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FLASH VACUUM THERMOLYSIS OF SPIROCYCLOHEXADIENONES

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Abstract - In an attempt to prepare short-bridged hydroxymetacyclophanes 1b-d, the spirocyclohexadienones 2b-d were pyrolyzed by flash vacuum thermolysis (FVT). Instead of 1b-d, variable amounts of 4-(5-hexenyl)phenol (4b), β-hydroxybenzocycloalkenes (5b-d) and 4-(*trans*-1-alkenyl)phenols (6c-d) were obtained. The formation of these products is explained by invoking cleavage of a spiro bond in 2 under formation of the intermediate diradical 3 which, depending on the length of the aliphatic chain and on the temperature, has several pathways open for isomerization to spin-paired products.

In connection with our studies on the synthesis of short-bridged [n]paracyclophanes and [n]metacyclophanes, we recently reported that 9-hydroxy[7]metacyclophane (1a; n = 7) was formed on flash vacuum thermolysis (FVT) of the spirocyclohexadienone 2a; 4-(6-heptenyl)phenol (4a) was another product from this reaction.[1] While the formation of 1a could be explained by invoking the intermediacy of the diradical 3a (Scheme 1), the mode of formation of 4a was less obvious.

It appeared of interest to investigate the scope of this approach; in particular, the synthesis of smaller hydroxy[n]metacyclophanes 1b-d (n = 6,5,4, respectively) was desirable. We here report that on FVT of 2b-d, no metacyclophanes were obtained; instead, the β-hydroxysubstituted benzocycloalkenes 5 were formed, together with 4-alkenylphenols 4 and/or 6. Although the primary synthetic goal could therefore not be realized, the interesting dependence of product formation on the chain length n permitted a more detailed analysis of the mechanism of these reactions.

RESULTS AND DISCUSSION

Compounds 2 were prepared by published procedures.[2,3] When 2 were subjected to FVT (4.10^{-2} mbar, alumina tube; see Experimental), pyrolysates were obtained with good recovery of material (usually 90% or better). They were analyzed by ^{1}H NMR spectroscopy and analytical and preparative GLC and shown to be mixtures of starting material 2 and the new, isomeric, products 4, 5 and 6, depending on the length n of the oligomethylene chain and on the temperature. As previously reported, 2a gave only 1a and 4a; 2b furnished 4b, 5b and 6b; 2c gave 5c and a trace of 6c; 2d was found to yield 5d exclusively (Table 1). On FVT of 5b-d at temperatures up to 800°, the starting material was recovered in practically quantitative yield.

The structures of the new compounds were derived from their spectral data (see Experimental). Compounds 5b-d were independently synthesized by treatment of 2b-d, respectively, with aluminium trichloride in dichloromethane at 0°C; this cationic rearrangement[4] proceeded quantitatively.

Scheme 1

(**a**: n=7 ; **b**: n=6; **c**: n=5; **d**: n=4)

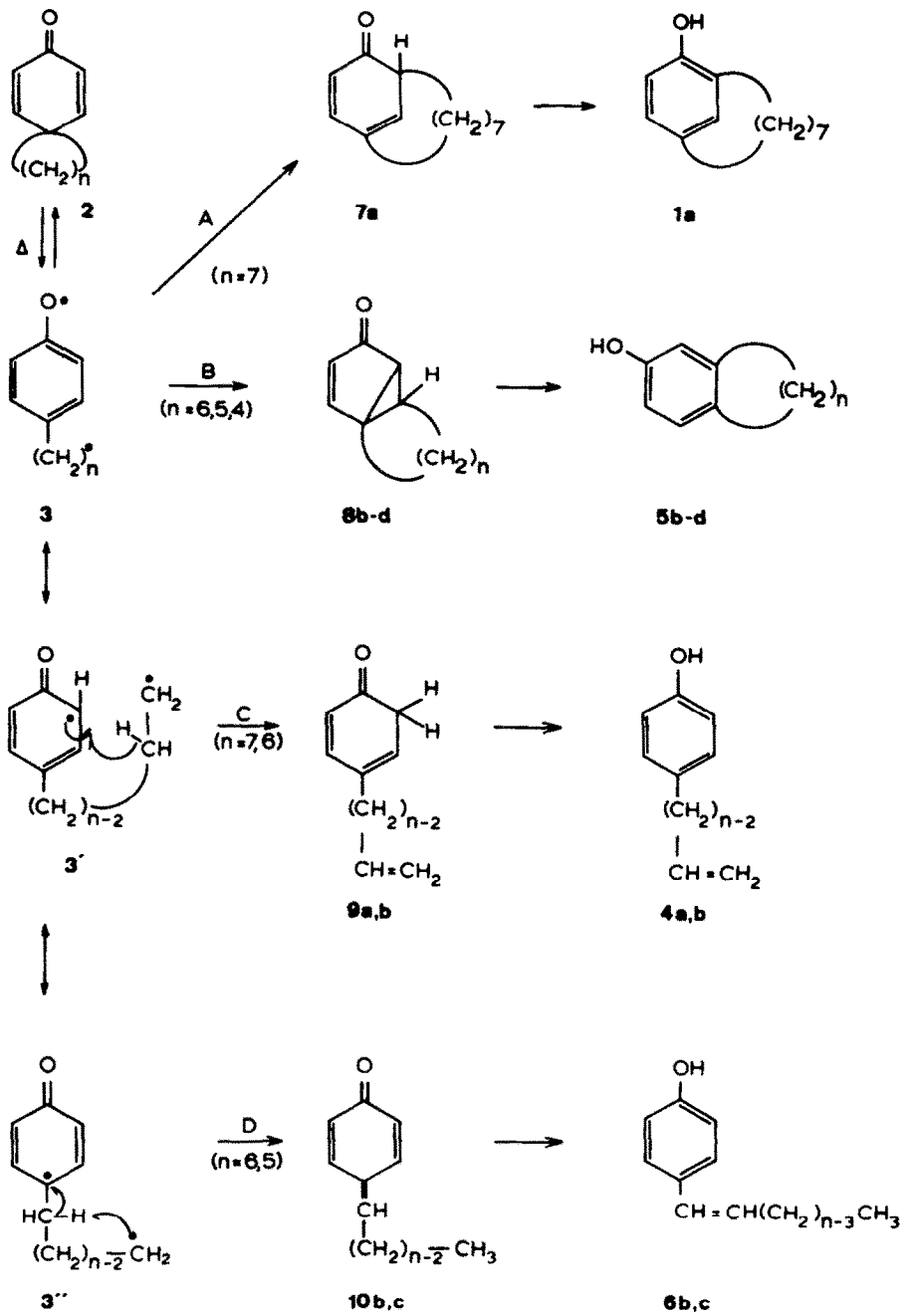

Table 1. Products of the flash vacuum thermolysis of 2 (%) [a]

2	n	T [°C]	2	1	4	5	6
a [b]	7	520	38	29	23	0	0
		560	14	23	53	0	0
		600	0	15	75	0	0
		650	0	0	90	0	0
b	6	520	65	0	0	25	0
		560	45	0	26	19	0
		600	11	0	63	16	trace
		650	0	0	56	11	23
c	5	520	51	0	0	39	0
		560	21	0	0	69	0
		600	14	0	0	76	0
		650	0	0	0	90	trace
d	4	520-650	0	0	0	90	0

[a] Total recovery ca. 90%; product ratios determined from integral ratios of ^{1}H NMR spectra of the pyrolysate. [b] From ref. 1.

As previously postulated in the case of 2a,[1] we feel that the initial step in all reactions 2b-d is the cleavage of one of the spiro bonds to furnish the diradical intermediate 3 (Scheme 1). As 2 and 3 are isomeric, the ease of this bond cleavage reaction should parallel differences of strain in the ground state of 2. With the exception of 2d, this seems roughly to be the case; the six- and seven-membered rings of 2c and 2b, respectively, open with comparable ease, while the slightly more strained eight-membered ring of 2a reacts faster. In fact, we feel that the amount of 2 recovered in the lower temperature range does not fully reflect the ease of ring opening, but rather is a balance of ring opening and ring closure, the latter being one of the options available to 3. Only 2d does not fit into this picture, as it is much too reactive. However, 2d has been reported to be a rather sensitive compound which rearranges to 5d under a variety of conditions.[5] Therefore, it cannot be excluded that other pathways are competing in the thermolysis of 2d; on the other hand, the nearly exclusive formation of 5c from 2c, even at temperatures where starting material is partially recovered, illustrates that a radical process may be operating in all cases.

In view of the high spin density of phenoxy radicals of the *ortho*- and *para*-positions (cf. the resonance structures 3' and 3" in Scheme 1), one may expect that 3 can form stable, spin-paired products by two modes of intramolecular radical combination: either the unproductive *para*-attack to give 2, or *ortho*-attack to give 7 (Scheme 1, pathway A); the latter could rearrange to the aromatic cyclophane 1. Clearly, this reaction pathway is only possible when the aliphatic chain is long enough. At first sight, it would appear that this condition is only fulfilled for n = 7, as only 1a is obtained. However, a closer investigation of the heats of formation of possible intermediates (Table 2) reveals that even in the d-series (n = 4), 3 has sufficient energy to form 7; entropy should favour the ring closure of the shorter bridges even more.

Absence of 1b,c,d among the pyrolysis products of the corresponding 2 is therefore not so much a consequence of the fact that the formation of 7 is impossible. Rather, the following step, the rearrangement of 7 to 1, is unfavourable even in the most favourable case of 7b, this rearrangement to 1b is endothermic by about 10 kcal.mol^{-1}, and the activation barrier is apparently considerably higher. So 7 is reconverted to 3 instead.

Table 2. Estimated heats of formation (ΔH_f° in kcal.mol^{-1})

Compound	n	1 [a]	2 [b]	3 [c]	5 [b]	7 [d]	8 [c]
a	7	-26.9	-17.1	46.9	-41.0	-24.0	-5.0
b	6	- 8.7	-15.7	51.9	-40.5	-18.3	-3.0
c	5	- 5.5	-17.1	56.8	-36.5	-10.8	-1.5
d	4	36.9	- 5.9	61.8	-35.2	6.5	-3.0

[a] Calculated from the heat of formation of the parent hydrocarbon (obtained from MNDO[9] calculations) with group increments for the conversion to the phenol.[10]
[b] Calculated from the heat of formation of 4,4'-dimethylcyclohexa-2,5-dienon (the dimethyl analogue of 2; obtained from MNDO[9] calculations) and group increments.[10]
[c] Calculated from the equation $\Delta H_f^\circ(3) = \Delta H_f^\circ(HOC_6H_4(CH_2)_{n-1}CH_3)$ [b] + D(O-H) + D(-CH_2-H) - 2 ΔH_f°(H·).[10]
[d] Calculated from the heat of formation of 4,6-dimethylcyclohexa-2,4-dienon (the dimethyl analogue of 7; obtained from MNDO[9] calculations) and group increments;[10] strain energies of *trans*-cycloalkene substructures were taken from ref. 11.
[e] Calculated from the heat of formation of 1,6-dimethylbicyclo[3.1.0]hex-2-en-4-one (the dimethyl analogue of 8; obtained from MNDO[9] calculations) and group increments.[10]

The same considerations apply a fortiori to 3c and 3d. Pathway A being (highly) unfavourable in these cases for geometric reasons, other pathways get a chance which are normally not competing because of an inherently higher activation barrier. We first consider the formation of the olefinic phenols 4a, 4b, 6b and 6c (trace), which can be rationalized on the basis of the spin distribution in the phenoxy radical 3. From resonance structure 3'a, transfer of the activated β-hydrogen of the aliphatic radical to the *ortho*-position (Scheme 1, pathway C) leads also to a spin-paired product, i.e. 9. Neither the formation of 9 nor its aromatization to 4 is hampered by ring strain in the products. However, only in 3a and 3b, the aliphatic chain appears to be long enough for this hydrogen to reach the *ortho*-position. In 3c, this is obviously impossible, and another process with still higher activation energy becomes discernible: trace amounts of 6c indicate attack of the aliphatic radical center at the hydrogen α to the six-membered ring which is activated towards β-cleavage by the spin indicated in resonance structure 3" (Scheme 1, pathway D). This results in the formation of the quinomethane 10c which aromatizes to 6c. In 3b, this process leading to 6b becomes increasingly prominent at higher temperatures at the expense of both pathway C and B (products 4b and 5b, respectively). This, too, implies a higher enthalpy of activation for pathway D. Presumably, the β-hydrogen cleavage is more activated by the localized radical of the aliphatic chain (pathway C) than by the delocalized phenoxy radical (pathway D); also, the C-H bond formed in the latter proces is stronger.

Finally, the formation of the aromatic "*ortho*-cyclophane" 5 has to be explained. Initially, we discussed the possibility that 5 might be formed by pathway A via 7 and 1 as intermediates: a thermal isomerization of 1 to 5 would find a precedent in the postulated thermal isomerization of [5]metacyclophane to benzocycloheptene.[7,8] However, we consider this sequence of events less likely for two reasons. In the first place, 1a was thermally stable at 800°C; secondly, valence isomerization of 1 to 5 would be expected to give, besides 5, also the α-hydroxyisomer which was never observed. We therefore prefer pathway B of Scheme 1 to explain the formation of 5, invoking the intermediacy of the bicyclo[3.1.0]hexenone-intermediate 8. Formally, 8 is formed by attack of the aliphatic radical in 3 on the position *meta*-relative to the oxygen. This attack does not profit from the spin density at the *ortho*- and *para*-positions of the phenoxy radical. However, it should not be worse than radical attack at any normal aromatic ring, and the calculated heats of formation of 8 (see Table 2) indicate that 8, while somewhat energetic, is thermodynamically accessible from 3. Although both pathway B and D seem geometrically feasible, pathway B apparently wins in the lower temperature range because of its lower activation enthalpy. Once formed, 8 probably rearranges rapidly and irreversibly to 5.

CONCLUSION

The pyrolytic conversion of spirodienones 2 to hydroxy[n]metacyclophanes 1 is limited to the a-series (n = 7). Although very likely the same intermediate diradical 3 is primarily formed in all instances, the shorter-bridged representatives (n = 6,5,4) undergo escape reactions as rationalized in Scheme 1.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker WM 250 or WH 90 spectrometer at a frequency of 250 MHz or 90 MHz respectively. All products were analyzed by GCMS, using a Finnigan 4000 mass spectrometer; exact mass measurements were performed with a Varian CH-5 DF mass spectrometer at an ionization potential of 70 eV.

Spirodienones 2b-d

These compounds were prepared as described in the literature[2,3].

Spiro[5,6]dodeca-1,4-dien-3-one (2b)

^{1}H NMR (250 MHz, $CDCl_3$, δ in ppm) 7.00 and 6.19 (AB system, J_{AB} = 10.1 Hz, 4H), 1.67 (m, 12H).
Mass spectrum m/z (%): 176 (19) $2b^{+\cdot}$, 107 (100); calc. for $C_{12}H_{16}O$ 176.1201, found 176.1200.

Spiro[5,5]undeca-1,4-dien-3-one (2c)

^{1}H NMR (250 MHz, $CDCl_3$, δ in ppm) 7.10 and 6.26 (AB system, J_{AB} = 10.0 Hz, 4H), 1.63 (m, 10H).
Mass spectrum m/z (%): 162 (38) $2c^{+\cdot}$, 91 (100); calc. for $C_{11}H_{14}O$ 162.1044, found, 162.1036.

Spiro[4.5]deca-6,9-dien-8-one (2c)

Its physical data were in agreement with reported data[3].

Flash vacuum theromlysis (FVT) of 2b-d

The FVT apparatus was modelled after the design of R.F.C. Brown.[12] We thank Prof. B. Zwanenburg Dr. A.J.H. Klunder and their coworkers for assistance and advice.
In our experiments, a 28 cm aluminium oxide tube and a pressure of 0.04 mbar were applied. In a typical run, 2 was evaporated into the hot zone at a rate of 50 mg per hour, using a sublimation furnace (Büchi GKR50) to heat the sample bulb. The pyrolysate was trapped in a cold trap, cooled with dry ice in acetone at -70°C. After pyrolysis of the substrate the pyrolysate was collected from the cold trap by washing with diethyl ether. The solvent was evaporated at reduced pressure; the residue was ~ 90% by weight. Products were isolated by preparative GLC (15% SE-30 on Chromosorb W, length 1.5 m). The products were identified on the basis of their spectral data.

4-(5-Hexenyl)phenol (4b)

^{1}H NMR (250 MHz, $CDCl_3$, δ in ppm) 7.05 and 6.74 (AB system, J_{AB} = 10.0 Hz, 4H), 5.82, 5.00 and 4.94 (ABX system, J_{AB} = 1.5 Hz, J_{AX} = 17 Hz, J_{BX} = 10.0 Hz, 3H, CH_2=CH-), 4.60 (bs, OH), 2.55 (t, ^3J = 7.3 Hz, 2H, benzylic CH_2), 2.08 (m, ^3J = 6.7 Hz, ^3J = 7.2 Hz, 2H, allylic CH_2), 1.67-1.33 (m, 4H).
Mass spectrum m/z (%): 176 (23), $4b^{+\cdot}$, 107 (100); calc. for $C_{12}H_{16}O$ 176.1201, found 176.1207.

5,6,7,8,9,10-Hexahydro-2-hydroxybenzocyclooctene (5c)

^{1}H NMR (90 MHz, $CDCl_3$, δ in ppm) 6.99 and 6.62 (AB system, J_{AB} = 9.0 Hz, on B part J_{BX} = 2.0 Hz, 2H), 6.57 (d, J_{BX} = 2.0 Hz, 1H), 5.31 (bs, OH) 2.69 (m, 4H) 1.67 (m, 4H).
Mass spectrum m/z (%): 176 (78) $5b^{+\cdot}$, 133 (100); calc. for $C_{12}H_{16}O$ 176.1201, found 176.1197.

6,7,8,9-Tetrahydro-2-hydroxy-5*H*-benzocycloheptene (5c)

^{1}H NMR (250 MHz, $CDCl_3$, δ in ppm) 6.96 and 6.55 (AB system, J_{AB} = 7.9 Hz, on B part J_{BX} = 2.7 Hz, 2H) 6.61 (d, J_{BX} = 2.7 Hz, 1H), 4.52 (bs, OH), 2.73 (m, 4H), 1.81 (m, 2H), 1.63 (m, 4H).
Mass spectrum m/z (%): 162 (100) $5c^{+\cdot}$ 133 (66); calc. for $C_{11}H_{14}O$ 162.1044, found 162.1050.

6-Hydroxytetralin (5d)

Its physical data were in agreement with those reported.[3]

4-(*trans*-1-Hexenyl)phenol (6b)

^{1}H NMR (250 MHz, $CDCl_3$, δ in ppm) 7.22 and 6.76 (AB system, J_{AB} = 10.0 Hz, 4H), 6.30 and 6.06 (AB system, J_{AB} = 15.0 Hz, on B part, ^3J = 7.5 Hz, 2H) 4.50 (bs, OH), 2.19 (m, ^3J = 7.5 Hz, ^3J = 7.0 Hz, 2H, allylic CH_2) 1.36 (m, 4H), 0.93 (t, ^3J = 7.5 Hz, 3H).
Mass spectrum m/z (%): 176 (86) $6b^{+\cdot}$, 133 (100); calc. for $C_{12}H_{16}O$ 176,1201, found 176.1207.

4-(*trans*-1-Pentenyl)phenol (6c)

^{1}H NMR (250 MHz, $CDCl_3$, δ in ppm) 7.20 and 6.84 (AB system, J_{AB} = 8.7 Hz, 4H), 6.31 and 6,07 (AB system, J_{AB} = 17.5 Hz, on B part ^3J = 7.5 Hz, 2H), 4.50 (bs, OH), 2.13 (m, ^3J = 7.5 Hz, ^3J = 6.8 Hz, 2H, allylic CH_2), 1.55 (m, 2H), 0.95 (t, ^3J = 7.3 Hz, 3H).

Mass spectrum m/z (%): 162 (65) $\underset{\sim}{6c}^{+\cdot}$, 147 (100); calc. for $C_{11}H_{14}O$ 162.1044, found 162.1050.

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