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THE PAGODANE ROUTE TO DODECAHEDRANES - FUNCTIONAL GROUP MANIPULATIONS ON THE DODECAHEDRANE SPHERE

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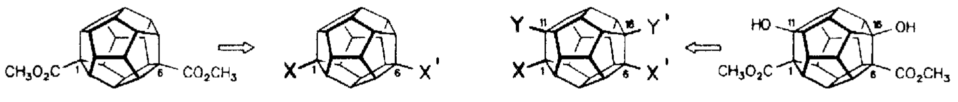
Summary: Reductive and halogenative Barton decarboxylation methodologies provide an expeditious access to variously 1,6- di- and 1,6,11,16-tetrasubstituted pentagonal dodecahedranes. Vicinal CO_2R and Cl substituents cause increasing competition in the radical transfer step.

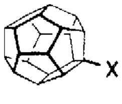
Pentagonal dodecahedranes 1,6-disubstituted with methoxycarbonyl groups (**1**) and 1,6,11,16-tetrasubstituted with additional hydroxy functions (**2**) are expeditiously prepared by S_N2 and aldol cyclization from appropriately tetrafunctionalized bisseco-precursors$^{1,2)}$. In this paper we report on the utilization of these functionalities for further chemical modification of the dodecahedrane sphere ('A','B') - with i.a. the installation of multiple C=C double bonds and charges being ultimate goals$^{3)}$. Activities by the Paquette group based on the availability of bromo- and 1,16-dibromo dodecahedrane$^{4)}$ from electrophilic substitution of the parent hydrocarbon are thus significantly extended.



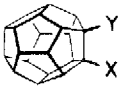
1 'A' 'B' 2

For the evaluation of reactivity and selectivity phenomena tied to polyfunctionalization of the dodecahedrane sphere, the differential strain energies calculated (MM2) for selected mono-, 1,2- and 1,3-difunctionalized derivatives are informative (Tab. 1)$^{5)}$. It is understood that the steric/ electronic effects$^{6)}$ hampering the installation and transformation of larger vicinal groups can be taken to advantage in the pursuit of particular substitution patterns$^{7)}$.

Tab. 1. Differential strain energies (kcal/mol) for mono-, 1,2- and 1,3-difunctionalized dodecahedranes



I



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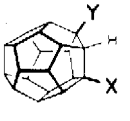
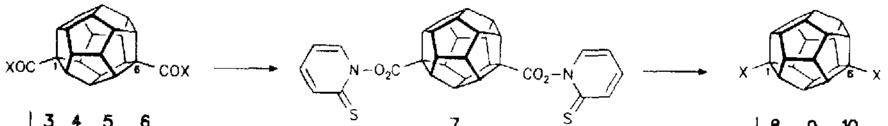


III

X	Y	I	II	III
H	H	0	0	0
OH	OH	0.07	0.12	0.10
Cl	Cl	1.91	5.95	3.81
Br	Br	4.32	11.96	8.58
CO_2CH_3	Cl	4.63	8.95	6.59
CO_2CH_3	Br	" "	12.10	8.96
SCH_3	CO_2CH_3	0.10	2.79	−1.20

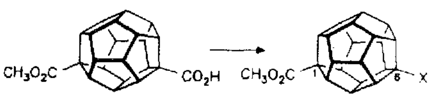
For the conversion of 1 into the 1,6-dihalides 8-10, particularly the dibromide 9[7], the Hunsdiecker reaction in its variations is an established procedure. Yet, in a series of experiments, the results were not satisfactory for our purposes. For dichloride 8 and dibromide 9, the Barton halodecarboxylation methodology[9] proved superior with yields of 80-85% for 8/9 (one-pot version with no isolation of the bisthiohydroxamic ester 7, CCl_4 and $BrCCl_3$ as solvents)[10]. External irradiation (300 Watt Osram daylight lamp) has no beneficial effect. The drop to 10-15% in case of diiodide 10 is probably due to an insufficient concentration of the iodide donor (CF_3CH_2I in benzene). The tolerance of ester groups by the Barton procedure allows the extension to the preparation of the corresponding dodecahedrane haloesters, as exemplified with the transformation of monoester 11 into the 1,6-haloesters 12 and 13. Conditions for an efficient dimerization of intermediate radicals 14 are being explored (with R groups enhancing the solubility of dimers 15).



	3	4	5	6
X	OH	Cl	NH_2	H

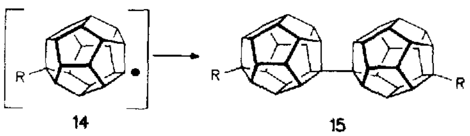
7

	8	9	10
X	Cl	Br	I



11

	12	13
X	Br	Cl

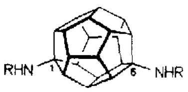


14

15

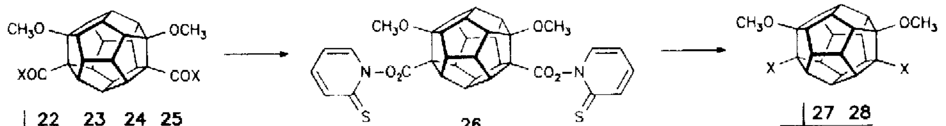
1,6-dimethylether 16 is accessible via reductive bisdecarboxylation of 23 (see below) and is cleaved by either $(CH_3)_3SiI$ ($(CH_3)_3SiCl/NaI$, CH_2Cl_2/CH_3CN, refl.) or CF_3CO_2H (refl.) to selectively furnish 1,6-diol 17 and its bistrifluoroacetate 18, respectively. 1,6-diamide 19 is almost quantitatively isolated (92%) from the reaction of dibromide 9 with $AgOCOCF_3/CH_3CN$ (refl.) followed by hydrolysis[4,11]. More modest is the result in the Hofmann degradation of dicarboxamide 5 ($C_6H_5IO(COCF_3)_2$, *tert*-butanol, refl.) with 60% of 1,6-diamine 20 being reproducibly isolated as bishydrochloride 21.

	16	17	18
R	CH_3	H	$COCF_3$



	19	20	21
R	$COCH_3$	H	H_2Cl

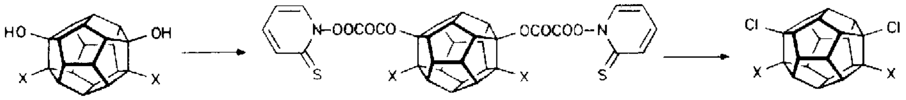
For halodecarboxylation, dihydroxydiester 2 is first transformed into its dimethyl ether 22 (DMF, CH_3I, >90%) and than via 23 into bis(acidchloride) 24 ($(COCl)_2$, CH_2Cl_2). In all three steps, steric constraints necessitate rather forcing conditions. As judged from the 75-85% yield of the 11,16-dimethoxy-1,6-dihalogenides 27 (m/z (%) = i.a. 388(100, M^+), 322(35), 291(19), 257(18)) and 28 (m/z (%) = i.a. 476(38,M^+), 367(9), 339(100), 257(31)), secured along the one-pot protocol (c.f. 8/9) for the preparation and decomposition of bisthiohydroxamic ester 26, the vicinal OCH_3 group does not impede the radical transfer to a significant degree. The potential appearence of small amounts of 36 besides 27 - the "mixed" product has not been detected in the formation of 8 - attests to a limited competition in the second radical transfer step. The reductive decarboxylation of 23 (via 24/26, with *tert*-butylmercaptan as hydrogen source) provides 16 with a somewhat reduced efficiency (50-60%). "Deprotection" of 27/28 to afford the dichloro(dibromo) diols **29** and **30** is bound to extended (12 h) boiling in 35% HCl or 46% HBr, yet is highly selective (90-95%). The OH groups in **29**/**30**, vicinal to the halogens, do obviously survive (in contrast, diol **17** under such conditions is quantitatively converted into **8**/**9**). The OH-groups in **2** similarly resist standard conditions for their substitution to afford dichlorodiester **33**. The 60% of the latter obtained by the Barton procedure ($(COCl)_2$, **31**)[12] - besides some 10-15% **37** - could be indicative of a stronger impediment of the second [Cl•] transfer by the vicinal ester group. The meager 10-15% yield of much wanted tetrachloride **34** analogously produced from **29** via **32** - besides substantial quantities of **38** (up to 15%, no **39**) - advocates an even stronger "selection" exerted by the vicinally Cl-substituted carbon radical. Comparably unselective is the formation of **34** (ca. 10%) in the Hunsdiecker degradation of **35**; the saponification **33** → **35**, not amenable to base-catalysis, needs prolonged refluxing in 35% HCl/CF_3CO_2H.



	22	23	24	25
X	OCH_3	OH	COCl	NH_2

26

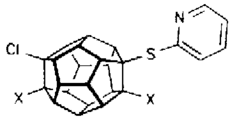
	27	28
X	Cl	Br



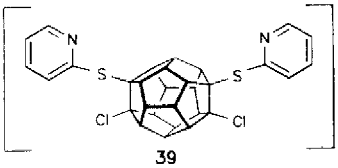
	2	29	30
X	CO_2CH_3	Cl	Br

	31	32
X	CO_2CH_3	Cl

	33	34	35
X	CO_2CH_3	Cl	CO_2H



	36	37	38
X	OCH_3	CO_2CH_3	Cl



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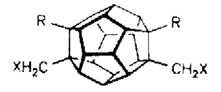
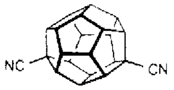
Diesters **1** as well as **2** and **22** are neatly reduced by $LiAlH_4$; after workup under non-acidic conditions, the bismethylols **40**-**42** are isolated in very high yields (90-97%). With 1,6-dinitrile **47** being conveniently aquired from biscarboxamide **5** (70%), 1,6-bismethylamine **43** (characterized as bishydrochloride **44**) is accessible through catalytic hydrogenation. The known propensity of the dodecahedrane skeleton for ring enlargement[5] shows up in the product composition resulting from the reaction of **42** with 35% aqueous $HCl/ZnCl_2$ (refl.); bismethylchloride **45** is accompanied by several isomers



	40	41	42	43	44	45	46
R	OH	OCH_3	H	H	H	H	H
X	OH	OH	OH	NH_2	NH_3Cl	Cl	Br



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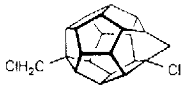

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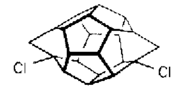

49

(GC/MS) as e.g. the mono-/bishomododecahedranes **48**/**49**. As judged from their relative energies (MM2)[13], not much preference for one of the possible bishomododecahedrane isomers can be expected. Skeletal isomerization is largely avoided in the preparation of bismethylbromide **46** from **42** and 48% $HBr/ZnBr_2$ (refl., 70%).

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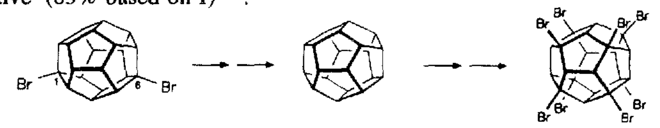
6) INDO calculations of the energetic consequences of substitution of fluorine for hydrogens in dodecahedrane had led to an energy difference of 3.5 (0.30) kcal/mol for 1,2(1,3)-difluorododecahedrane: J.W. Schulman, R.L. Disch, *J. Am. Chem. Soc.* **1978**, *100*, 5677-5681.
7) From a systematic study towards the utilization of 1,6-disubstituted dodecahedranes for a more expeditious synthesis of the parent hydrocarbon **50**, the reductive debromination of **9** emerged as superior alternative (83% based on **1**)[8].



9 **50** **51**

In the complex product mixture resulting from photoperbromination of **50**, an octabromide ($C_{20}H_{12}Br_8$) is detected in a better than statistical percentage and assigned the T_h symmetrical structure **51** on the basis of spectral data, i.a. the MS fragmentation pattern (m/z (%) = i.a. 888, 889, 890(3,M$^+$), 807, 808, 810, 812, 815(6), 729, 731, 733, 735(20), 655(22), 571, 573(12), 491(12), 411, 413(12), 331, 333(14), 252(27), 250(44)), 125(100)) with a base peak supposedly due to a doubly charged (conjugated) dodecahedrapentaene, c.f. **6** in lit. 3. Its non-appearance in the analogous perbromination of **9** (only heptabromides) is in line with the hypothesis that vicinal Br/Br arrangements (Tab. 1) are avoided[8].

8) F. Wahl, J. Wörth, H. Prinzbach, in preparation.
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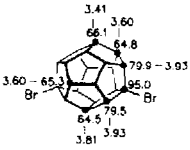
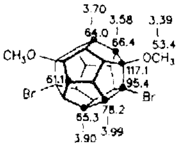
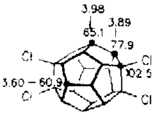
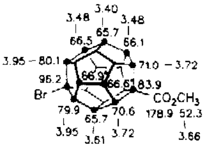
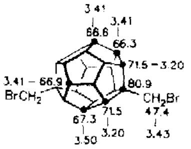
10) The new compounds are generally characterized by elemental analysis and spectral data (IR, ^1H-, ^{13}C-NMR, MS); e.g.











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