Synthesis of polysubstituted 1,3-cyclohexadienes from β-branched α,β-alkenals and monoesters of ylidenemalonic acids

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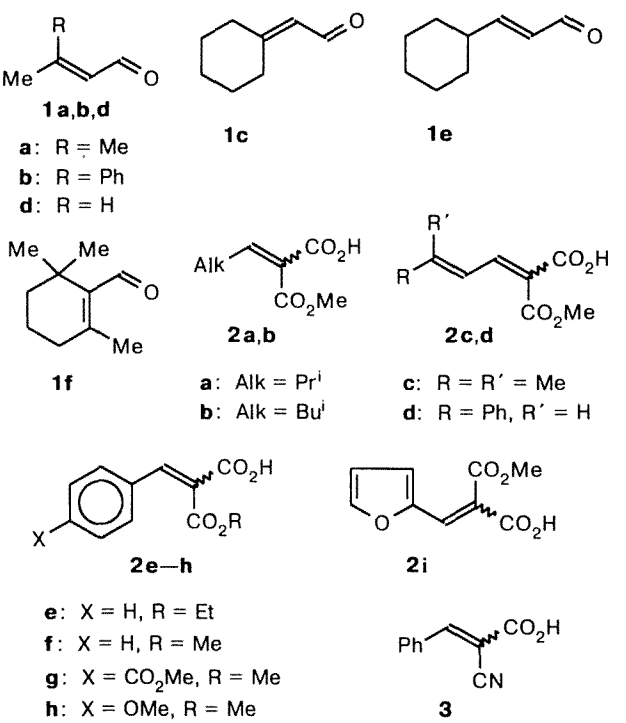
3-Methyl- and 3-phenyl-2-butenal react with monoesters of alkylidene-, alkenylidene-, and arylmethylenemalonic acids in the presence of piperidine as the catalyst to give esters of 4,6-disubstituted 1,3-cyclohexadienecarboxylic acids in 23—96 % yields. Under the same conditions cyclohexylideneacetic aldehyde reacts with the monoesters of prenylidene- and benzylidenemalonic acid to afford mixtures of 1,8a-*trans*- and 1,8a-*cis*-isomers of 1-substituted alkyl 1,5,6,7,8,8a-hexahydronaphthalene-2-carboxylates, the ratios and configurations of which were determined by means of ^{1}H NMR spectroscopy. In some cases the formation of cyclic dienes is impeded by the competing process of decarboxylation of acidic ylidenemalonates. The derivatives of 4,6-diphenyl-1,3-cyclohexadienecarboxylic acid were shown to be convenient precursors for the preparation of *meta*-terphenyls.

Key words: α,β-alkenals, β-branched; monoesters of ylidenemalonic acids; piperidine; polysubstituted 1,3-cyclohexadienes; 1,2-disubstituted 1,5,6,7,8,8a-hexahydronaphthalenes, synthesis, stereochemistry; *meta*-terphenyls.

Earlier,[1—4] we found that under the conditions of secondary amine-catalyzed Knoevenagel condensation acyclic isoprenoidal α,β-enals reacted with monoethyl malonate[1] or with the monoesters of prenylidene- and citrylidenemalonic[2—4] and benzylidenemalonic acid[4] as well as with 2-cyanocinnamic acid[2] to afford polysubstituted 1,3-cyclohexadienes in preparatively attractive yields. It was also shown[2,3] that the process is mediated by transiently formed isoprenoidal 1,3-dienamines, which quickly enter the Diels—Alder reaction with monoalkyl ylidenemalonates (prepared in advance or generated *in situ* from an enal and monoethyl malonate). The resulting cycloadducts undergo spontaneous 1,2-elimination of CO_2 and HNR_2, which gives rise to 1,3-cyclohexadienes and regenerates a molecule of catalytically active amine.

Now with a view of assessing the scope and limitations of this synthesis of 1,3-cyclohexadienes we have studied the reactions of prenal (**1a**), 3-phenyl-2-butenal (**1b**), cyclohexylideneacetaldehyde (**1c**), 2-butenal (**1d**), 3-cyclohexylpropenal (**1e**), and β-cyclocitral (**1f**) with such carboxyl-containing dienophiles as the acidic monoesters of alkylidene- (**2a,b**), alkenylidene- (**2c,d**), and arylmethylene- or α-furfurylidenemalonic acids (**2e—i**) as well as 2-cyanocinnamic acid (**3**) in presence of piperidine (0.1 equiv.) as the catalyst.



Dienophiles **2a—i** were prepared by Knoevenagel condensation of the respective aldehydes with dialkyl malonates followed by a controlled saponification of the resulting dialkyl ylidenemalonates with one equivalent of alkali (see Experimental and Table 1). Compounds **2a—i** were obtained as mixtures of *E*- and *Z*-isomers in various proportions and were made to react as such with the enals and piperidine.

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Table 1. Yields, melting points, spectral data, and isomeric composition of acidic derivatives of ylidenemalonic acids **2a—i**, **3**

Product	Yield (%)	M.p. /°C [n_D^{20}]	^{1}H NMR ($CDCl_3$), δ (*J*/Hz)				IR, ν/cm^{-1}	Isomer ratio (*E* : *Z*)
			C(3)H	C(4)H	C(5)H	Other signals		
2a	59	Oil [1.4595]	7.21 (d, 0.55 H); 7.26 (d, 0.45 H)	3.42 (d, 0.55 H); 2.92 (m, 0.45 H)	—	1.1 (d, 6 H, *J* = 7); 3.86 (s, 1.7 H); 3.89 (s, 1.3 H); 10.4 (br.s, 1 H)	3650—2500, 1734, 1705 (sh), 1640	~1 : 1
2b	43	Oil [1.4610]	7.22 (m, 1 H)	2.7 (m, 0.6 H); 3.3 (m, 0.4 H)	1.45 (m, 2 H)	0.88 (m, 3 H); 1.08 (d, 3 H, *J* = 7); 3.88 (s, 3 H); 11.2 (br.s, 1 H)	3600—2350, 1732	~4 : 6
2c	45	65—68 (heptane)	8.41 (d, 0.8 H); 8.20 (d, 0.2 H, *J* = 12.5)	6.86 (m, 0.8 H); 7.56 (m, 0.2 H)	—	2.06 (s, 6 H); 3.97 (s, 3 H); 10.4 (br.s, 1 H)	3600—2400, 1738, 1600	~1 : 4
2d	74	156—157 (benzene)	8.37 (d, 1 H, *J* = 12.5)	~7.5—7.9 (m, 2 H)[a]		7.3—7.5 (m, 6 H)[a]; 4.12 (s, 3 H); 10.9 (br.s, 1 H)	3400—2500, 1738, 1660, 1600, 1580	<1 : 100[b]
2e	80	82—84 (cyclohexane)	7.90 (s, 0.92 H); 7.83 (s, 0.08 H)	—	—	1.30 > 1.37 (both t, 3 H); 4.35 (q, 2 H); 9.1 (br.s, 1 H); 7.4—7.5 (m, 5 H)	3650—2300, 1733, 1705 (sh), 1640	~1 : 12[c]
2f	70	112—113 (cyclohexane—benzene, 4 : 1)	7.91 (s, ~1 H)	—	—	3.90 (s, 3 H); 7.47 (m, 5 H); 11.35 (br.s, 1 H)	3650—2300, 1735, 1700, 1630	<1 : 10
2g	95	142—145	7.83 (s, 1 H)[d]	—	—	3.82 (s, 3 H); 3.92 (s, 3 H); 7.67 + 8.08 (dd, 4 H, A_2B_2-system, J_{AB} = 9); 10.7 (br.s, 1 H)[d]	3600—2900, 1724, 1684, 1623, 1566	<1 : 100[b]
2h	90	139—141	7.83 (s, 0.84 H); 7.80 (s, 0.16 H)	—	—	3.82 (s, 3 H); 3.88 (s, 3 H); 6.90 + 7.42 (dd, 4 H, A_2B_2-system, J_{AB} = 9); 9.8 (br.s, 1 H)	3600—2200, 1730, 1685, 1625, 1600	~1 : 5
2i	60	141—142	7.61 (s, 0.6 H); 7.58 (s, 0.4 H)	—	—	3.95 (s, 3 H); 6.56 (dd, 1 H, *J* = 3.5, *J'* = 1.5); 6.95 (d, 1 H, *J* = 3.5); 7.73 (d, *J'* = 1.5)	3330—2400, 1720, 1680, 1610	~4 : 6
3	45	181—182	8.48 (s, 1 H)[d]	—	—	7.67 (m, 3 H) + 8.12 (d, 2 H, *J* = 9); 4.5 (s, 1 H, OH)[d]	3600—2100, 2220, 1684, 1600 (sh), 1590, 1570	~1 : 100[b]

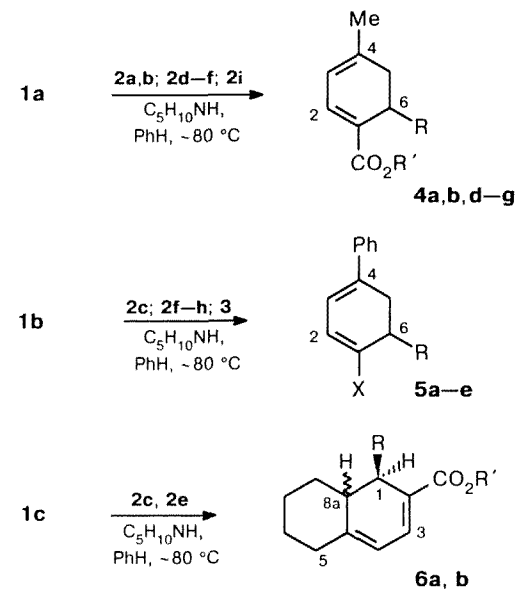
[a] Partly overlaps a neighboring group of signals. [b] Apparently homogeneous substance (TCL and ^{1}H NMR data), tentatively formulated as the *Z*-isomer. [c] Repeated recrystallization of the specimen from heptane—cyclohexane changes the *E* : *Z* ratio to ~1 : 17. Evaporation of the mother liquor affords another crystalline specimen with *E* : *Z* = 1 : 4; the NMR data of **2e** presented in Table 1 relate to this specimen. [d] For solutions in acetone-d_6.

In the ^{1}H NMR spectra of alkenylidene-, arylmethylene-, and α-furfurylidene malonates (**2c**, **2g—i**) the protons at C(3) of preponderant stereoisomers resonate in a somewhat lower field than their counterparts in the minor isomers. On the other hand, in the case of diene **2c** the signal of the proton at C(4) in the minor stereoisomer is markedly shifted downfield with respect to analogous signal of major isomer. Comparison of

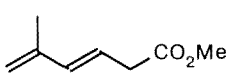
these spectra with the ^{1}H NMR data reported for related polyene systems[5–7] makes it possible to assign the *Z*-configuration to the preponderant isomers of monoesters **2c—i**. This assignment is compatible with a better accessibility of the sterically less congested *trans*-positioned ester group of dialkyl ylidenemalonates to alkaline hydrolysis.

Using enals **1a—c** and dienophiles **2a—i** and **3** we carried out the following transformations (Scheme 1).

Scheme 1



4a: R = Pr^i, R′ = Me
4d: R = *E*-PhCH=CH, R′ = Me
4f: R = Ph, R′ = Me
4b: R = Bu^t, R′ = Me
4e: R = Ph, R′ = Et
4g: R = α-C_4H_3O, R′ = Me
5a: R = Me_2C=CH, X = CO_2Me
5b: R = Ph, X = CO_2Me
5c: R = *p*-$MeO_2CC_6H_4$, X = CO_2Me
5d: R = *p*-$MeOC_6H_4$, X = CO_2Me
5e: R = Ph, X = CN
6a: R = Me_2C=CH, R′ = Me
6b: R = Ph, R′ = Et



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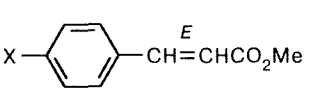


8a—c

PhCH=CHCN
9

X = H (**a**), CO_2Me (**b**), OMe (**c**)

At 80 °C these transformations occur rapidly to give the products with 1,3-cyclohexadienic (**4**, **5**) or 1,5,6,7,8,8a-hexahydronaphthalenic structures (**6**) in preparatively attractive yields. Similar reaction of enal **1a** with monoester **2c** was carried out earlier[8] at 4—5 °C in the presence of a chiral secondary amine, (*S*)-(+)-prolinol; in that case the resulting cyclohexadiene **4c** (R = Me_2C=CH, R′ = Me) was optically active. On the other hand, 2-butenal **1d**, which has only one alkyl substituent at C(3), does not enter the cyclocondensation reaction with monoesters **2c** and **2f**, but undergoes resinification instead.

Under standard conditions the reaction of another β-monosubstituted acrolein, **1e**, with monoester **2c** gives rise to a complex mixture of products. Its analysis using GC-MS technique revealed the presence of no less than seven components. Two of them had molecular masses which corresponded to the dienamine derived from **1e** and/or its isomer $C_{14}H_{23}N$ (*m/z* 206 [M+1], I_{rel} = 89 and 3.1 %). Two other components (in an 8 : 1 ratio), accounting for only 10 per cent of the total peaks area, displayed molecular masses corresponding to the cyclocondensation product formed from **1e** and **2c**, *i.e.*, to the cyclic 1,3-diene and/or to its isomer $C_{17}H_{24}O_2$ (*m/z* 260 $[M]^+$, I_{rel} = 41.7 % for the former and *m/z* 258 $[M-2]^+$, I_{rel} = 47.8 % for the latter; subsequent fragmentation patterns of these two isomers was reminescent of those observed earlier for polysubstituted 1,3-cyclohexadienes[1,2]). These compounds were not studied in more detail. Finally, β-cyclocitral (**1f**) reacted with monoesters **2c** and **2f** very slowly. Although the ^{1}H NMR spectrum of the crude reaction product contained some signals characteristic of the cyclic diene, it was a competing process that predominated under standard reaction conditions, namely, gradual decarboxylation of both dienophiles. In the case of **2c** it gave rise to methyl 5-methyl-3,5-hexadienoate (**7**) whereas **2f** fragmented to methyl benzylideneacetate (**8a**); these esters were isolated and characterized spectroscopically.

Decarboxylation of dienophiles was also observed upon reacting **1a** with **2f**, **1b** with **2f—h** and **3**, and **1c** with **2e** (Table 2). This process becomes particularly prominent when the dienophile or the intermediate dienamine tends to be a reluctant partner in [4+2]-cycloaddition. Decarboxylation is likely to be initiated by the addition of piperidine or a molecule of water (which is formed simultaneously with dienamine) to the conjugated α,β-olefinic bond of the dienophile; this is followed by the well-known[9,10] elimination of CO_2 and HY (Y = NC_5H_{10} or OH) from the respective β-amino or β-hydroxy acid.

To the exclusion of compounds **5a,b**, which are crystalline, the remaining cyclic dienes are either colorless or pale-yellow oils (**4a—g**; **5e**; **6a,b**) or amorphous solids (**5c,d**). For all three types of dienes there are observed characteristic two-spin AB-systems in the ^{1}H NMR spectra with $J_{AB} \approx 6$ Hz, which correspond to the internal H atoms in the diene moiety (Table 3). Compounds belonging to the types **4** and **6** display in their UV spectra a characteristic absorption at λ = 300—310 nm, while compounds of the type **5** absorb at

Table 2. Synthesis of polysubstituted derivatives of 1,3-cyclohexadienecarboxylic (**4**, **5**) and 1,5,6,7,8,8a-hexahydronaphthalene-2-carboxylic acid (**6**)

Reactants		Time,	Product	Yield	M.p./°C	Side
Enal	Dienophile	*t*/min		(%)	[n_D^{20}]	product (yield (%))
1a	**2a**	45	**4a**	88	[1.5035]	—
1a	**2b**	30	**4b**	86	[1.5085]	—
1a	**2d**	45	**4d**	90	[1.5860]	—
1a	**2e**	40	**4e**	95	[1.5580]	—
1a	**2f**	1440[a]	**4f**	59	[1.5540]	**7** (~35 %)[a]
1a	**2i**	40	**4g**	96	[1.5468]	—
1b	**2c**	45	**5a**	93	64—65	—
1b	**2f**	60	**5b**	50[b]	107—108	**8a** (~35 %)
1b	**2g**	120	**5c**	23[b]	Amorphous	**8b** (~45 %)
1b	**2h**	100	**5d**	34[b]	Amorphous	**8c** (~40 %)
1b	**3**	30	**5e**	45	[1.6220]	**9** (~40 %)
1c	**2c**	45	**6a**	57	[1.5270][c]	—
1c	**2e**	45	**6b**	28[b]	[1.5645][c]	**8d** (~65 %)

[a] The reaction was performed at room temperature; when it was carried out on boiling, side product **8** became the preponderant one. [b] After chromatographic separation from the side product. [c] For the mixture of two stereoisomers which differ in their configuration relative to the C(1)—C(8a) bond.

$\lambda \approx 340$ nm. All of the cyclic dienes except for **5e** contain in their IR spectra strong carbonyl absorption bands in the region of 1705—1720 cm^{-1} (Table 4).

As follows from the GC and ^1H NMR spectroscopy data, bicyclic dienes **6a** and **6b** were obtained as the binary mixtures of 1,8a-*trans*- and 1,8a-*cis*-isomers. Interestingly, the ratio of stereoisomers in diene **6a** was ~33 : 67, although in the monoester **2c**, from which the latter was prepared, the ratio of *E*- and *Z*-isomers (determined from the ^1H NMR spectrum, *cf.* Table 1) was ~20 : 80. Similarly, stereoisomer ratio for diene **6b** was 10 : 90 whereas in its precursor (**2e**) the *E* : *Z* ratio was slightly different (~7.5 : 92.5, *cf.* Table 1). In both cases the configuration of preponderant isomers in **6a** and **6b** is *trans*. This conclusion is based on the data discussed below.

In the ^1H NMR spectrum of **6a** (R = Me_2C=CH, two stereoisomers) the signals of the proton H_C at the C(1) atom of hexahydronaphthalene system appear as double doublets. Comparison with the spectra of compounds **4c** (*cf.* Refs. 1, 2), **4d**, and **5a**, where the vicinal coupling of H_C with the adjacent proton in the lateral group R is possible, as well as with that of the nearest analog of **6a**, *i.e.*, **6b**, where such a kind of interaction cannot exist, shows that one of the large spin-spin coupling constants observed for the signals of H_C both in the major and minor isomer corresponds to the vicinal coupling of H_C with the vinylic proton in the group R ($J_{HC,R} \approx 6.5$—11 Hz). Another coupling constant observable for the signal of H_C from the major isomer (1.4 Hz) might be attributed either to the vicinal coupling between H_C and H_D or to a strong allylic coupling between H_C and H_B. In the former case the dihedral angle formed by H_C and H_D should be in the range of 90±20°, and the allylic interaction between H_C and H_B should be practically nonexistent; in the latter case one should have to assume that $J_{CD} = 0$, *i.e.*, that the dihedral angle between H_C and H_D is 90°.

^1H NMR spectrum of the prevailing (90 wt. %) component of the binary mixture of stereoisomeric 1-phenyl-substituted hexahydronaphthalenes **6b** is analogous to that of the major isomer in **6a** with the difference that the lateral Ph group in the molecule of **6b** has no protons in the vicinity of H_C, and thus no interaction of this kind is possible. Consequently, the signal of H_C is narrowed.

As is known,[11] the derivatives of 1,3-cyclohexadiene (including polycyclic ones) can exist in two stable conformations where the substituents at the allylic carbon atoms adopt either quasi-equatorial or quasi-axial positions. The consideration of molecular models of **6a** and **6b** for both conformations of 1,8a-*cis*-isomers ($\mathbf{C}_{eq} \rightleftharpoons \mathbf{C}_{ax}$) and 1,8a-*trans*-isomers ($\mathbf{T}_{eq} \rightleftharpoons \mathbf{T}_{ax}$) revealed that the first of the assumptions made above to account

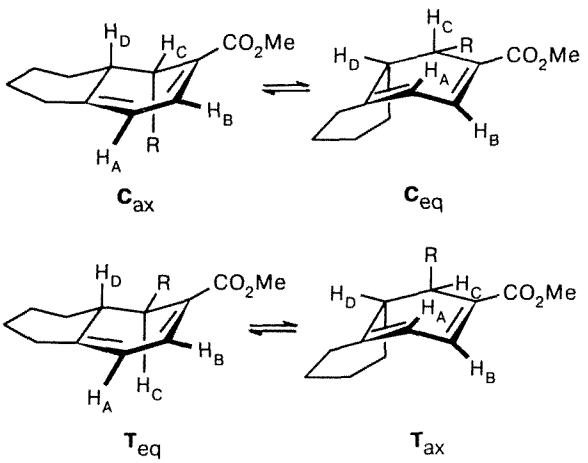
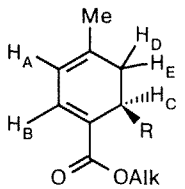
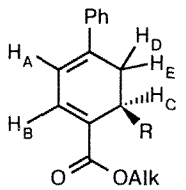


Table 3. ^{1}H NMR data ($CDCl_3$) for the derivatives of 1,3-cyclohexadienecarboxylic (**4**, **5**) and 1,5,6,7,8,8a-hexahydronaphthalene-2-carboxylic (**6**) acid



4 (R = H)



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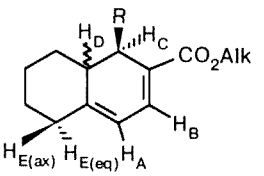

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Di-ene	δ (*J*/Hz)[a]								
	H_A	H_B[b]	H_C	H_D[c]	H_E[c]	4-Me	4-Ph	OAlk	R, $-(CH_2)_4-$
4a	5.72 (m)	7.03 (d)	2.60 (dd)[d,e]	2.21 (d)	2.41 (ddm)[e]	1.84 (s, 3 H)	—	3.74 (s, 3 H)	0.79 (d, 3 H)[f]; 0.87 (d, 3 H)[f]; 1.8 (m, 1 H)
4b	5.71 (m)	7.04 (d, 0.4 H); 7.06 (d, 0.6 H)	2.72 (m)	2.17 (d)	2.40 (ddm)[d]	1.83 > > 1.86 (both s, 3 H)	— —	3.74 (s, 3 H)	0.77 (m, 3 H); 0.88 (m, 3 H); 1.25—1.6 (m, 3 H)
4d	5.90 (m)	7.13 (d)	3.55 (ddd)[e,g,h]	2.27 (dd)[h]	2.71 (ddm)[g]	1.94 (s, 3 H)	—	3.78 (s, 3 H)	6.12 (dd, 1 H)[e,i]; 6.48 (d, 1 H)[i]; 7.32 (m, 5 H)
4e	5.91 (m)	7.4 (d)	4.02 (dd)[d,j]	2.36 (dd)[j]	2.90 (ddm)[d]	1.95 (s, 3 H)	—	1.22 (t, 3 H)[f]; 4.18 (q, 2 H)[f]	7.27 (m, 5 H)
4g	5.84 (m)	7.17 (d)	4.12 (dd)[g,h]	2.62 (m, 2 H)		1.86 (s, 3 H)	—	3.75 (s, 3 H)	5.92 (1 H, J = 0.5); 6.22 (dd, 1 H, J = 1.8, J' = 2.5); 7.28 (br.s, 1 H)
5a	6.48 (d)[b,k]	7.17 (d)	3.74 (ddd)[d,e,j]	2.70 (dd)[j]	2.95 (ddm)[d,k]	—	7.38 (m, 3 H); 7.52 (d, 2 H)	3.78 (s, 3 H)	1.65 (s, 3 H); 1.80 (s, 3 H); 5.20 (d)[e]
5b	6.55 (d)[b,k]	7.42 (d)[l]	4.20 (dd)[d,j]	3.05 (dd)[j]	3.25 (ddd)[d,k]	—	7.35 (m, 5 H)[l]	3.72 (s, 3 H)	—
5c	6.55 (d)[b,k]	7.47 (d)	4.24 (dd)[d,j]	3.02 (dd)[j]	3.27 (ddd)[d,k]	—	7.35 (m, 5 H)[l]	3.72 (s, 3 H)	3.88 (s, 3 H); 7.39 (d, 2 H)[m]; 7.91 (d, 2 H)[m]
5d	6.53 (dd)[b,k]	7.45[l]	4.15 (dd)[d,j]	2.98 (dd)[j]	3.25 (ddd)[d,k]	—	7.2—7.4 (m, 5 H)[l]	3.72 (s, 3 H)	3.86 (s, 3 H); 6.32 (d, 2 H)[m]; 7.65 (d, 2 H)[m]
5e	6.50 (dd)[b,k]	7.02 (d)	3.90 (dd)[d,j]	3.12 (m, 2 H)		—	7.3—7.4 (m, 5 H)[l]	—	0.79 (d, 3 H)[f]; 0.87 (d, 3 H)[f]; 1.8 (m, 1 H)
6a	5.73 (d, 0.67 H)[b]; 5.78 (ddd, 0.33 H)[b,k,p]	6.90 (d, 0.67 H); 6.94 (d, 0.33 H)	3.27 (dd, 0.67 H)[e,j]; 3.5 (dd, 0.33 H)[e,h]	~2.6 (m, 1 H)		—	—	3.62 + + 3.63 (both s, 3 H)	1.2—2.5 (m, 8 H)[l]; 1.68 + 1.77 (both s, 4 H)[l,n]; 1.63 + 1.72 (both d, 2 H)[l,n]; 5.13 (dm, 0.67 H)[e,n]; 5.00 (dm, 0.33 H)[e,n]
6b	5.83 (d, 0.9 H)[b]; 5.88 (dt, 0.1 H)[b,k,p]	7.13 (d, 1 H)	3.61 (d, 0.9 H)[j]; 3.92 (d, 0.1 H)[h]	~2.5 (m, 1 H)		—	—	1.18 + 1.20 (both t, 3 H)[f]; 4.06 + 4.08 (both q, 2 H)[f]	1.25—2.40 (m, 8 H); 7.3—7.5 (m, 5 H)

[a] All H_B protons are characterized by a typical AB-doublet with J_{AB} = 6; for all H_D and H_E protons a characteristic geminal coupling is observed with J_{DE} = 17—18. The constant J_{CR} relates to the vicinal coupling of H_C with the hydrogen atom attached to the C(1′) atom of the lateral group R. [b] J_{vic} = 6 Hz. [c] J_{DE} = 17—18 Hz. [d] J_{CE} = 9.5—10.5 Hz. [e] J_{CR} = 6.5—11 Hz. [f] J_{vic} = 6.5—7 Hz. [g] J_{CE} = 1.5—4 Hz. [h] J_{CD} = 7—8 Hz. [i] J_{vic} = 15 Hz. [j] J_{CD} = 1.4—4.0 Hz. [k] J_{AE} = 2.8—3.0 Hz. [l] Partly overlaps neighboring signals. [m] J_o = 8—9 Hz. [n] J_{All} = 1.3—1.5 Hz (interaction of Me and C<u>H</u> in $Me_2C{=}CH$). [p] $J_{All} \approx 3$ Hz (interaction of H_A and $H_{E(ax)}$ in **6a**,**b**).

Table 4. Other spectral characteristics of cyclic dienes **4—6**[a]

Diene	IR (thin film)[b], ν/cm^{-1}	UV (EtOH), λ_{max}/nm (ε)
4a	1705 (s), 1645, 1590, 1276, 1250	307 (8500)
4b	1710 (s), 1650, 1590, 1245, 1080	307 (9000)
4d	3075, 1710 (s), 1645, 1588, 1280, 1234	254 (14000) 300 (9760)
4e	3080, 1700 (s), 1645, 1635, 1590, 1492, 1270, 1240, 835	254 (280) 307 (10350)
4f	3080, 1707 (s), 1650, 1640, 1490, 1260, 1235, 830	254 (280) 305 (10900)
4g	3060, 1708 (s), 1640, 1583, 1496, 1435, 1273, 1250, 1234, 770	218 (7800) 302 (9270)
5a	3075, 1708 (s), 1664, 1592, 1560, 1445, 1432, 1260, 1240, 830	230 (19600) 338 (40000)
5b	3080, 1707 (s), 1610, 1560, 1435, 1260, 1235	235 (19500) 342 (23000)
5c	1718 (s), 1710 (s), 1610, 1560, 1260	238 (22400) 342 (16000)
5d	1710 (s), 1710 (sh), 1605, 1590, 1250	235 (21000) 346 (18000)
5e	3070, 2208, 1682, 1600, 1550, 1438, 745	237 (8300) 341 (14000)
6a	3040, 1708 (s), 1645, 1585, 1440, 1280, 1250, 1232	310 (10600)
6b	3090, 1710 (s), 1650, 1590, 1250	255 (240) 304 (9000)

[a] For compounds of series **4** mass spectrometric determination of molecular ions (EI, 70 eV) gave the following values of *m/z*: **4a** — 194, **4b** — 208, **4d** — 254, **4e** — 242, **4f** — 228, **4g** — 218. [b] For compounds **5a—5d**, in KBr pellets.

for the observed values of the spin-spin coupling constants in the ^1H NMR spectra of **6a** and **6b** was in good agreement with the conformation $\mathbf{T}_{ax}$, while the second assumption was not compatible with any of the four conformations. The fact that 1,8a-*trans*-isomers of **6a** and **6b** are in the $\mathbf{T}_{ax}$ conformation demonstrates once more the tendency of bulky substituents at the allylic carbon atom of 1,3-cyclohexadienes to occupy axial positions (*cf.* Ref. 11).

trans-Configuration of the major stereoisomers in products **6a** and **6b** was also confirmed by applying the MM2 technique to the modeling of spin-spin coupling constants. Optimization of geometric parameters for each of the stable conformers of 1,8a-*cis*- and 1,8a-*trans*-isomers of **6a** and **6b** employing a PC MODEL program that takes into account π-conjugation of sp^2-hybridized atoms afforded values of the dihedral angles φ between the vicinal atoms H_C and H_D, and dihedral angles ψ relevant to the allylic interactions of H_C with H_B as well as of H_A with H_D, H_E, and $H_{E'}$ (Table 5). The constants of vicinal interaction corresponding to the angle φ ($^3J_{CD}$) were obtained automatically, while the constants of allylic interactions ($^4J_{BC}$, $^4J_{AD}$, $^4J_{AE}$, and $^4J_{AE'}$) were calculated by using the semiempirical Barfield's equation.[12]

Comparison of the splitting patterns corresponding to the major and minor components of the binary mixtures of **6a** and **6b** (see Table 3) with the calculated dihedral angles and spin-spin coupling constants (see Table 5) showed that the best fit of experimental and calculated values of $^3J_{CD}$ and $^4J_{BC}$ occurs in the conformation $\mathbf{T}_{ax}$. Moreover, in this case all the three constants relating to the proton H_A ($^4J_{AD}$, $^4J_{AE}$, and $^4J_{AE'}$) are close to zero; as a consequence, in ^1H NMR spectra **6a** and **6b** the signals of H_A of the major stereoisomers appear as typical AB-doublets of a two-spin system.

In the spectra of **6a** and **6b** the signals of H_C attributable to the minor components are splitted with a large constant characteristic of vicinal H—H interaction ($^3J_{CD}$ = 7—8 Hz), but no allylic splitting is visible ($^4J_{BC} \approx 0$ Hz). On the other hand, the signals of H_A in the minor components are markedly broadened due to the allylic interaction of H_A with H_D and with the quasi-axial hydrogen atom in the methylene group at C(5). Comparing the data of Tables 3 and 5 suggests that the minor components are 1,8a-*cis*-isomers. Again, it is the axial conformation ($\mathbf{C}_{ax}$) that is favored since in this case the calculated values of $^4J_{AD}$ and $^4J_{AE}$ best fit those found experimentally (*ca.* 3 Hz).

Assuming that the 1,8-*trans*-configuration of the preponderant stereoisomers of dienes **6a,b** correlates with the *Z*-configuration of the main components of the respective dienophiles **2c** and **2e** one has to conclude that the configuration of *trans*-**6a** and *trans*-**6b** arises from the *exo*-addition of the dienamine **10** (which is formed *in situ* from **1c**) to (*Z*)-**2c** or (*Z*)-**2e**, *i.e.*, that the [4+2]-cycloaddition step proceeds mostly with disregard to the Alder principle of the maximum accumulation of π-bonds. At the same time, the content of 1,8a-*trans*-isomers in the reaction products is somewhat lower than the content of *Z*-isomers in the starting dienophiles: the former in **6a** and **6b** is ~67 and ~90 %, respectively, while the latter in their precursors **2c** and **2e** amounts to ~80 and 92 %, respectively. It seems plausible that the *exo*-addition of **10** to (*Z*)-**2c** and (*Z*)-**2e** takes place largely *via* an oriented complex **A** (Scheme 2) in which the amino group of the dienamine and the carboxy group of the dienophile are drawn together due to the formation of a labile dienammonium salt (*cf.* Ref. 13). However, to a certain extent the reaction of dienamine **10** with (*Z*)-**2c,e** proceeds as well through the alternative complex **B** where the mutual orientation of the reactants corresponds to the *endo*-cycloadducts and, eventually, to the 1,8a-*cis*-isomers of **6a** and **6b**.

Both in the *exo*- and *endo*-cycloadducts mutual arrangement of the amino and carboxy groups is favorable to their synchronous elimination (through a cyclic or a *trans*-periplanar transition state, respectively), which results in formation of a 1,3-cyclohexadiene system and regeneration of the amine catalyst.

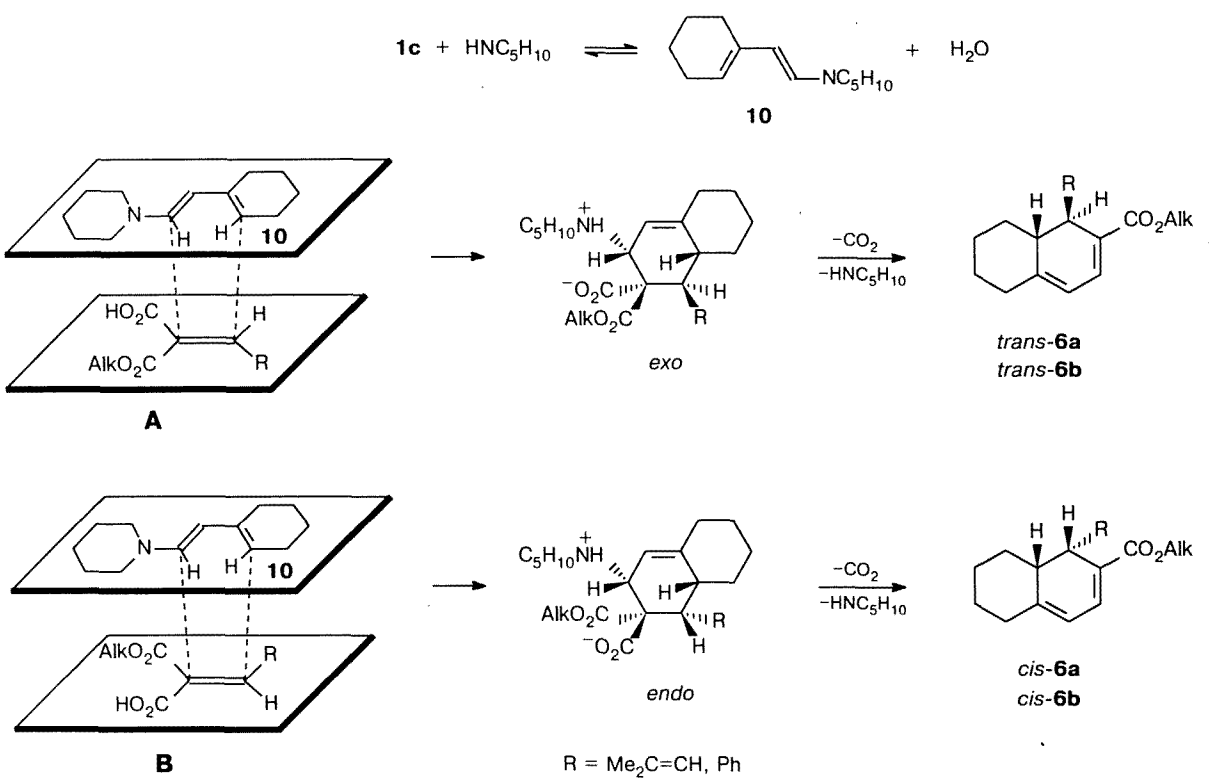
Table 5. Calculated values of dihedral angles H_C—C(1)—C(8a)—H_D (φ_{CD}), H_C—C(2)—C(3)—H_B (ψ_{BC}), H_D—C(8a)—C(4)—H_A (ψ_{AD}), H_E—C(5)—C(4)—H_A (ψ_{AE}), and $H_{E'}$—C(5)—C(4)—H_A ($\psi_{AE'}$) in the energy optimized conformations of compounds **6a** and **6b** and the respective constants of vicinal ($^3J_{CD}$) and allylic spin-spin coupling

Configuration and conformation of diene	Angle/deg					J_{H-H}/Hz				
	φ_{CD}	ψ_{BC}	ψ_{AD}	ψ_{AE}	$\psi_{AE'}$	$^3J_{CD}$	$^4J_{BC}$	$^4J_{AD}$	$^4J_{AE}$	$^4J_{AE'}$
1,8a-*cis*										
6a (C_{ax})	49.2	150.1	84.5	98.7	19.8	4.6	0.5	−2.7	−2.5	0.5
6b (C_{ax})	40.4	142.9	87.6	96.5	22.0	6.3	−0.1	−2.8	−2.5	0.4
6a (C_{eq})	34.7	92.2	137.6	130.0	10.9	6.5	−2.8	−0.4	−0.7	0.9
6b (C_{eq})	41.5	86.6	138.4	130.0	10.3	6.0	−2.8	−0.4	−0.7	0.9
1,8a-*trans*										
6a (T_{eq})	172.9	86.1	86.3	22.5	96.1	12.4	−2.8	−2.8	0.4	−2.6
6b (T_{eq})	177.2	80.3	85.1	21.0	97.0	12.5	−2.7	−2.8	0.4	−2.6
6a (T_{ax})	86.8	145.2	139.0	130.2	10.6	0.4	0.0	−0.3	−0.7	0.9
6b (T_{ax})	96.3	138.3	135.4	128.0	8.0	0.4	−0.4	−0.6	−0.8	0.9

Note. In all cases the energy minima for **6a,b** correspond to the disruption of conjugation between the CO_2Alk group and the C(2)—C(3) double bond. The former lies in a plane, the inclination of which over the plane of the Δ^2 double bond is 45±3° (135±3°); the groupings R and OAlk are situated on opposite sides of the ring system.

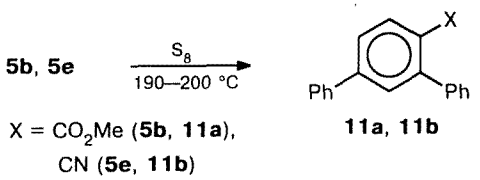
Summing up, the results of the study imply that the reaction of β,β-disubstituted α,β-alkenals with the acidic monoalkyl ylidenemalonates in presence of a secondary amine is a fairly simple and general way to 1,4,6-trisubstituted 1,3-cyclohexadienes and their fused polycyclic analogs. In the latter case the process affords preponderantly the products corresponding to the *exo*-addition of the intermediate dienamine to the dienophile. Although the formation of cyclohexenes from 1-amino-1,3-butadienes and olefinic dienophiles was reported long ago,[14] their conversion to cyclohexadienes (which formerly was carried out in two steps[15]) made so far little appeal to

Scheme 2



synthetic organic chemists. Present modification of this approach, which unites in one operation three consecutive reactions (the formation of a dienamine, [4+2]-cycloaddition, and 1,2-elimination) makes it possible to obtain various functionally substituted cyclohexadienes in preparatively attractive yields. These products may be of interest as intermediates in the synthesis of polynuclear carbocycles.

With a view of demonstrating synthetic usefulness of 1,3-cyclohexadienes obtained in this work compounds **5b** and **5e** were subjected to dehydrogenation with elemental sulfur. This procedure afforded the respective aromatization products, **11a** and **11b**, in about 30 % yields; the structures of **11a,b** were confirmed by their spectral characteristics.



Thus, transforming enals of the type **1b** into adducts of the type **5** and submitting the latter to dehydrogenative aromatization appears to be a convenient protocol for the regiocontrolled synthesis of functionally substituted *meta*-terphenyls.

Experimental

Reactions were monitored and the purity of isolated products was controlled by TLC on Silufol plates. Compounds **4f**, **5c**, **5d**, **6a**, and **6b** and the products formed upon reacting enal **1c** with **2c** were additionally analyzed by GC using an LKhM-8 MD instrument equipped with a flame ionization detector and a stainless steel column (1.5×0.003 m) filled with 5 % XE-60 on Chromaton N-AW-DMCS (deactivated with hexamethyldisilazane) as the stationary phase; N_2 was used as the eluent (injector temperature 200 °C, oven temperature program 80 °C + 3 °C min^{-1}). Column chromatography was performed on Silicagel L (particle size 40—100 μm). ^1H NMR spectra were recorded on a Bruker WM-250 (250 MHz) spectrometer in $CDCl_3$. IR spectra were taken using a Perkin-Elmer 577 instrument either in thin films (for liquids) or in KBr pellets (for solids). UV spectra were measured in EtOH using a Specord UV-Vis spectrophotometer. Molecular masses of the products were determined on a Varian MAT-311A mass spectrometer (EI, 70 eV).

Aldehydes **1a—c** were obtained by the vanadate-catalyzed rearrangement of isomeric acetylenic carbinols employing a known procedure[16]; the aldehyde **1b** thus prepared contained the *E*- and *Z*-isomers in a ratio of ~1 : 5. Aldehydes **1e** and **1f** were kindly provided by Dr. Zh. A. Krasnaya (N. D. Zelinsky Institute of Organic Chemistry of the RAS); nitrile **3** was obtained according to Ref. 17. Melting points are not corrected.

Acidic monoesters of ylidenemalonic acids 2a—i (general procedure). To a solution of an aldehyde (2-methylpropanal, 3-methylbutanal, 3-methyl-2-butenal, 3-phenyl-2-propenal, benzaldehyde, 4-(methoxycarbonyl)benzaldehyde, anisaldehyde, furfural) (50 mmol) with dimethyl or diethylmalonate (50 mmol) in dry benzene (20 mL) piperidine (0.43 g, 5 mmol) and glacial AcOH (0.3 g, 5 mmol) were added. The reaction mixture was left for 12 h at 20—25 °C and then evaporated under reduced pressure. The residue was fractionated *in vacuo* to give the respective dimethyl or diethyl ylidenemalonate, which was characterized by its GC or TLC data and ^1H NMR spectroscopy.

The diester (20 mmol) was dissolved in methanol (13 mL, for the synthesis of **2e** MeOH was replaced by EtOH) and treated with a solution of KOH (1.23 g, 22 mmol) in water (7 mL), and the mixture was diluted with a minimum volume of THF to provide for its homogeneity (7 mL to prepare **2b**, 8 mL for **2d**, 1.5 mL for **2i**; in the synthesis of **2g** a mixture made of 110 mL of THF and 70 mL of water was used instead of MeOH). The reaction mass was stirred at 20—25 °C for 16 h and concentrated in a rotative evaporator to deposit the potassium salt of the monoester. This residue was dissolved in a minimum of water, and the non-polar admixtures were extracted with Et_2O (2×5 mL). The aqueous layer was acidified with diluted (17.5 %) hydrochloric acid to pH 5.5—6.0 and extracted with Et_2O (3×5 mL). The ethereal extract was washed with water (2×3 mL), dried with Na_2SO_4, and evaporated. Solid products (**2c—i**) were purified by recrystallization or by precipitating them with hexane from the ethereal solution, the oily products (**2a,b**) were column chromatographed on SiO_2 using a hexane—Et_2O gradient system.

Derivatives of 1,3-cyclohexadienecarboxylic acid (4, 5) and 1,5,6,7,8,8a-hexahydronaphthalene-2-carboxylic acid (6) (general procedure). To a mixture of an aldehyde (**1a—c**) with a dienophile (**2a—i** or **3**), dissolved in 2 mL of dry benzene, 1 mL of a 0.1 *M* solution of piperidine (8.5 mg, 0.1 mmol) was added in the same solvent, and the reaction mass was refluxed and periodically analyzed (TLC) until the reactants had disappeared. Then the solvent was stripped off under reduced pressure, and the residue was dissolved in hexane or in hexane—Et_2O (4 : 1, v/v) and purified by column chromatography on SiO_2 using gradient hexane—Et_2O systems as the eluent. Solid products (**5a—d**) were purified by recrystallization or reprecipitated with hexane from their ethereal solutions.

In the case of the reaction of **1b** with **3** THF (2 mL) was added to make the reaction mixture homogeneous.

***m*-Terphenyls 11a,b (general procedure).** Diene **5b** or **5e** (0.35 mmol) was thoroughly mixed with elemental sulfur (11.2 mg, 0.35 mmol), and the mixture was heated for 90 min at 195—200 °C in a slow stream of argon. The residue was dissolved in benzene and column chromatographed on SiO_2 using a gradient hexane—Et_2O system as the eluent.

Methyl 2,4-diphenylbenzoate (11a) was isolated in a 30 % yield. M.p. 74—75 °C (from MeOH), R_f 0.43 (heptane—Et_2O, 1 : 1). Lit.[18]: m.p. 75.5—76 °C. MS, *m/z* (I_{rel} (%)): 288 $[M]^+$ (100), 257 (98), 229 (17), 228 (28). UV, λ_{max}/nm: 250 (ε 28000), 268 sh (ε 24700). IR, ν/cm^{-1}: 3070, 1725 (s), 1600, 1580, 1560, 1480, 1432, 1255, 1190, 840. ^1H NMR, δ: 3.68 (s, 3 H, Me); 7.42 (m, 9 H, Ar); 7.65 (m, 3 H, Ar); 7.98 (d, 1 H, AB-doublet, C(6)H, J_o = 8 Hz).

2,4-Diphenylbenzonitrile (11b) was isolated in a 33 % yield. M.p. 67—68 °C (from MeOH), R_f 0.38 (heptane—Et_2O, 1 : 1). Lit.[18]: m.p. 69—70 °C. MS, *m/z* (I_{rel} (%)): 255 $[M]^+$ (100). UV, λ_{max}/nm: 257 (ε 22000), 276 (ε 19500). IR, ν/cm^{-1}: 3070, 2217, 1605 (sh), 1600, 1478, 902, 840. ^1H NMR, δ: 7.5 (m, 6 H); 7.66 (m, 5 H); 7.75 (d, 1 H, C(3)H, J_m = 1.4 Hz); 7.85 (d, 1 H, AB-doublet, C(6)H, J_o = 8 Hz).

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