

[A019]

BEHAVIOUR OF 2-NITROHETEROCYCLES IN CYCLOADDITION REACTIONS

Claudia Della Rosa, Maria Kneeteman, Pedro M. E. Mancini*

Área Química Orgánica- Departamento de Química - Facultad de Ingeniería Química, Universidad Nacional del Litoral. Santiago del Estero 2829- 3000 Santa Fe, Argentina.
FAX: +54-342-4571162. *e-mail: pmancini@fiquis.unl.edu.ar

Abstract. Five membered aromatic 2-nitroheterocycles are studied in Diels-Alder reactions. 2-nitrofuran and 1-tosyl-2-nitropyrrole yielded normal cycloadducts with isoprene and Rawal's diene. Formation of pyrrolyl-derivatives are observed in reactions of 2-nitrothiophene and 2-nitroselenophene with isoprene.

Keywords: 2-nitroheterocycles, dienophiles, Diels-Alder

Introduction

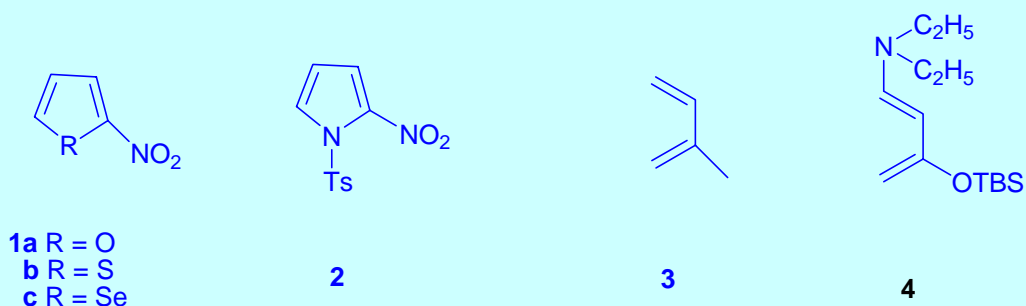
In view of their electron-rich constitution and electron-donor properties five-membered aromatic heterocycles have involved mostly as the diene component in cycloaddition reactions. There exists a limited number of examples of them acting as dienophiles in Diels-Alder reactions with normal electron demand, e.g. aromatic heterocyclepentadienes holding an electron-withdrawing group at β -position have shown to be excellent dienophiles on interaction with isoprene at elevated temperature. In contrast, α -acylheterocycles proved to be a very poor dienophile toward isoprene.^{1,2}

Considering our interest in cycloaddition chemistry of substituted aromatic heterocycles with electron-withdrawing groups,^{3,4} we attempt to determine if a very strong withdrawing group, such as nitro group in 2-position induces reactivity at cycloaddition reactions.

The purpose of the present work is to compare the thermal behaviour of 2-nitrofuran, 1-tosyl-2-nitropyrrole, 2-nitrothiophene and 2-nitroselenophene in their exposure to dienes strongly and poorly activated.

Results and Discussion

The dienophiles used were 2-nitrofuran (**1a**), 2-nitrothiophene (**1b**), 2-nitroselenophene (**1c**) and 1-tosyl-2-nitropyrrole (**2**). isoprene (**3**) and 1-diethylamino-3-*tert*-butyldimethylsiloxy-1,3-butadiene (**4**) (Rawal's diene) were chosen as diene partners.



Scheme 1

2-nitro substituted furan reacted with isoprene in different reaction conditions (Table 1) to give a mixture of dihydrobenzofurans (**5a**, **5b**) and benzofurans (**6a**, **6b**) resulting from thermal extrusion of nitrous acid followed by a further aromatization of the primary cycloadduct. Treatment with Rawal's diene yielded the benzofuran (**7**) with very good yields.⁵ (Scheme 2)

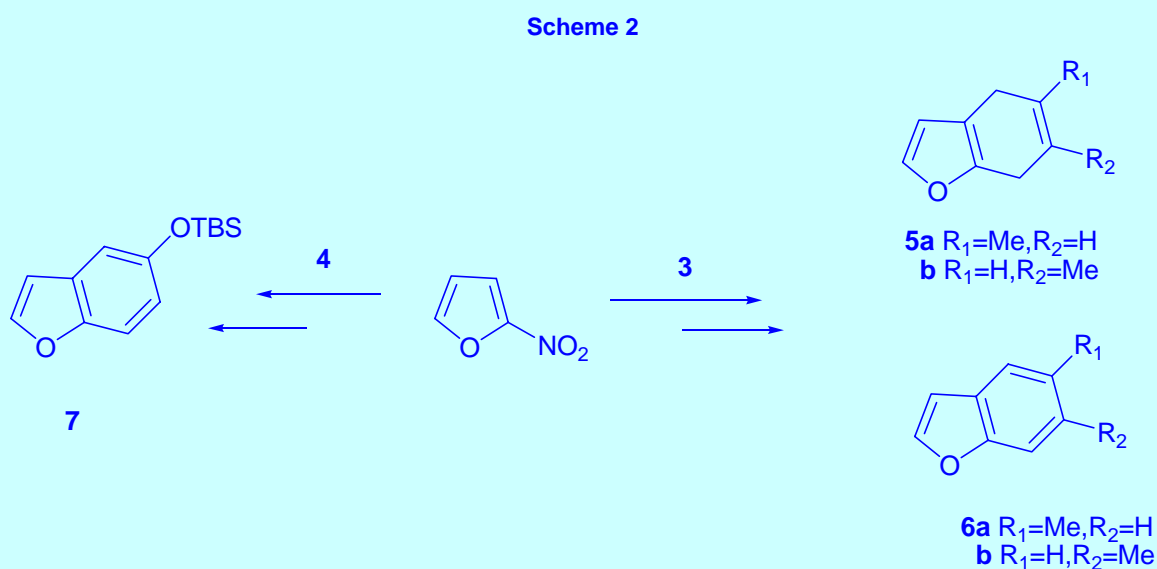


Table 1

Dienophile	Diene	D:D ^a	T(°C)	Time	Product	Yield ^b
1a	3	12:1	200	72 h	5a,5b,6a,6b	60%
		12:1	150	72 h	5a,5b,6a,6b	50%
	4	3:1	150	72 h	7	50%
		3:1	Ref. Tol.	96 h	7	80%

- ^a ratio diene/dienophile
^b based on consumed dienophile

The reaction of 1-tosyl-2-nitropyrrole with **3** under the after mentioned conditions (Table 2) produced a mixture of dihydroindoles (**8a**, **8b**) and indoles (**9a**, **9b**). In the reaction with **4** the indole **10** was obtained with moderate to high yield and complete regioselectivity. The ease of thermal extrusion of nitrous acid accompanying the Diels-Alder reaction of α -nitropyrrole followed by a further aromatization makes this reaction sequence a simple method of indole synthesis.

Scheme 3

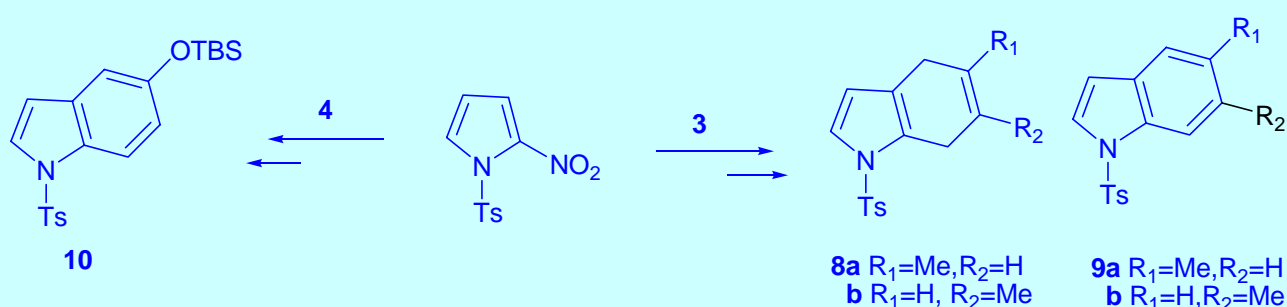


Table 2

Dienophile	Diene	D:D ^a	T(°C)	Time	Products	Yield ^b
2	3	12:1	200	72 h	8a,8b,9a,9b	50%
		12:1	150	72 h	8a,8b,9a,9b	45%
	4	3:1	150	72 h	10	55%
		3:1	Ref. Tol.	96 h	10	70%

- ^a ratio dieno/dienophile
^b based on consumed dienophile

On the other hand, when isoprene was used, **1b** gave the corresponding pyrrolylthiophene (**11**) formed by an assumed hetero cycloaddition followed by thermal rearrangement.⁶ No normal adduct was detected. The formation of pyrroles by reaction of the diene with a nitro group was already observed in experiments with nitronapthalenes. Dienophile **1b** and Rawal's diene **4** underwent cycloaddition with the formation of adduct **12**. This reaction showed complete regioselectivity.

Scheme 4

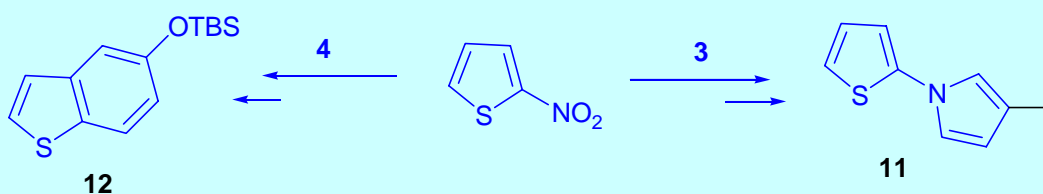


Table 3

Dienophile	Diene	D:D ^a	T (°C)	Time	Product	Yield ^b
1b	3	12:1	200	72 h	11	20%
		12:1	150	72 h	11	15%
	4	3:1	150	72 h	12	30%
		3:1	Ref. Tol.	96 h	12	40%

^a ratio dieno/dienophile

^b based on consumed dienophile

This unexpected behavior was also found in 2-nitroselenophene. Exposure of **1c** to isoprene at different temperatures and reaction times afforded the pyrrolyl-selenophene **13** (Table 4). In contrast, the reaction with **4** yielded the cycloadduct **14** with complete regioselectivity.

Scheme 5

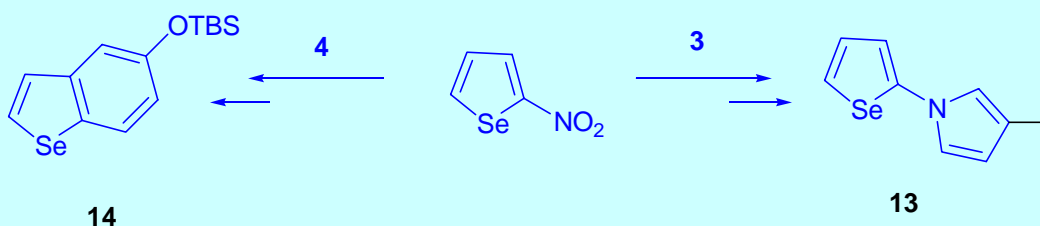


Table 4

Dienophile	Diene	D:D ^a	T (°C)	Time	Product	Yield ^b
1c	3	12:1	200	72 h	13	18%
		12:1	150	72 h	13	10%
	4	3:1	150	72 h	14	20%
		3:1	Ref. Tol.	96 h	14	35%

^a ratio diene/dienophile

^b based on consumed dienophile

Conclusion

It has been demonstrated that in opposition to the 2-acylated heterocycles, 2-nitrofurans and 1-tosil-2-nitropyrrole reacts 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 conditions, giving cycloadducts of high interest

as intermediaries in the synthesis of some alkaloid families as serotonin, tryptamine and gramine.

Furthermore, 2-nitrothiophene and 2-nitroselenophene when was heated with less reactive isoprene, they gave the heterocycloaddition products. However with a highly activated 1,3-butadiene yielded the cycloaddition adducts.

Acknowledgement

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