

[4 + 2]Cycloaddition of *N*-Buta-1,3-dienylsuccinimide to *gem*-Substituted Vinyl Phosphonates

Nathalie Defacqz,^a Roland Touillaux^b and Jacqueline Marchand-Brynaert^{*a}

^aLaboratoire de Chimie Organique de Synthèse, Université catholique de Louvain, Département de Chimie, Bâtiment Lavoisier, Place Louis Pasteur, 1, B-1348 Louvain-la-Neuve, Belgium

^bLaboratoire de Chimie Physique et Cristallographie, Université catholique de Louvain, Département de Chimie, Bâtiment Lavoisier, Place Louis Pasteur, 1, B-1348 Louvain-la-Neuve, Belgium

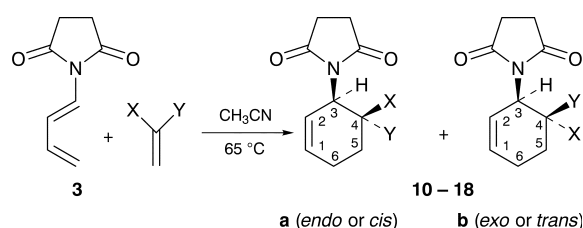
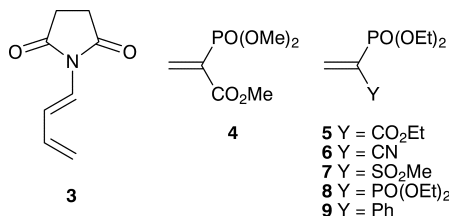
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Vinyl phosphonates α -substituted with carboxylate, nitrile, sulfone and phosphonate groups reacted with *N*-buta-1,3-dienylsuccinimide to give [4 + 2] *ortho*-cycloadducts as mixtures of *endo/exo* stereoisomers.

The use of vinyl phosphonates as dienophiles¹⁶ in [4 + 2]cycloaddition reactions is scarcely documented in the literature.^{17–20} Vinyl phosphonates are poorly reactive partners; however, they could be activated by the substitution in β -position with a strong electron-withdrawing group.^{21,22} In this case, the [4 + 2]cycloadducts formed by reaction with 1-substituted electron-rich dienes display the phosphonate substituent on the cyclohexene ring in the *meta*-position with regard to the electron-releasing group.^{21,22}

We have examined the reactivity of vinyl phosphonates activated by the geminal substitution (α -position) with various electron-withdrawing groups towards *N*-buta-1,3-dienylsuccinimide **3**^{16,30,31} which is considered to be a stable representative of the 1-aminobuta-1,3-diene family.



Scheme 3 Reactions of *N*-buta-1,3-dienylsuccinimide with vinylphosphonates and references

acrylonitrile **6** and α -(diethylphosphono)vinyl methyl sulfone **7** appeared to be less reactive; the *ortho*-cycloadducts **12** and **13** were recovered in 80 and 42% yields, respectively, after 8 and 20 days (Table 1, entries 3 and 4). Tetraethyl ethenyldene bis(phosphonate) **8** gave < 10% yield of cycloadduct **14** after 25 days, while diethyl 1-phosphonostyrene **9** was totally inert (entries 5 and 6).

We obtained equimolar mixtures of *endo* (*cis*, N axial/P equatorial) and *exo* (*trans*, N axial/P axial) stereoisomers (**12**, **13**), or a modest preference for the *endo* stereoisomers (**10**, **11**) which were characterized in their ¹³C NMR spectra by the $J_{\text{P-C}(3)}$ and $J_{\text{P-C}(6)}$ coupling constant values of 5.4 and 10.8 Hz, respectively.¹⁶ In the presence of ZnI₂ (2 equivalents), an *exo* (*trans*, N axial/P axial) stereoselectivity was observed; for instance, the reaction of **3** with **4** furnished a 18:82 mixture of **10a** and **b**.

The 1,1-disubstituted vinyl phosphonates **4–9** have been prepared according to standard procedures.^{33–38}

Trimethyl 2-phosphonoacrylate **4** and triethyl 2-phosphonoacrylate **5** reacted with *N*-buta-1,3-dienylsuccinimide **3** to furnish the *ortho*-cycloadducts **10** and **11** in > 90% yield, after 2 and 4 days respectively, in acetonitrile at 65 °C (Scheme 3, Table 1: entries 1 and 2). α -(Diethylphosphono)-

Table 1 Cycloaddition results

Entry	Dienophile		No equiv.	Compound no.	Conditions ^a	Yield(%) ^b	Cycloadduct no.	a:b ^c
	X	Y						
1	PO(OMe) ₂	CO ₂ Me	0.8	4	2	95	10	65:35
2	PO(OEt) ₂	CO ₂ Et	0.8	5	4	93	11	55:45
3	PO(OEt) ₂	CN	0.8	6	8	80	12	46:54
4	PO(OEt) ₂	SO ₂ Me	1	7	20	42	13	52:48
5	PO(OEt) ₂	PO(OEt) ₂	1.2	8	25	ca. 10	14	Not isolated
6	PO(OEt) ₂	Ph	1	9	>10	No reaction		
7	CO ₂ Me	H	10		7	82	15	84:16
8	CO ₂ Et	H	2.5		8	79	16	73:27
9	CN	H	6		20	76	17	78:22
10	SO ₂ Me	H	3.5		25	13	18	58:42
11	PO(OEt) ₂	H	5		>10	No reaction		
12	Ph	H	10		>10	No reaction		

^aReaction time in days, CH₃CN, 65 °C. ^bYield after purification by column chromatography. ^cRatio determined from the ¹H NMR spectra of the crude mixtures.

As control experiments, we have performed cycloaddition reactions of *N*-buta-1,3-dienylsuccinimide **3** with the monosubstituted olefins structurally related to the *gem*-substituted vinyl phosphonates **4–9**. Methyl acrylate, ethyl acrylate and acrylonitrile (dienophiles used in excess) gave good yields of *ortho*-cycloadducts **15–17**, with a good *endo*-selectivity, but only after 7 to 20 days (Scheme 3, Table 1, entries 7–9). Methyl vinyl sulfone furnished a 13% yield of adduct **18** after 25 days (entry 10), while vinyl phosphonate and styrene were totally unreactive towards **3** (entries 11 and 12).

Thus, the monosubstituted dienophiles appeared to be systematically less reactive than the corresponding *gem*-disubstituted vinyl phosphonates. This could result from favourable interactions¹⁶ in the pre-reactive complex (van der Waals complex) between the imide substituent of the diene **3** and the phosphonate group of the dienophiles **4–8** that govern the cycloaddition reactions, despite the steric factors resulting from the geminal substitution.

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Techniques used: ¹H and ¹³C NMR, MS, IR

References: 44

Scheme 1: Reactivity of the 1-aminobuta-1,3-dienes

Scheme 2: Preparation of the dienophiles

Table: 1

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