CONJUGATED NITROALKENES IN CYCLOADDITION REACTIONS. PART 2.+ DIELS–ALDER REACTIONS OF *E*-2-ARYL-1-CYANO-1-NITROETHENES WITH CYCLOPENTADIENE

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The reaction between *E*-2-aryl-1-cyano-1-nitroethenes **1a–1e** and cyclopentadiene (**2**) occurs according to the carbodiene [4+2]cycloaddition scheme and leads to the corresponding 6-*endo*-aryl-5-*endo*-cyano-5-*exo*-nitronorbornenes **3a–3e** and 6-*exo*-aryl-5-*exo*-cyano-5-*endo*-nitronorbornenes **4a–4e** as the only reaction products. The attempts to detect the products of heterodiene [4+2]cycloaddition in the reaction environment were not successful.

Keywords: [4+2]Cycloaddition; Nitroalkenes; Cyclopentadiene; Nitronorbornenes; Diels–Alder reaction; Carbocycles; Heterocycles.

Reactions of simple nitroalkenes with conjugated dienes proceed according to the carbodiene [4+2]cycloaddition scheme[2,3]. However, in the case of extremely electrophilic nitroalkenes, the carbodiene [4+2]cycloaddition (CDA) may compete with the heterodiene [4+2]cycloaddition (HDA), in which one of the N=O bonds of the nitro group participates in the reaction as a part of the 4π electron system[3–5]. For example, HDA products are formed in addition to the CDA products in the reactions of 2,3-dimethylbutadiene and cyclohexa-1,3-diene with 1-nitro-1-(phenylsulfonyl)ethene[6,7]. Competition between these pathways is an interesting issue both from the practical and theoretical perspective. Therefore, while continuing our studies on the reactivity of nitroalkenes in [4+2] π-electron cycloadditions[1,8–10], in the present work we have focused on structures of the products formed in the reaction between *E*-2-aryl-1-cyano-1-nitroethenes **1a–1e** and cyclopenta-

+ For Part 1, see ref.[1]

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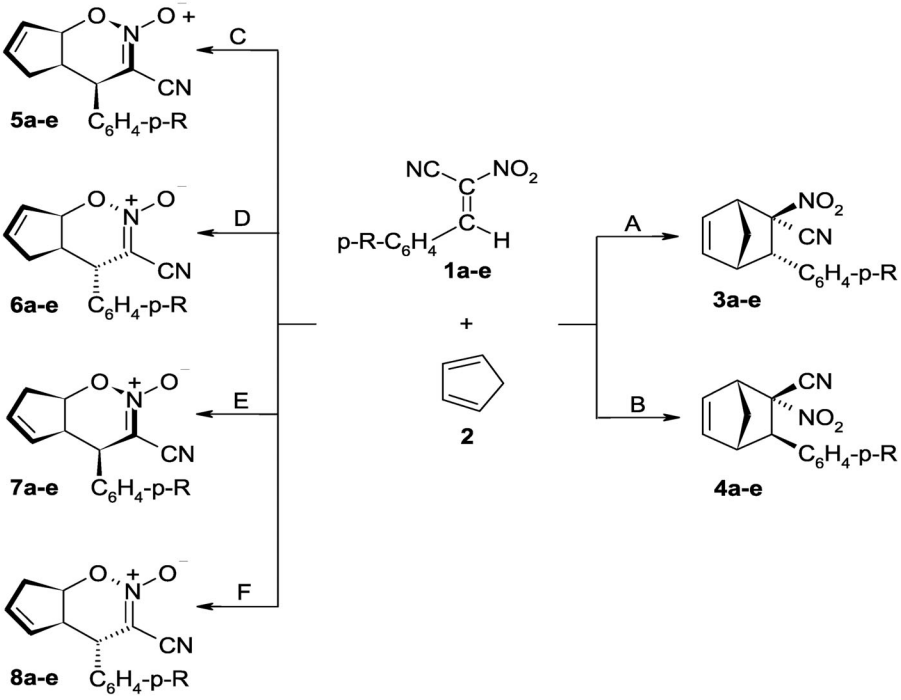
diene (**2**). In the dienophiles selected for our research, steric hindrance is very similar, but the dienophiles electrophilicity is different due to the presence of the substituent R in the phenyl ring. This is proved by the electronic chemical potentials (μ) and the electrophilicity power (ω), calculated by us according to the expressions recommended by Domingo et al.[11,12].

Assuming the concerted reaction mechanism, we could expect six cycloadducts in the reactions studied (Scheme 1). The aim of the present work was to determine experimentally which of the theoretically possible pathways were really favored. Previously[1], we carried out detailed analysis of the A–F pathways of **1d** + **2** reaction using B3LYP/6-31G(d) calculations.



	1a	1b	1c	1d	1e	2
R	$COOCH_3$	Br	Cl	H	CH_3O	-
μ [a.u.]	-0.2019	-0.1953	-0.1970	-0.1939	-0.1771	-0.1108
ω [eV]	3.80	3.71	3.68	3.42	3.14	0.83
Δω [eV]	2.97	2.88	2.85	2.59	2.31	-

SCHEME 1

These calculations suggest that the reaction on kinetically most favorable path leading finally to *endo*-nitronorbornene **4d** proceeds according to a two step mechanism (in nitromethane $\Delta G^{\neq}$ = 27.5 kcal/mol). The initially formed 4-cyano-5-phenyl-2-oxa-3-azabicyclo[4.3.0]nona-3,8-diene-3-oxide (**5d**) is converted to *endo*-nitronorbornene **4d** by [3.3]-sigmatropic shift. On less preferred paths B, D, E and F ($\Delta G^{\neq}$ = 28.0, 28.5, 37.9 and 37.4 kcal/mol, respectively) the reaction proceeds according to a one step mechanism.

RESULTS AND DISCUSSION

All the cycloadditions studied in this work were carried out at room temperature, using a triple stoichiometric excess of cyclopentadiene (**2**) relative to the dienophiles and nitromethane as solvents. When the reaction was complete, the solvent and the excess of cyclopentadiene were removed in vacuum and the semi-solid residue was analysed by HPLC. It was found that independently of the nature of the substituent R, the reaction afforded only two products, whose retention times were different from those of the starting materials. For example, the reaction of methyl *E*-4-(2-cyano-2-nitroethenyl)benzoate (**1a**) with cyclopentadiene (**2**) led to the products with the retention times of 19.7 and 30.0 min (Fig. 1). The Δω index[11] suggests the cycloaddition of these substrates should have the highest polar character. The same types of products appeared in the reaction medium, when the reaction was carried out at 0 °C or in other solvents of various polarity

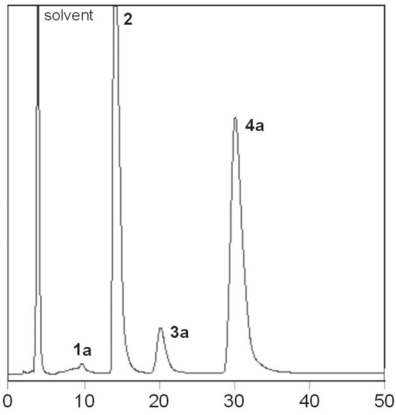


FIG. 1
The chromatogram of the reaction mixture of methyl *E*-4-(2-cyano-2-nitroethenyl)benzoate (**1a**) with cyclopentadiene (**2**)

(Table I). The compounds were effectively separated by semipreparative HPLC, which yielded individual compounds in an analytically pure form (Table II).

The IR spectra of the reaction products show the absorption bands, which confirm[13] the presence of cyano, nitro and methoxycarbonyl groups, a bridging methylene group, a double bond, and a *para*-substituted benzene ring (Table III). However, there are no bands confirming the presence of six-membered cyclic nitronates that usually occur in the range of 1570–1610 cm^{-1} (refs[5,14–16]). Similarly, the UV spectra do not show the presence of a derivative of 1,2-oxazine-*N*-oxide with a substituent at the carbon atom of >C=N(O)O– moiety capable of conjugation with the C≡N bond. This is confirmed by the absence of a band in the 260–320 nm range[14]. A strong band (log ε > 4.1) at ~235 nm is observed instead, which is most likely related to the $\pi \rightarrow \pi^*$ transitions in the *para*-substituted benzene ring[13,17]. Therefore, the pathways leading to the products of heterodiene [4+2]cycloaddition (paths C–F) can be excluded.

The mass spectra of both compounds are nearly identical. The molecular weight of the molecular ions ($M^{\bullet+}$) is equal to the sum of molecular weights of the substrates **1a** and **2** (*m/z* = 298), which allowed us to assign the molecular formula of $C_{16}H_{14}N_2O_4$. The formula is consistent with the results of elemental analysis.

TABLE I
Selectivity of reaction between compounds **1a–1e** and **2**

Reaction	Condition		Isomer ratio [**3**]/[**4**]
	t, °C	Solvent	
1a + **2**	25	nitromethane	0.19
1a + **2**	0	nitromethane	0.17
1a + **2**	25	THF	0.18
1a + **2**	25	dioxane	0.14
1b + **2**	25	nitromethane	0.15
1c + **2**	25	nitromethane	0.15
1d + **2**	25	nitromethane	0.14
1e + **2**	25	nitromethane	0.08

TABLE II
Yields and essential physical properties of compounds **3a–3e** and **4a–4e**

Compound	R	R_t[a], min	M.p., °C	Formula	MS, $M^{\bullet+}$ (m/z, %)	Found, %/Calculated, %		
						C	H	N
3a	$COOCH_3$	19.7	100–101	$C_{16}H_{14}N_2O_4$	298 (0.4)	64.28/64.49	4.61/4.74	9.30/9.40
4a	$COOCH_3$	30.0	123–124	$C_{16}H_{14}N_2O_4$	298 (1.4)	64.35/64.49	4.73/4.74	9.34/9.40
3b	Br	41.9	106–108	$C_{14}H_{11}N_2O_2Br$	318 (37.2)	52.51/52.88	3.38/3.49	8.65/8.81
4b	Br	62.2	121.5–123	$C_{14}H_{11}N_2O_2Br$	318 (10.1)	52.59/52.88	3.42/3.49	8.82/8.81
3c	Cl	35.2	89–92	$C_{14}H_{11}N_2O_2Cl$	274 (20.2)	61.15/61.37	3.91/4.05	10.06/10.22
4c	Cl	52.2	103–105	$C_{14}H_{11}N_2O_2Cl$	274 (5.9)	61.22/61.37	4.03/4.05	10.09/10.22
3d	H	19.4	53–56	$C_{14}H_{12}N_2O_2$	240 (14.8)	69.86/70.06	4.84/5.04	11.54/11.67
4d	H	28.8	76–78	$C_{14}H_{12}N_2O_2$	240 (6.1)	70.07/70.06	4.93/5.04	11.61/11.67
3e	CH_3O	21.7	98–99	$C_{15}H_{14}N_2O_3$	270 (10.0)	65.78/66.73	5.11/5.23	10.20/10.38
4e	CH_3O	32.5	104–105	$C_{15}H_{14}N_2O_3$	270 (4.5)	65.52/66.73	5.03/5.23	10.21/10.38

[a] Methanol–water (65:35 v/v) was used as an eluent at the flow rate 0.7 ml/min. The analyses were carried out at 10 °C and λ = 254 nm.

The ^{1}H NMR spectra of both compounds are very similar. Nevertheless, the proton chemical shifts and their coupling constants (Table IV) clearly indicate arylnorbornene structures[18–20]. As expected, the resonance signals of H8 and H7 protons of methylene bridge occur at higher fields than the aromatic ring protons, which appear at the lowest ones. The H4 proton signal in both isomers occurs in a field slightly lower than that of the H1 proton. This is caused by location of the H4 protons in vicinity of the CN and NO_2 groups, which cause larger deshielding than the aromatic ring does in vicinity of the H1 proton. For the major isomer **4a**, the doublet from the H6 proton is at δ 3.91 ppm, while for the minor isomer **3a**, at δ 4.39 ppm. It is probably caused by the anisotropy of double bond in the norbornene ring[18,19]; H6 seems to be closer to the *endo* proton than to the *exo* one. The protons of the vinylidene moiety of both isomers have similar chemical shifts as well.

On the basis of the IR, UV, MS and ^{1}H NMR spectra, it was possible to assign the structure of methyl (6-cyano-6-nitronorbornen-5-yl)benzoate to the products obtained. However, their stereochemistry could not be assigned from those spectra. This was determined from the NOESY experiments.

In the NOESY spectrum of the minor compound (Fig. 2), a correlation signal occurs at the intersection of projection lines of chemical shifts of H6 and H7 protons on the spectrum diagonal, which proves their spatial prox-

TABLE III
Essential IR data for compounds **3a–3e** and **4a–4e** (cm^{-1})

Compound	ν(CN)	ν(R)	ν(NO_2)	δ(CH_2)	δ(HC=CH)	δ(Ar)
3a	2256 vw	1729 s	1556 s, 1338 m	1459 w	715 m	853 m
4a	2255 w	1724 s	1567 s, 1342 m	1458 w	719 m	858 m
3b	–	1011 m	1559 s, 1384 m	1460 m	727 m	840 m
4b	2249 w	1011 m	1567 s, 1330 s	1456 w	727 m	839 m
3c	–	1012 m	1572 s, 1336 s	1459 w	728 m	842 m
4c	2250 w	1015 m	1568 s, 1332 m	1456 m	728 m	840 m
3d	–	–	1560 s, 1340 s	1459 w	739 m	696 m
4d	2254 w	–	1562 s, 1341 s	1454 w	735 m	695 s
3e	–	1031 m	1560 s, 1337 s	1459 m	737 m	844 m
4e	2253 w	1032 m	1560 s, 1333 m	1459 m	728 m	838 m

TABLE IV
Essential ^{1}H NMR data for compounds **3a–3e** and **4a–4e**

Compound	Chemical shift δ, ppm							Coupling constant *J*, Hzt				
	H1	H2	H3	H4	H6	H7	H8	1,2	2,3	3,4	1,6	7,8
3a	3.54 m	6.82 dd	6.45 dd	3.86 m	4.39 d	2.18 m	2.01 m	2.9	5.6	3.4	2.7	9.9
4a	3.44 m	6.76 dd	6.13 dd	3.98 m	3.91 d	2.36 m	2.12 m	3.3	5.7	2.8	2.9	10.2
3b	3.37 m	6.75 dd	6.46 dd	3.95 m	4.25 d	2.19 m	2.04 m	2.8	5.6	3.6	2.7	10.0
4b	3.37 m	6.75 dd	6.11 dd	3.96 m	3.80 d	2.33 m	2.07 m	3.3	5.6	2.9	2.7	10.2
3c	3.38 m	6.79 dd	6.43 dd	3.96 m	4.33 d	2.20 m	2.02 m	3.0	5.6	3.5	2.9	10.0
4c	3.37 m	6.75 dd	6.11 dd	3.96 m	3.87 d	2.33 m	2.11 m	3.4	5.6	2.9	2.6	10.1
3d	3.44 m	6.82 dd	6.40 dd	3.84 m	4.33 d	2.21 m	1.96 m	2.7	5.6	3.1	2.7	9.9
4d	3.42 m	6.75 dd	6.10 dd	3.95 m	3.87 d	2.39 m	2.07 m	3.2	5.7	2.8	2.7	10.2
3e	3.39 m	6.86 dd	6.41 dd	3.79 m	4.24 d	2.19 m	1.94 m	2.7	5.1	3.4	2.6	10.8
4e	3.34 m	6.73 dd	6.08 dd	3.92 m	3.81 d	2.37 m	2.04 m	3.1	5.7	2.7	2.9	10.0

imity and suggests the *exo*-position of the H6 proton in the molecule. Indeed, according to the B3LYP/6-31G(d) calculations[1], the H6–H7 proton distance in the **3a** isomer does not exceed 2.4 Å, while in the **4a** isomer, it is more than 3.7 Å. The absence of the correlation signal between the H7 proton and the *ortho* protons of the phenyl ring proves that the ring is in the *endo*-position. Therefore, a structure of methyl (6-*endo*-cyano-6-*exo*-nitronorbornen-5-yl)benzoate (**3a**) can be assigned to the compound. In the NOESY spectrum of the major product, a correlation signal between the H6 and H7 protons is not observed. This fact indicates that the H6 proton is located below the plane of the carbocyclic ring. Due to the presence of the correlation signal between the H7 proton and the *ortho* protons of the phenyl ring, a structure of methyl (6-*exo*-cyano-6-*endo*-nitronorbornen-5-yl)-benzoate (**4a**) can be assigned to the compound.

The configuration of the CN and NO_2 groups in **3a** and **4a** was confirmed by HPLC analysis of the products of their retro [4+2]cycloaddition reactions, which were carried out in boiling nitromethane. It was found that both reaction mixtures, apart from cyclopentadiene oligomers and the un-

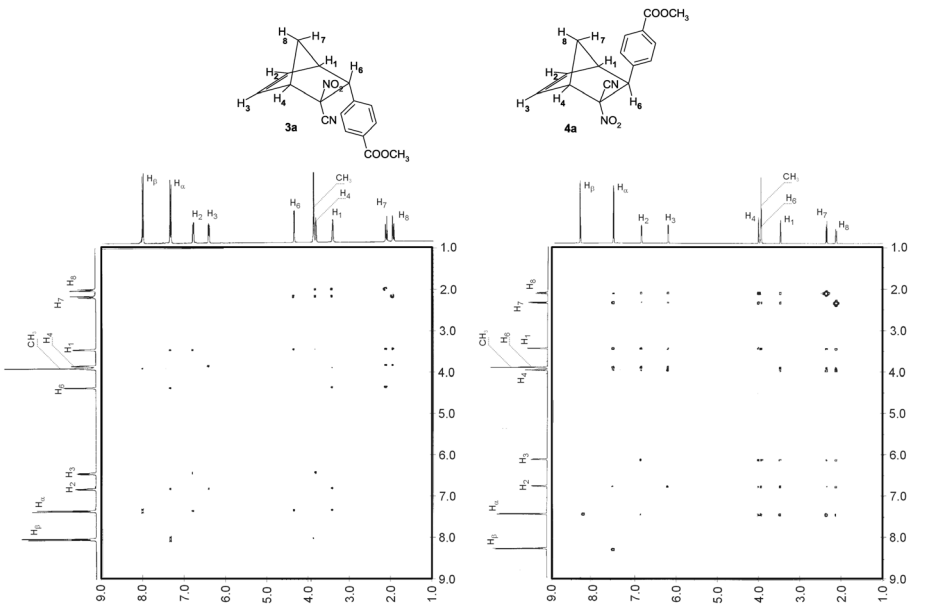
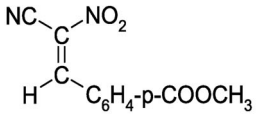
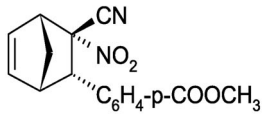


FIG. 2
The NOESY correlations for nitronorbornenes **3a** and **4a**

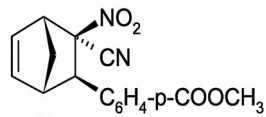
reacted substrates, contained methyl *E*-4-(2-cyano-2-nitroethenyl)benzoate (**1a**) and no methyl *Z*-4-(2-cyano-2-nitroethenyl)benzoate (**9a**). The latter should be found, if the substrates used in the retro reactions had the structure of methyl (6-*exo*-cyano-6-*endo*-nitronorbornen-5-yl)benzoate (**10a**) or methyl (6-*endo*-cyano-6-*exo*-nitronorbornen-5-yl)benzoate (**11a**).



9a



10a



11a

The [4+2]cycloaddition reactions that involve the *E*-2-aryl-1-cyano-1-nitroethenes **1b–1e** proceed analogously. Regardless of their electrophilicity, only the carbodiene [4+2]cycloaddition products were formed in each case. Their physical properties are listed in Tables II–IV.

Thus, our experimental observations indicate that the reaction between *E*-2-aryl-1-cyano-1-nitroethenes **1a–1e** and cyclopentadiene (**2**) leads to 6-*endo*-aryl-5-*endo*-cyano-5-*exo*-nitronorbornenes **3a–3e** and 6-*exo*-aryl-5-*exo*-cyano-5-*endo*-nitronorbornenes **4a–4e** as the final reaction products.

According to the B3LYP/6-31G(d) calculations, the reaction path leading finally to *endo*-nitronorbornenes **3a–3e** should be the most favored one from the kinetic point of view, independently on polarity of the reaction medium. The experimental results confirm this prediction (Table I). However, it was not possible to prove the existence of HDA intermediates during conversion of substrates into *endo*-nitronorbornenes. All attempts to identify heterocyclic intermediates in the reaction medium (^{1}H NMR, HPLC) were not successful. Therefore, it has to be assumed that the reactions of *E*-2-aryl-1-cyano-1-nitroethenes with cyclopentadiene are proceeding according to carbodiene cycloaddition. However, the mechanism of the cycloaddition itself is a separate issue. Despite large electrophilicity of the dienophiles, the reaction on both competing pathways proceeds with retention of stereochemical configuration of nitroalkenes. This fact suggests concerted mechanism of the reaction. Nevertheless, we are aware that final confirmation of this mechanism can be acquired only from kinetic measurements.

EXPERIMENTAL

General

For reaction testing, a HPLC Knauer apparatus equipped with a UV-Vis detector and a Lichrospher 100-5 RP18 column (4 × 250 mm) was applied. Methanol–water or THF–water mixtures were used as eluents. For separation of the cycloadducts from post-reaction mixtures, a semipreparative HPLC equipped with a Lichrospher 100-10 RP18 column (16 × 250 mm) was applied, and methanol–water (65:35 v/v) was used as an eluent at the flow rate 10 ml/min. Melting points were determined on a Boetius apparatus and are not corrected. IR spectra were recorded on a Bio-Rad 175C spectrophotometer in KBr pellets. UV spectra were taken with a StellarNet EPP-2000C spectrometer in methanol. The mass spectra were obtained using a Finningan 955 apparatus, operated at 70 eV ionization energy and 100–130 °C ion source temperature. ^{1}H NMR spectra were taken on a Bruker AMX 500 spectrometer using $CDCl_3$ as a solvent and TMS as an internal reference. The *E*-2-aryl-1-cyano-1-nitroethenes **1a**–**1e** and cyclopentadiene (**2**) were prepared according to the method described in literature[21,22].

Synthesis of 6-Aryl-5-cyano-5-nitronorbornenes

A mixture of nitroalkene **1** (4 mmol) and freshly distilled cyclopentadiene (**2**) (12 mmol) in 5 ml of dry nitromethane was stirred at room temperature for 24 h. The excess of cyclopentadiene and the solvent were then evaporated to dryness in vacuo and the residue was separated by semipreparative HPLC. Evaporation of the eluent from the obtained fractions gave pure 6-aryl-5-cyano-5-nitronorbornenes. The products were recrystallized from ethanol. Their physical constants are given in Tables II–IV.

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