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Diene Condensation of Cyclopentadiene with Dienophiles of Allylacetylene Series

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Abstract—Diene condensation of cyclopentadiene with 2-substituted allylacetylenes occurs nonselectively at a double and triple bonds; therewith the dienophile activity grows in parallel with the electron-withdrawing properties of the substituent. Depending on electronic character of functional groups the reaction proceeds as "neutral" diene synthesis. The relative activity of cyclopentadiene and 1,3-cyclohexadiene in reactions with allylacetylenes is essentially governed by the different distance between the 1,4-reactive sites in these systems.

The behavior of allylacetylenes and their functional derivatives in Diels–Alder reactions is poorly understood [1–4]. The compounds under study attract interest on the one hand because of practical value of the arising adducts [5, 6], and on the other hand due to the possibility to reveal the factors controlling the reactivity of addends [7, 8].

The scanty available data on cycloaddition of conjugated and nonconjugated enynes to cyclic dienes show that the reaction occurs regioselectively at the double bond affording adducts of *endo*-configuration [9–11]. We reported previously [12, 13] on diene condensation of 1,3-cyclohexadiene, hexachlorocyclopentadiene, 5,5-dimethoxytetrachlorocyclopentadiene with allyacetylene and its derivatives. It was shown that the reaction occurred at the double bond and furnished *endo*-adducts. We studied chemical reactions and the structure of the bicyclic adducts obtained.

In extension of our research we investigated the diene condensation of cyclopentadiene (**I**) with allylacetylene dienophiles **IIa–i** and 2-substituted allylacetylenes **Va–d** in order to reveal the relations between the donor-acceptor properties of addends and the factors governing their reactivity.

We found that diene **I** enters into the diene condensation with dienophiles **IIa–i** regioselectively at the double bond at heating to 165–170°C providing alongside monoadducts **IIIa–i** also biadducts **IVa–i**. The yield of mono and biadducts depended on the chosen reaction conditions. It was established that at equimolar ratio of reagents within 8 h at 160–165°C formed 75–80% of bicyclic compounds **IIIa–i** and 8–10% of tetracyclic adducts **IVa–i** whereas at the double excess of diene **I** within 20 h at 170–175°C the yield of adducts **IIIa–i** was 15–20%, and that of **IVa–i** 65–69.5%. The biadducts obtained are thick dark-yellow syrupy substances soluble in most organic solvents. Yields, physicochemical characteristics, and elemental analyses of compounds synthesized are compiled in Table 1. The structure of adducts **IIIa–i, IVa–i** was proved by ^{1}H NMR and IR spectra and by chemical transformations: by esterification of the corresponding alcohols and by reaction of monoadducts with cyclopentadiene (**I**).

In the IR spectra of compounds **IIIa–i, IVa–i** appear strong absorption bands of stretching and bending vibrations in the regions 3400, 3300, 2230, 1615, 2140, 1720, 1155, 805, 750, 630 cm^{-1}, characteristic of bonds O–H, ≡C–H, C≡C, CH=CH,
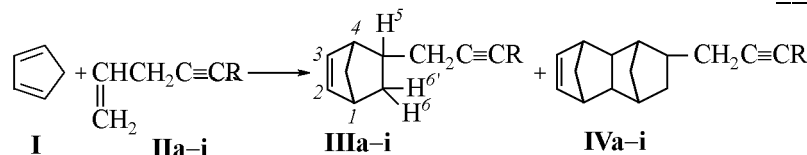
II–IV, R = H (**a**), C(CH$_3$)$_2$OH (**b**), C(CH$_3$)$_2$OCH$_3$ (**c**), C(CH$_3$)$_2$OCOCH$_3$ (**d**), C(CH$_3$)$_2$OCH$_2$CH$_2$CN (**e**), C(CH$_3$)$_2$OCH$_2$CH$_2$OH (**f**), C(CH$_3$)$_2$OCH$_2$CH–CH$_2$ (**g**), C(CH$_3$)$_2$Cl (**h**), C(CH$_3$)$_2$Br (**i**).

Table 1. Yields, physical constants, and elemental analyses of cycloaddition products of allylacetylene derivatives to cyclopentadiene **IIIc–i, IVc–i, VIa–d, VIIb–d**[a]

Compd. no.	Yield, %	bp, °C (*p*, mm Hg), mp,°C	n_d^{20}	d_4^{20}	Found, %			Formula	Calculated, %		
					C	H	Cl(Br)		C	H	Cl(Br)
IIIc	84.3	92–93 (2)	1.4916	0.9506	82.12	10.07	–	$C_{14}H_{20}O$	82.30	9.86	–
IIId	76.2	98–99(1)	1.4885	0.9864	77.49	8.77	–	$C_{15}H_{20}O_2$	77.55	8.67	–
IIIe	86.0	124–126 (1)	1.4904	1.0312	78.79	8.75	5.59 (N)	$C_{16}H_{21}NO$	78.97	8.69	5.75 (N)
IIIf	75.2	127–128 (2)	1.5051	1.0190	76.84	9.53	–	$C_{15}H_{22}O_2$	76.88	9.46	–
IIIg	70.0	123–124 (2)	1.4956	1.0051	78.22	9.02	–	$C_{16}H_{20}O_2$	78.01	9.00	–
IIIh	76.3	68–70 (1)	1.4980	0.9287	75.60	8.33	16.7	$C_{13}H_{17}Cl$	74.81	8.21	16.99
IIIi	68.4	61–62 (1)	1.5178	1.1282	61.02	6.47	31.6	$C_{13}H_{17}Br$	61.65	6.77	31.56
IVc	76.3	126–127 (2)	1.5170	0.9970	84.55	9.44	–	$C_{19}H_{26}O$	84.39	9.69	–
IVd	64.0	130–131 (1)	1.5086	1.0265	80.69	8.60	–	$C_{20}H_{26}O_2$	80.49	8.78	–
IVe	75.4	163–165 (1)	1.5170	1.0303	81.55	8.66	4.53 (N)	$C_{21}H_{27}NO$	81.59	8.79	4.52 (N)
IVf	66.6	156–157 (2)	1.5220	1.0480	80.16	9.26	–	$C_{20}H_{28}O_2$	79.95	9.36	–
IVg	61.2	152–153 (2)	1.5210	1.0501	80.89	9.27	–	$C_{21}H_{28}O_2$	80.72	9.03	–
IVh	61.5	104–105 (1)	1.5180	0.9720	78.40	8.25	12.45	$C_{18}H_{23}Cl$	78.68	8.44	12.45
IVi	60.2	146–147 (1)	1.5373	1.2375	66.50	7.01	25.10	$C_{18}H_{23}Br$	67.70	7.26	25.02
VIa	81.4	97–98 (1)	1.5202	1.0030	81.45	8.76	–	$C_{11}H_{14}O$	81.43	8.69	–
VIb	45.0	98–99 (1)	1.5195	0.9996	81.69	9.15	–	$C_{12}H_{16}O$	81.77	9.15	–
VIc	73.3	92–93 (0.5)	1.5200	1.1004	67.1	6.69	18.12	$C_{11}H_{13}ClO$	67.18	6.66	18.03
VId	56.3	110–111 (0.5)	1.5565	1.3676	54.86	5.38	33.22	$C_{11}H_{13}BrO$	54.79	5.43	33.14
VIIb	14.8	102–103(1)	1.5230	1.0102	81.85	9.29	–	$C_{12}H_{16}O$	81.77	9.15	–
VIIc	17.2	95–96 (0.5)	1.5260	1.1106	67.23	6.72	18.17	$C_{11}H_{13}ClO$	67.18	6.66	18.03
VIId	15.0	114–115 (0.5)	1.5610	1.3718	54.67	5.42	33.29	$C_{11}H_{13}BrO$	54.79	5.43	33.14

[a] Physicochemical data of compounds **IIIa, b** and **IVa, b** not indicated in Table 1 are presented in [11].

C≡N, C=O, C–C, C–O–C, C–Br and C–Cl respectively [14].

The lack of signals from three protons at the double bond of allyl fragment in the ^{1}H NMR spectra and also the presence in the IR spectra of adducts

Table 2. Values of coupling constants (Hz) of protons H[6] and H[6'] in the bicycloheptene skeleton of compounds **IIIc–i**

| Compd. no.	$J_{6,6'}$, Hz	$J_{5,6}$, Hz
IIIc	11.5	4.2
IIId	11.0	4.3
IIIe	11.4	4.1
IIIf	11.3	4.2
IIIg	11.4	4.3
IIIh	12.1	4.1
IIIi	12.6	4.6
Publ. data [16, 17]	10.4–13.7	2.5–5.0, $J_{5,6'}$ 6.0–7.0

IIIa–i, IVa–i of stretching vibration bands at 2200–2260 cm^{-1} [ν (C≡C)] proves the strict regiospecificity of the reaction proceeding exclusively at the double bond of the allyl group and conserving the triple bond intact [15–17]. The observed coupling constants of protons H_{endo}^6, $H_{exo}^{6'}$ and H^5 of adducts **IIIa–i** permit an unambiguous assignment the *endo*-configuration to the substituent (Table 2).

Note that the most active diene **I** in contrast to 1,3-cyclohexadiene [12] formed not only normal adducts of diene condensation but also added the second molecule of diene **I**. Increased substitution at the double bond (at the use of 2-substituted dienophiles) affected the reactivity of enyne and required higher temperature for adducts formation at the double bond. As a result the selectivity of reaction is reduced, and the product contains a mixture of adducts formed both at the double and the triple bonds. The relative amounts of reaction products from addition at the double and the triple bonds were determined by TLC and GLC. The content of adducts **VIIb–d** equaled to 20–25%. The deviation from selectivity may be ascribed to sterical hindrance to formation of the reaction complex.

Table 3. Characteristic of diene condensation of cyclopentadiene with allylacetylene dienophiles $CH_2 = CHCH_2C\equiv CR$ **IIa–e**

R	Rate constant value ($k \times 10^4$, l mol^{-1} min^{-1})				E_A, kJ mol^{-1}	$\Delta H^{\neq}$, kJ mol^{-1}	$-\Delta S^{\neq}$, J mol^{-1} deg^{-1}	$-\Delta G^{\neq}$, kJ mol^{-1}
	100°C	120°C	140°C	160°C				
H	2.5	3.75	4.2	6.7	20.5	13.8	278.1	109.32
C(CH$_3$)$_2$OH	3.4	4.25	5.61	8.31	19.3	16.0	266.2	106.4
C(CH$_3$)$_2$OCH$_3$	5.1	7.44	10.21	14.24	17.4	17.8	243.5	103.1
C(CH$_3$)$_2$OCOCH$_3$	6.7	8.32	13.5	18.10	21.2	14.5	255.0	105.0
C(CH$_3$)$_2$OCH$_2$CH$_2$CN	9.2	13.0	17.5	24.5	25.6	16.9	230.3	101.1

The formation of adducts at the double bond **VIa–d** and at the triple bond **VIIb–d** is confirmed by IR and ^{1}H NMR spectra. As show GLC analyses the product mixtures contain 70–75% of adducts **VIa–d** and 20–25% of adducts **VIIb–d**. Besides in the course of reaction arose also the corresponding bi-adducts in an overall yield no more than 10–15%. Adducts **VIa–d** and **VIIb–d** were isolated in an individual state by means of TLC. Compounds **VIa–d** and **VIIb–d** were separated from the obtained alcohols mixtures by column chromatography similarly to procedures [18, 19] under TLC monitoring (Table 1).

I Va–d

VIa–d VIIb–d
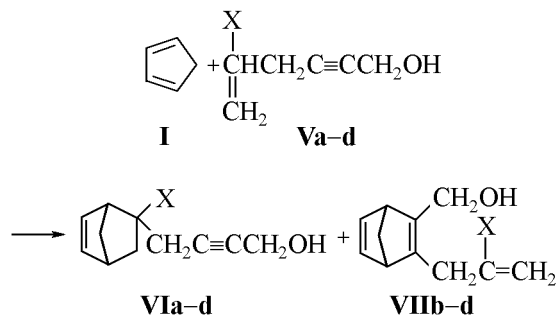
V–VII, X = H (**a**), CH$_3$ (**b**), Cl (**c**), Br (**d**).

In the IR spectra of adducts **VIa–d** are present absorption bands at 2240, 1615 cm^{-1} characteristic of C≡C and C–C bonds, and also the bands at 3450 cm^{-1} characteristic of a hydroxy group. In the IR spectrum of adducts **VIIb–d** instead of the band at 2240 cm^{-1} appears a band at 3090 cm^{-1} (=CH$_2$). In the ^{1}H NMR spectra of compounds **VIa–d** are observed the proton signal belonging to the geminal system H^6, H$^{6'}$, and in the spectra of compounds **VIIa–d** appear the signals from =CH$_2$ protons characteristic of an iso-propenyl group. These data also show that the reaction occurs both at the double and triple bonds. The study of diene condensation of the 2-substituted allylacetylenes with cyclopentadiene demonstrated that

the activity of a double bond depends both on the nature of the functional groups [12] and on the type of substituents attached to the double bond, and it decreases in the series H > Br > Cl > CH$_3$.

In order to reveal the effect of electronic factors on the reactivity of allylacetylene dienophiles in cycloaddition to diene **I** we measured the reaction kinetics and estimated the corresponding kinetic parameters [20] compiled in Table 3.

The rate constants were calculated along equations of bimolecular reactions. For all dienophiles **IIa–d** the dependence of log rate constants on the reciprocal temperature for the reaction series investigated fits to the Arrhenius equation (see the figure). Basing on these data the thermodynamical parameters were evaluated (Table 3).
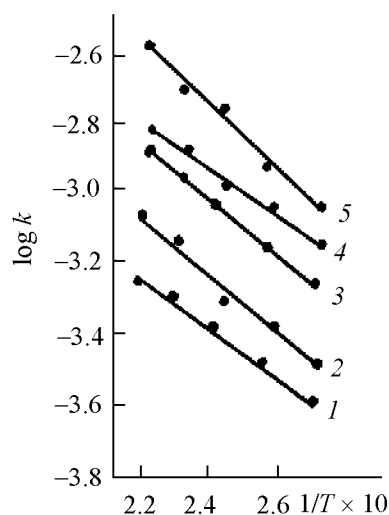
Arrhenius plot for reaction rate constants of diene cyclocondensation between cyclopentadiene and allylacetylenes $CH_2=CHCH_2C\equiv CR$. R = H (*1*), C(CH$_3$)$_2$OH (*2*), C(CH$_3$)$_2$OCH$_3$ (*3*), C(CH$_3$)$_2$OCOCH$_3$ (*4*), C(CH$_3$)$_2$CH$_2$CH$_2$CN (*5*).

Table 4. Characteristics of energy levels of HOMO and LUMO for some dienes and dienophiles

C°mpd.	HOMO, eV	LUMO, eV
Cyclopentadiene	−8.62	0.98
Cyclohexadiene	−8.566	0.814
$CH_2=CH-C\equiv CH$	−9.261	1.466
$CH_2=CHCH_2-C\equiv CH$	−9.758	1.737
$CH_2=CHCH\equiv CH_2$	−8.853	1.125
$CH_2=CHCH_2CH\equiv CH_2$	−9.526	1.695
$CH_2=CHCH_2C\equiv CCH_2OH$	−9.420	0.811
$CH_2=C(CH_3)CH_2C\equiv CCH_2OH$	−9.656	1.286

The data obtained show that all reactions are characterized by large negative values of activation entropy and small values of activation energy which is typical for Diels–Alder reaction [21]. Therewith we also found that although diene **I** is more active than cyclohexadiene (**VIII**) the relations concerning effects of functional groups remain the same [12].

The qualitative rationalization of molecular reactivity is often based on consideration of interaction of LUMO (lowest unoccupied molecular orbital) of one reactant with the HOMO (highest occupied molecular orbital) of the other reactant molecule [22]. The stronger is the interaction of LUMO and HOMO the higher is energy stabilization of the transition state and therefore the faster is the reaction. In its turn this interaction varies as the reciprocal of the energy difference between LUMO (E^{LUMO}) and HOMO (E^{HOMO}) and depends on the symmetry of the corresponding MO. In this respect it was obviously interesting to analyze from the viewpoint of the theory of frontier molecular orbitals the behavior of some dienophiles (vinylacetylene, allylacetylene, 1,3-butadiene, 1,3-pentadiene, allylethynylcarbinol, methallylethynylcarbinol) in reactions with cyclopentadiene and cyclohexadiene [23]. To this end the calculation of these molecules was carried out according to quantum-chemical method MINDO-3 [24], and energy levels of LUMO and HOMO for dienes and dienophiles were determined (Table 4). The analysis of data compiled in Table 4 leads to the following conclusions: In allylacetylene molecules the contribution of the ethylene fragment to HOMO is large, and therefore the reaction should occur at this site. An introduction of a methyl group to the ethylene fragment reduces this contribution with simultaneous increase in the contribution of the acetylene fragment, although the latter still remains smaller. These conclusions are consistent with the experimental facts, for the unsubstituted allylacetylenes react as dienophiles with cyclic dienes by the double

bond, and those substituted in 2-positions afford a mixture of adducts at the double and the triple bond, the former prevailing.

In Table 5 are presented the differences ΔE between LUMO and HOMO of the molecules listed above and the differences ΔE between MO of dienes and dienophiles. These data show that the diene synthesis between the mentioned dienophiles and cyclopentadiene proceeds by the type of "neutral" diene synthesis (the diene and the dienophile can play the part of HOMO and LUMO components).

Note that the distance between the 1,4-reactive sites in diene **I** is smaller than in the cyclopentadiene; therefore in reactions with the latter the degree of overlapping of the atomic orbitals is lower, and consequently the contribution of the donor-acceptor interaction to decreasing the energy barrier to reaction is smaller. This reasoning is in agreement with the lower activity of cyclohexadiene (**VIII**) as compared to cyclopentadiene (**I**).

Thus the study of Diels–Alder reactions of dienes **I** and **VIII** with dienophiles of the allylacetylene series revealed a correlation between the yields of the final products and the location of the frontier MOs on the energy scale. This result evidences that the orbital interaction governs the mechanism of this reaction.

EXPERIMENTAL

IR spectra were recorded on spectrophotometer UR-20, ^{1}H NMR spectra were registered on spectrometer Tesla B-4878 (80 MHz) with HMDS as internal reference. The purity of compounds obtained was checked by TLC on unfixed layer of alumina of the **II** grade activity, eluent benzene–ether, 3:1, development in iodine vapor.

Compounds **VIb–d** and **VIIa–c** were separated by column chromatography along procedures [18, 19]: column 800 × 21 mm packed with Al_2O_3 (neutral, II grade Brockmann activity), amount of substance to be separated 1 g per 200 g of adsorbent, eluent benzene–ether, 5:3, monitoring by TLC on Silufol-254 plates, development in iodine vapor.

Reaction mixtures were analyzed and kinetic measurements were performed by GLC on LKhM-8MD chromatograph equipped with a column 200 × 0.4 cm, stationary phase 3% SE on Chromaton-W, carrier gas helium, flow rate 30 ml min^{-1}.

The second-order rate constants were evaluated from the decrease in dienophile concentration with time carrying out the reaction at temperatures 100–160°C. The given values are averaged from 3 runs performed under identical conditions. The diene

Table 5. Difference in LUMO and HOMO energy levels in dienofiles (A) and some dienes (B)

Dienofily (A)	Dienes (B)	$E_1 = E_A^{LUMO} - E_B^{HOMO}$, eV	$E_2 = E_B^{LUMO} - E_A^{HOMO}$, eV	$E_3 = E_A^{LUMO} - E_A^{HOMO}$, eV	$E_4 = E_B^{LUMO} - E_B^{HOMO}$, eV
$CH_2=CHC\equiv CH$	C_5H_6 [a]	10.08	10.24	10.73	9.59
	C_6H_8 [b]	10.03	10.07	10.73	9.38
$CH_2=CHCH_2C\equiv CH$	C_5H_6	10.35	10.73	11.50	9.59
	C_6H_8	10.30	10.57	11.50	9.38
$CH_2=CHCH\equiv CH_2$	C_5H_6	9.74	9.83	9.98	9.59
	C_6H_8	9.69	9.67	9.98	9.38
$CH_2=CHCH_2CH\equiv CH_2$	C_5H_6	10.31	10.50	11.22	9.59
	C_6H_8	10.26	10.34	11.22	9.38
$CH_2=CHCH_2C\equiv CCH_2OH$	C_5H_6	9.43	10.40	10.23	9.59
	C_6H_8	9.38	10.23	10.23	9.38
$CH_2=C(CH_3)CH_2C\equiv CCH_2OH$	C_5H_6	9.90	10.63	10.94	9.59
	C_6H_8	9.85	10.47	10.94	9.38

[a] C_5H_6 cyclopentadiene; [b] C_6H_8 cyclohexadiene.

synthesis was carried out in ampules at the equimolar ratio of reagents; reaction time 4–12 h, toluene was used as solvent. Compounds **IIIa, b** were obtained before [11], and their characteristic were consistent with the published data.

General procedure for preparation of adducts **IIIc–i, IVc–i,** and **VIa–d, VIIb–d**. A mixture of 0.1 mol of diene **I** and 0.1 mol of dienophile **IIb–i, Va–d** was heated in a sealed ampule to 150–180°C for 8–10 h in the presence of 0.05 g of hydroquinone. On completing the reaction the products were subjected to vacuum distillation. On removing the unreacted reagents the target product was repeatedly distilled. The yields, physical constants, and elemental analyses of adducts synthesized are given in Table 1.

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