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Molecular baskets based on tetramercaptotetrathiacalix[4]arene and tetrathiacalix[4]arene

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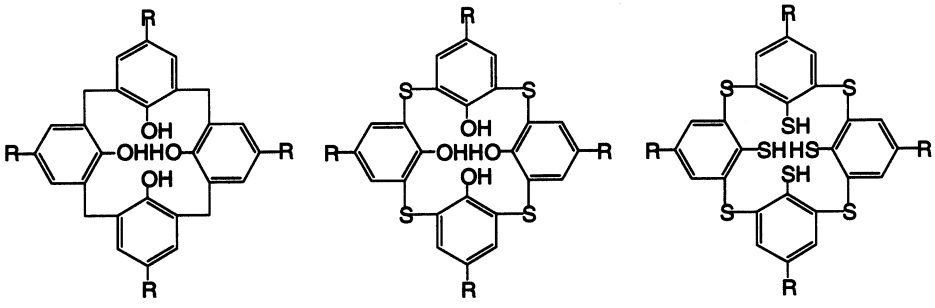
Abstract—Upon treatment of *p*-*t*but-tetrathiacalix[4]arene and *p*-*t*but-tetrathiatetramercaptocalix[4]arene by 1,2-dibromoethane in the presence of K_2CO_3 two new basket-type derivatives are obtained and their structures characterised in the solid state by X-ray diffraction on single crystals.

Calixarenes are very useful macrocyclic frameworks.[1,2] In particular, the calix[4]arene **1** has been widely used as a scaffold for the design of a variety of new receptors. Dealing with cyclic tetramers of phenol, an efficient procedure was recently reported leading to the tetrathiacalix[4]arene **2** for which the methylene junctions between the phenolic moieties are replaced by sulfur atoms was reported (Scheme 1).[3–5] The remarkable binding ability of the thiacalix[4]arene **2** towards transition metals was investigated.[6,7] The synthesis of the tetramercaptotetrathiacalix[4]arene **3**, in which the methylene junctions between the aromatic moieties are replaced by S atoms and all four OH groups are substituted by SH moieties has also been reported.[8] The syntheses of di[9,10] and tetra[11,12] mercaptocalix[4]arenes in which two or four OH groups were replaced by SH groups was also reported, as well the *O*-alkylation of **2**.[13,14]

Pursuing our effort on the design of new koilands[15] (multicavity receptor molecules) based on fusion of two thiacalix units by connecting chains, we have investigated the formation of compounds **4**–**7** (Scheme 2). These derivatives, due to the presence of the halogen atoms, are interesting precursors for the design of koilands and other calixarenes.

In order to prepare compound **4**, the calix **2**, prepared according to a published procedure,[4] was treated at 80°C with an excess of dibromoethane in dry DMF and in the presence of K_2CO_3. However, after purification of the mixture, NMR studies revealed that the isolated compound (22% yield) could not be the expected one. In order to establish its structure, single crystals were grown from a $CHCl_3$/MeOH solution. The X-ray diffraction[16] study revealed that the isolated compound was the basket type derivative **8**.[17] This compound



1 R = $(CH_3)_3C$ **2** R = $(CH_3)_3C$ **3** R = $(CH_3)_3C$

Scheme 1.

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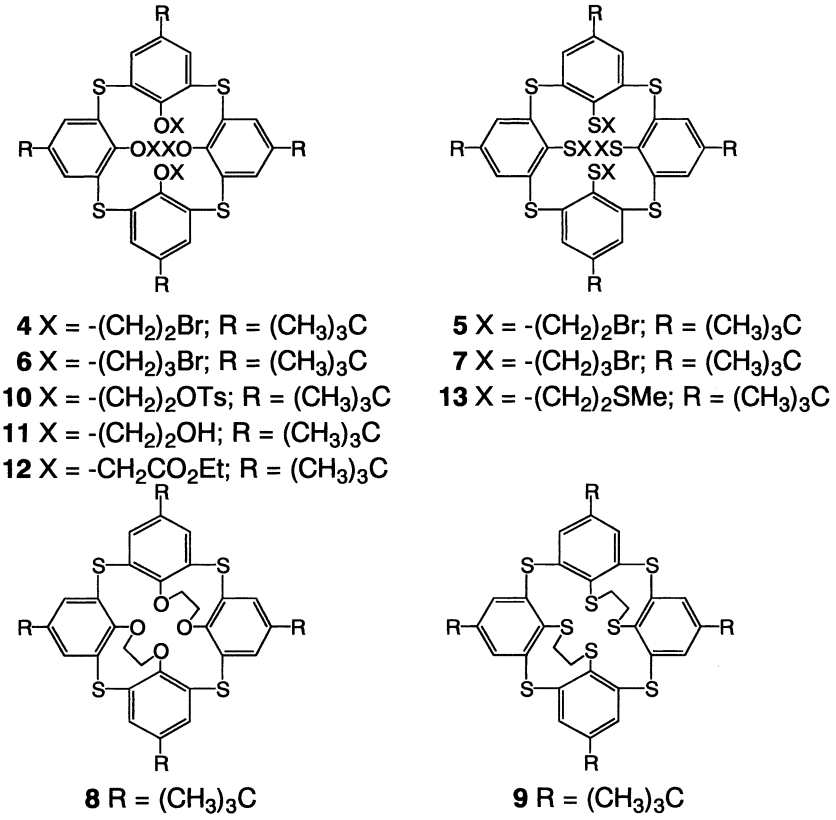


Scheme 2.

results from the double bridging by two ethylene fragments of two adjacent OH groups of the calix unit **2** adopting the cone conformation (see Fig. 1). This type of bridging has been reported for a lactone derivative of the compound **2**.[18]

Although, in solution, the interconversion between all four limit conformations of the thiacalix backbone is rather rapid, we have previously demonstrated that the thiacalix **2** adopts in the solid state the cone conformation in the presence of a variety of solvent molecules.[5] The structural characteristics revealed by the study are (Fig. 2): the thiacalix unit adopts a flattened cone conformation with two opposite phenyl rings almost parallel and perpendicular to the plan formed by the four S atoms and the other two aromatic rings adopting a rather open conformation. The CS bond distance varies between 1.77 and 1.81 Å. Whereas for the C–O(Ph) junctions, the distance is between 1.37 and 1.40 Å, for the C–O(CH_2) the bond distance varies between 1.41 and 1.44 Å. The OCCO dihedral angle varies between 71.2 and 75.3°.

Surprisingly, the same compound **8** was obtained in 65% yield when the thiacalix **2** was allowed to react with its tetratosylate derivative **10**[19] in the presence of Cs_2CO_3 in CH_3CN. The compound **10** was obtained upon tosylation of the corresponding tetraol **11** using TsCl in pyridine.[19] The latter was obtained in 70% yield upon reduction by $LiAlH_4$ of the corresponding tetraethyl ester **12** in dry THF. Compound **12** was prepared as previously described.[20]

A possible mechanistic explanation for the formation of **8** from **2** and **10** under basic conditions may be the following (Scheme 3). In the presence of Cs_2CO_3, the

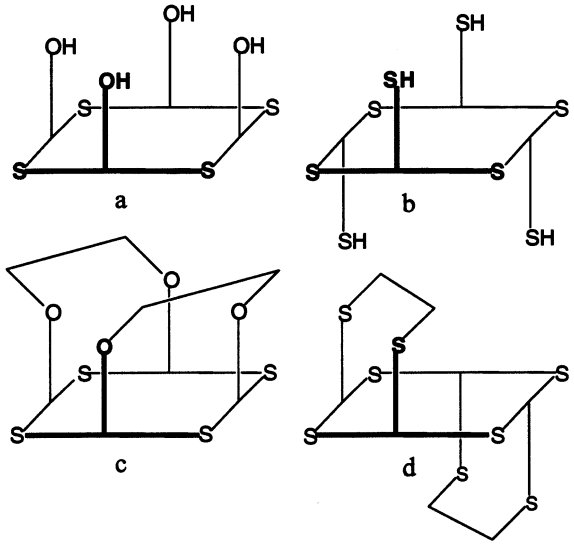


Figure 1. Schematic representations of compound **2** in cone conformation (a) compound **3** in 1,3-alternate conformation (b) and the corresponding two ethylene bridged derivatives **8** (c) and **9** (d).

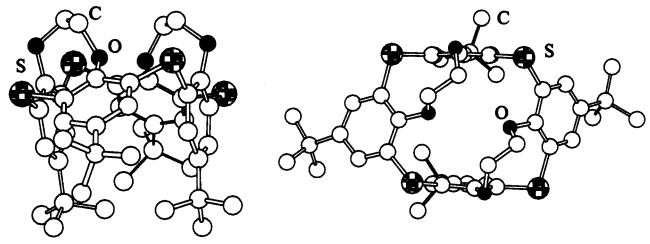
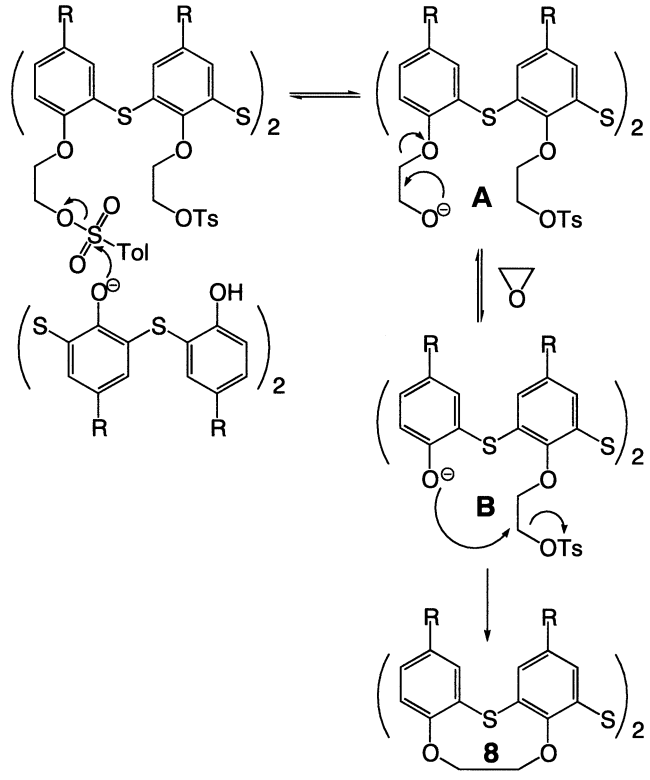


Figure 2. Solid state structure of compound **8** (side (left) and top view (right)). The calix unit adopts the cone conformation and the adjacent oxygen atoms are bridged by ethyl fragments. One of the four tertiobutyl group was found to be disordered. H atoms are not represented for clarity. For bond distances and angles see text.



Scheme 3.

deprotonation of the compound **2** would generate a phenoxide anion which, through a transesterification process, would lead to the anionic intermediate **A**. The latter, upon elimination of ethylene oxide, would lead to the intermediate **B**. This elimination seems reasonable since the leaving group is a pheoxide. Finally, the intramolecular attack of the remaining adjacent tosylate group by the pheoxide would lead to compound **8**.

In marked contrast, the treatment of compound **2** at 80°C for 3 h by an excess of 1,3-dibromopropane in acetone and in the presence of K_2CO_3 afforded the expected tetrabromo derivative **6**[21] (see Scheme 2) in 92% yield, indicating that the distance between the adjacent OH groups in **2** is adequate for bridging by a C_2 fragment. The structure of compound **6** was again investigated by X-ray diffraction on single crystals grown from a $CHCl_3$/MeOH solution.[16] The study revealed the 1,3-alternate conformation for compound **6** (Fig. 3a). The structure was found to be disordered and therefore the corresponding data set is not reported here.

In the case of the mercapto derivative **3**, treatment by an excess of 1,2-dibromoethane in acetone and in the presence of K_2CO_3 afforded a mixture of the bridged compound **9**[22] and the tetrabromo derivative **5**. Although compound **9** could be isolated by chromatography, the bromo derivative **5** decomposed upon purification. For that reason, the mixture of the two compounds was further treated with NaSMe affording after chromatography compound **9** and the tetrathioether **13**[22] in 33 and 19% yields, respectively.

The structure of the bridged compound **9** was also investigated by a X-ray diffraction study on a single crystal obtained from a $CHCl_3$/MeOH solution (Fig. 4).[16] In contrast with the parent compound **3** which was shown to adopt the 1,3-alternate conformation,[10] the calix unit in **9** adopts the 1,2-alternate conformation. The adjacent S atoms on the same face of the unit are bridged by ethylene fragments. For the S atoms connecting the aromatic rings, a CS bond distance of ca. 1.79 Å is observed, whereas for S atoms connected by the ethylene fragments, the SC(Ph) distance is ca. 1.76 Å. The bridging by the CH_2–CH_2 fragment of the two S atoms on the same face of the calix takes place through a one short (1.67 Å) and one long (2.05 Å) CS bond distances with SCCS dihedral angles of 143.6 and −143.6°.

The structure of compound **13** was also investigated by an X-ray diffraction study on a single crystal obtained from a $CHCl_3$/MeOH solution (Fig. 3b).[16] As in the case of the parent compound **3**,[10] the calix unit in **13** adopts the 1,3-alternate conformation. All four SMe units are oriented towards the outside of the cavity of the calix unit. The CS bond distance varies between ca. 1.74 and 1.79 Å.

Finally, treatment of **3** with 1,3-dibromopropane in acetone and in the presence of K_2CO_3 afforded, as in the case of compound **2**, the tetrabromo derivative **7**[23] in 60% yield. The structure of **7** was again studied in the solid state by X-ray diffraction on single crystal obtained from a CH_2Cl_2/MeOH mixture (Fig. 3c). For compound **7**, the calix unit adopts the 1,3-alternate conformation, and the two opposite aromatic rings on each face of the calix are almost parallel and perpendicular to the plan formed by the four sulfur atoms. The C–S bond distances are all around 1.79 Å and the C–Br distance is 1.95 Å.

In conclusion, whereas the treatment of the tetrathiacalix[4]arene derivative **2** by 1,2-dibromoethane in DMF and in the presence of K_2CO_3 leads to the bridging of consecutive phenolic moieties, affording thus the new basket type derivative **8** for which the calix unit adopts the cone conformation, the same

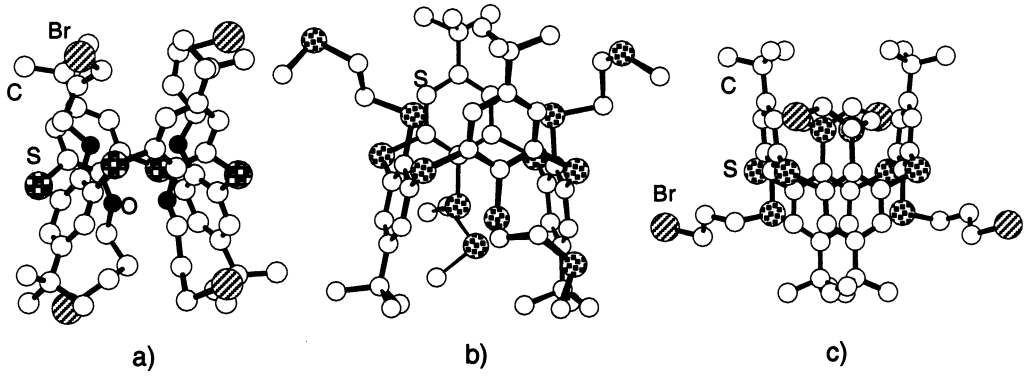


Figure 3. Solid state structure of compounds **6** (a), **13** (b) and **7** (c). In all three cases, the calix unit adopts the 1,3-alternate conformation. H atoms and solvent molecules are not represented for clarity.

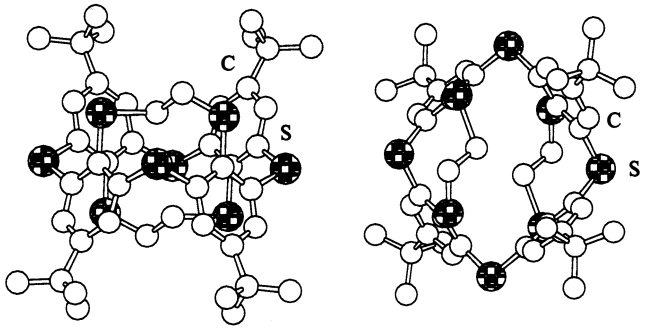


Figure 4. Solid state structure of compound **9** (side (left) and top view (right)). The calix unit adopts the 1,2-alternate conformation and the adjacent sulfur atoms are bridged on each face of the backbone by ethyl fragments. One of the four tertiobutyl group and an ethyl group are disordered. H atoms are not represented for clarity. For bond distances and angles see text.

reaction with 1,3-dibromopropane leads to the expected tetrabromo compound **6**. On the other hand, treatment of the tetramercaptotetrathia derivative **3** by 1,2-dibromoethane in acetone and in the presence of K_2CO_3 affords a mixture of the bridged compound **9** for which the calix adopts the 1,2-alternate conformation, and the tetrabromo derivative **5** which was isolated as its SMe derivative **13** in 1,3-alternate conformation. Under the same condition, the reaction with 1,3-dibromopropane leads to the expected tetrabromo compound **7** in which the calix adopts again the 1,3-alternate conformation.

Acknowledgements

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16. **X-Ray studies**: For compound **8**, data were measured at 294 K on a Enraf–Nonius CAD4 diffractometer with graphite-monochromated Mo-Kα radiation. For the other two compounds **9** and **14**, data were measured at 173 K on a kappa CCD diffractometer with graphite-monochromated Mo-Kα radiation. All structures were solved by direct methods using OpenMoleN 2.2 and refined anisotropically using absorption corrected data. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
17. **Compound 8**: A mixture of *p-tert*-butylthiacalix[4]arene **2** (0.5 g, 0.70 mmol), 1,2-dibromoethane (1.0 ml, 11 mmol), K_2CO_3 (1.5 g, 11 mmol) in dry dimethylformamide (50 ml) was heated under argon to 80°C overnight. After cooling at rt, the mixture was poured onto ice and the yellow solid obtained was washed with water (100 ml). The solid was redissolved in CH_2Cl_2 (50 ml), dried on $MgSO_4$ and evaporated to dryness. Upon purification by column chromatography (SiO_2, hexane/CH_2Cl_2 1:1) the pure compound **8** was obtained as a white solid (120 mg, 22% yield). Mp 310°C (decomp.). Anal. calcd for $C_{44}H_{52}O_4S_4$: C, 68.36; H, 6.78. Found: C, 68.27; H, 6.78%. ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ (ppm): 0.86 (s, 18H, *CH*$_3$); 1.38 (s, 18H, *CH*$_3$); 4.24 (d, $J=12$ Hz, 2H, *CH*$_2$); 4.34 (d, $J=11$ Hz, 2H, *CH*$_2$); 5.11 (t, $J=11$ Hz, 2H, *CH*$_2$); 5.58 (t, $J=12$ Hz, 2H, *CH*$_2$); 6.62 (d, $J=2.6$ Hz, 2H, arom.); 6.96 (d, $J=2.6$ Hz, 2H, arom.); 7.59 (d, $J=2.3$ Hz, 2H, arom.); 7.72 (d, $J=2.3$ Hz, 2H, arom.); ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ (ppm): 30.8 (CH_3); 31.3 (CH_3); 33.8 (*C*(CH_3)); 34.5 (*C*(CH_3)); 67.3 (O*CH*$_2$ CH_2); 72.4 (O*CH*$_2$ CH_2); 125.4; 129.9; 130.3; 130.9; 131.3; 132.5; 134.8; 146.8; 156.5 (arom.).
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19. **Compound 10**: ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ (ppm): 1.06 (s, 36H, CH_3); 2.43 (s, 12H, CH_3 (Tos)); 4.31 (t, 3.3 Hz, 8H, CH_2); 4.47 (t, 3.4 Hz, 8H, CH_2); 7.20 (s, 8H, Ar); 7.33 (d, 8H, Ar (Tos)); 7.79 (d, 8H, Ar (Tos)). **Compound 11**: mp 330°C (decomp.). Anal. calcd for $C_{48}H_{64}O_8S_4$, CH_3OH: C, 63.33; H, 7.38; S13.8. Found: C, 63.13; H, 7.00; S, 13.95%; ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ (ppm): 1.10 (s, 36H, CH_3); 4.00 (m, 8H, CH_2); 4.30 (m, 8H, CH_2); 4.97 (t, 6.6 Hz, 4H, OH); 7.35 (s, 8H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ (ppm): 31.17 (CH_3); 34.29 ($C(CH_3)_3$); 61.60; 79.22 (CH_2); 129.76; 134.69; 147.27; 158.34 (arom.).
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21. **Compound 6**: mp 310°C (decomp.). Anal. calcd for $C_{52}H_{68}O_4Br_4S_4.(CH_3)CO$: C, 52.30; H, 5.91; S, 10.15. Found: C, 52.72; H, 5.93; S, 10.45%; ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ (ppm): 1.34 (s, 36H, CH_3); 1.54 (t, $J=7.3$ Hz; 8H; CH_2); 3.07 (t, $J=7.1$ Hz, 8H, CH_2); 3.97 (t, $J=6.8$ Hz, 8H, CH_2), 7.35 (s, 8H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ (ppm): 30.46 (CH_2); 31.42 (CH_3); 32.28 (CH_2); 34.48 (**C**CH_3); 67.06 (OCH_2); 127.28; 128.19; 146.49; 156.32 (arom.).
22. **Compound 9**: mp 290°C (decomp.). Anal. calcd for $C_{44}H_{52}S_8$, 0.5 CH_2Cl_2: C, 60.75; H, 6.07. Found: C, 60.56; H, 6.61%; ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ (ppm): 1.34 (s, 36H, *C*H_3); 1.65 (m, 4H, *C*H_2); 2.65 (m, 4H, *C*H_2); 7.77 (d, 2.2 Hz, 4H, arom.); 7.90 (d, 2.2 Hz, 4H, arom.); ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ (ppm): 29.7 (O*C*H_2*C*H_2); 31.2 (CH_3); 32.8 (O*C*H_2*C*H_2); 34.7 (*C*(CH_3)); 135.1, 135.5, 138.8, 139.8, 143.1, 150.8 (arom.). **Compound 13**: ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ (ppm): 1.25 (s, 36H, CH_3); 2.06 (s, 12H, SCH_3); 2.58 (m, 8H, CH_2); 3.09 (m, 8H, CH_2), 7.75 (s, 8H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ (ppm): 15.5 (SCH_3); 30.9 (*C*CH_3); 34.3 (CH_2); 34.5 (*C*CH_3); 35.2 (CH_2); 135.0; 140.1; 142.6; 149.9 (arom.).
23. **Compound 7**: mp 265°C (decomp.). Anal. calcd for $C_{52}H_{68}Br_4S_8$: C, 49.21; H, 5.4; S, 19.54. Found: C, 49.64; H, 5.38; S, 20.21%; ^{1}H NMR (200 MHz, $CDCl_3$, 25°C): δ (ppm):1.32 (s, 36H, CH_3); 1.89 (m, $J=6.38$ Hz; 8H; CH_2); 3.06 (t, $J=6.4$ Hz, 8H, CH_2); 3.71 (t, $J=6.8$, 8H, CH_2), 7.69 (s, 8H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$, 25°C): δ (ppm):30.9 (CH_2); 31.0 (CH_3); 31.8, 33.2 (CH_2) 34.4 (*C*CH_3); 133.5, 138.7, 142.52, 151.0 (arom.).