, Kreysiginine and Codeine. Selecting the appropriate reagents (diene-dienophile), the DA adducts for the total synthesis of these natural products could be obtained in a simple way.

◆



MORPHINE



KREYSIGININE

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References

- 1- E. Wenkert, S. Piettre, *J. Org. Chem.* **1988**, 53, 5850-5853.
- 2- E. Wenkert, P. Moeller and S. Piettre, *J. Am. Chem. Soc.* **1988**, 110, 7188-7194.
- 3- Chien-Hsing Chen, Poliseti Dharma Rao, Chun-Chen Liao, *J. Am. Chem. Soc.* **1998**, 120, 13254-13255.

- 4- a) B. Biolatto, M. Kneeteman, E. Paredes, P. Mancini. *J. Org. Chem.* **2001**, 66, 3906-3912. b) B. Biolatto, M. Kneeteman, P. Mancini. *Tetrahedron Lett.* **1999**, 40, 3343.
- 5- a) E. Paredes, B. Biolatto, M. Kneeteman, P. Mancini. *Tetrahedron Lett.* **2000**, 41, 8079-8082. b) E. Paredes, B. Biolatto, M. Kneeteman, P. Mancini. *Tetrahedron Lett.* **2002**, 43, 4601-4603. c) E. Paredes, M. Kneeteman, M. Gonzalez Sierra, P. Mancini. *Tetrahedron Lett.* **2003**, 44, 2943-2945.
- 6- C. Della Rosa, E. Paredes, M. Kneeteman, P. Mancini. *Letters in Organic Chemistry.* **2004**, 1, 148-150.