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The Structural Basis of the Geminal-Dimethyl Effect

Reinhart Keese* and Marc Meyer

Institut für organische Chemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland

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Abstract: A systematic analysis of the X-ray structures of cyclohexanes, cylcopentanes and open-chain compounds containing gem.-dimethyl groups has revealed that a static scissor-type deformation at the quaternary C atom is absent. Unexpectedly the C-C-C bond angles in α-position to the quaternary C atom are significantly larger than the standard values in the unsubstituted reference structures. This distortion is interpreted in terms of gauche interactions. Based on the presently available data for structures containing gem.-dimethyl groups, the structure-reactivity relationship observed by Thorpe and Ingold for this class of compounds, has an origin different from static scissor-like distortions at the quaternary C atom.

INTRODUCTION

The formation of 3-, 5- and 6-membered ring compounds from open chain substances is enhanced by the presence of geminal dialkyl groups. This so-called gem.-dimethyl effect applies to both equilibria and rates.[1] Several interpretations of this structure-reactivity relationship have been forwarded. Thorpe and Ingold,[2] who first provided experimental evidence for this phenomenon, proposed in 1915, that this enhanced reactivity might be due to changes of the bond angles at the C atom bearing the gem.-dimethyl groups. Their interpretation is based on the well established fact, that the bulky CH_3 groups which replace the H atoms, require more space than the latter resulting in a larger CH_3-C-CH_3 bond angle. This increase in the bond angle would be transferred in a scissor-like deformation to the opposite bond angle, which subsequently should become smaller. This interpretation is based on the hypothesis, that the sum of the six bond angles at a tetracoordinated C atom is constant. However, this assumption is not justified; for example in cyclopropane, the sum of the six bond angles at one C atom is about 10° less than 656.8°, while it would be much larger for planar tetracoordinate carbon. Nevertheless the question remains, whether the static scissor-type deformation in compounds with gem.-dimethyl groups is apparent. More recently, v. R. Schleyer[3] has discussed the Thorpe-Ingold interpretation of the gem.-dimethyl effect on the basis of the extent of intramolecular H bonds with HO groups. He concluded, that the Thorpe-Ingold type angle deformation is of minor importance.

In a recent paper, M.E. Jung[4] has provided clear evidence, that the gem.-dimethyl effect is essentially enthalpic in nature and most likely due to the presence of reactive rotamers. In this paper we investigate the structural features of open chain compounds, cyclopentanes and cyclohexanes, all bearing geminal dimethyl groups.

Data Selection

The Cambridge Structural Data Base (updated version of May 1991 with 90'296 entries) was searched for carbocyclic rings with ring size 5 and 6 and open chain compounds containing geminal CH_3 groups. Although t.-butyl groups contain gem.-dimethyl groups, they were excluded. Only structures with R-factors <10% were included in the systematic analysis. No X-ray structures have been found containing geminal C_2H_5-, n- and i-C_3H_7 and t.-butyl groups. Also compounds with quaternary C atoms of type CH_3-C-R (R=C_2H_5, C_3H_7 or C_4H_9) and H_2C_5-C-R (R = n- or i-C_3H_7) were absent. The chair and boat conformations of cyclohexanes as well as the the C_s- and C_2-conformations of cyclopentane with geminal dimethyl groups in the different locations were each analyzed separately.

For comparison, the gas phase structural data of unsubstituted alkanes and cycloalkanes have been retrieved from the literature (table 1). For cyclohexane electron diffraction as well as an X-ray analysis have been reported. It should be noted that the 111° found for the internal bond angles in cyclohexane is very close to the C-C-C bond angle found in simple alkanes.

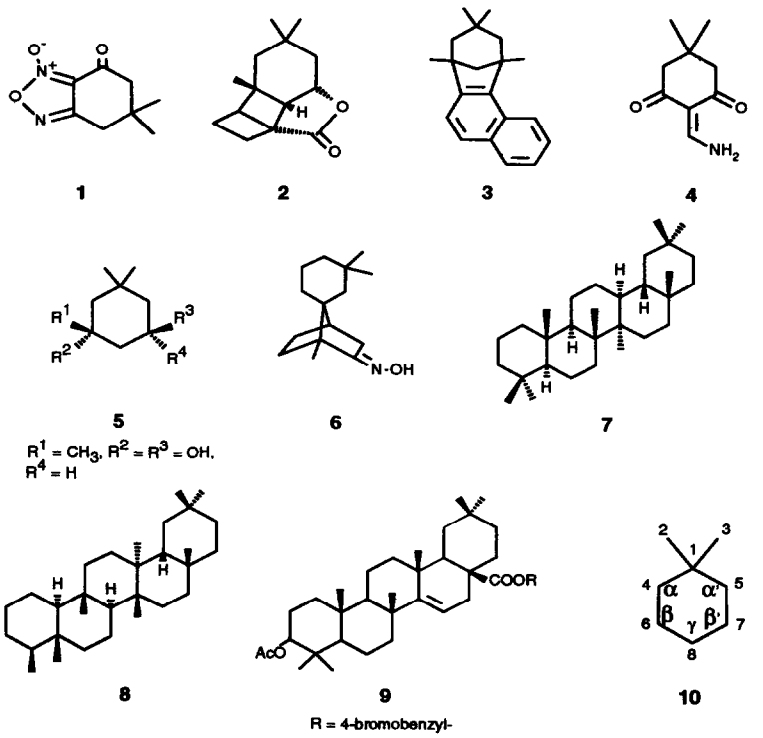
Table 1. Molecular Structure of Several Hydrocarbons

Substance	Bond lengths [Å]		Bond angles ω				Method[a]	Ref.
	C-C	C-H	C-C-C					
n-Propane	1.537		111.7°				MW	5
n-Butane	1.540±0.003	1.099±0.003	112.1±0.15°				ED	6
n-Pentane	1.531±0.002	1,118±0.004	112.9±0.2°				ED	7
n-Hexane	1.533±0.003	1.118±0.006	111.9±0.4°				ED	
n-Heptane	1.534±0.003	1.121±0.007	112.0±0.3°				ED	
Cyclopropane	1.509±0.001	1.088±0.003					ED	8
Cyclobutane	1.548±0.003	1.092±0.001						9
Cyclohexane	1.528±0.003	1.119±0.004	111.05±0.12°				ED	10
	1.523		111.34°				XR	11
			ω_{213}	ω_{415}	ω_{146}	ω_{157}		
Cyclopentane[b]	1.546±0.001	1.113±0.001		100°	102°	106° [c]	ED	12
				105°	105°	101° [d]		
1,1-Dimethyl-cyclohexane[b]	1.533±0.002	1.119±0.004	106.4°	109.8°	115.0°			13

a) MW = microwave, ED = electron diffraction, XR = X-ray structure analysis; b) for numbering see **10** and **11** respectively; c) C_s-conformation (12); d) C_2-conformation (13)

RESULTS AND DISCUSSION

The 59 gem.-dimethyl cyclohexanes in chair conformation were analyzed regardless of the presence of exocyclic double bonds, carbonyl groups, annulated or bridged rings as for example in **1-4** (set I). From this family of compounds a subset of 11 compounds was separated, which like **5** and **6** contain a cyclohexane ring with neither an exocyclic double bond nor substituents in α-position to the quaternary C atom C_q nor annulated



rings (set II). In order to avoid a bias by several closely related structures the 24 X-ray structures of the natural products oleane **7** and friedelane **8**, and related triterpenoid structures with the same basic skeleton have been analyzed separately (set III).

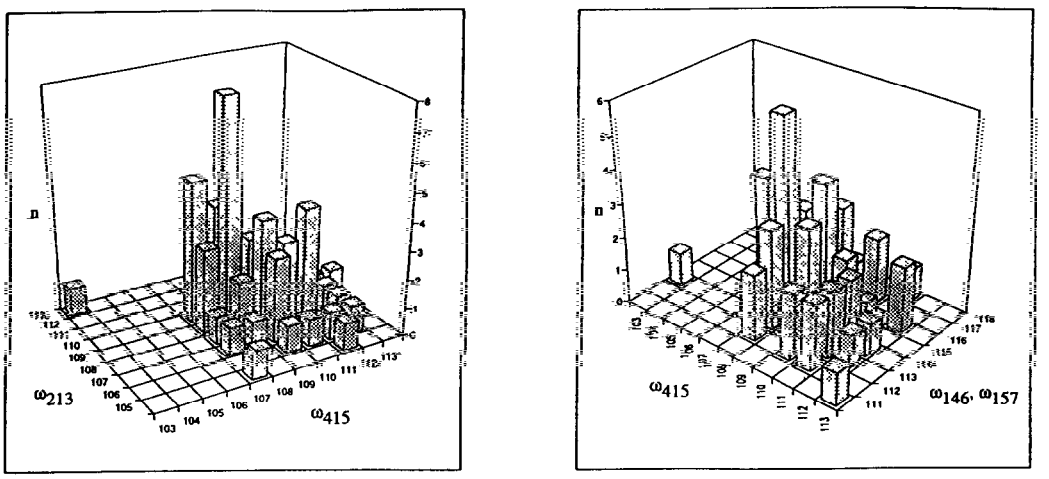
Table 2. Average Bond Angles ω[°] for Cyclohexanes with Gem.-Dimethyl Groups for Set I-III (cf. text)

ω[a]	I	II	III	
			chair	boat
213	107.22±1.58	108.57±1.56	108.56±1.97	108.56±0.62
415	108.87±1.25	108.94±1.77	108.39±1.60	109.66±0.21
214, 215, 314, 315 av.	110.15±2.03	109.82±1.87	109.93±2.32	109.64±1.42
146, 157 av.	115.10±2.1	114.34±2.28	113.60±2.60	114.58±1.50
468, 578 av.	109.82±2.20	113.61±4.39	112.20±1.69	112.69±0.77
687	113.700±2.32	115.06±5.84	110.26±1.10	109.45±0.47

a) for numbering see formula **10**

The bond angle between the gem.-dimethyl groups, ω_{213} (cf. formula **10**) is 108.6° in set I and 107.2° in the structurally more uniform set II. Both values are smaller than the 110° H-C-H bond angle of cyclohexane.[10] The opposite, internal bond angle ω_{415} being very close to 109° in both sets, is slightly smaller than that found in unsubstituted cyclohexane by electron diffraction or X-ray structural analysis (C-C-C = 111.1° [X-ray: 111.3°], cf. table 1).[14]

Since the external as well as the internal bond angle at C_q is smaller than those of cyclohexane, used as reference, it is clear, that a scissor-like deformation at C_q is absent in these structures. This is further supported by the histogram **A**, where the bond angles ω_{213} and ω_{415} are clearly related and cluster around 109°.



A **B**

Figure 1. Histograms for the correlation of ω_{213} with ω_{415} (**A**) and ω_{415} with the average value of ω_{146} and ω_{157} (**B**), respectively (cf. formula **10**)

Together with the other four bond angles at the quaternary C atom, which are also close to 109°, the bond angle situation at C_q in a $(H_3C)_2C(CH_2\text{-})_2$ fragment of gem.-dimethyl substituted cyclohexanes approaches that of neopentane.[15] It suggests, that the structure of $C(C)_4$ fragments in this type of molecule is rather robust, approaching local T_d symmetry avoiding large bond angle deviations.

The average bond angles in α-position to the quaternary C atom are with 115° and 114° surprisingly large. From a histogram it is apparent, that the small internal bond angle ω_{415} is correlated to a large bond angle at C_α and $C_{\alpha'}$ respectively (histogram **B**). This unexpected relationship is interpreted in terms of a synclinal or gauche 1,4-interaction between the axial CH_3 and the CH_2 groups in both β-positions. Concomitant with the widening of the bond angles at C_α and $C_{\alpha'}$, the average bond lengths $d_{1,4}$ and $d_{1,5}$ are slightly larger than the other four bond lengths in the cyclohexane ring, which themselves are close to those found in cylcohexane itself (cf. table 1). As a further corollary to the gauche effect exerted by the axial CH_3 group, the torsional an-

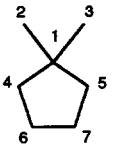
gles in the chair conformation of the cyclohexane ring as well as those to the gem.-dimethyl groups are changed with the overall result of a slight flattening of the chair.

Only chair conformations have been found for the ring E of molecules derived from oleane **7**, where the rings C and D are cis-fused or contain a bridgehead double bond, whereas the ring E is very close to a boat conformation in the 7 structures related to friedelane **8**.[16] This is due to the trans fusion of the rings C and D and the steric interactions emanating from the CH_3 groups at these ring junctions. The flagpole positions are at C(4) and C(7) (cf. formula **10**) with the gem.-dimethyl groups at the basal C(1).

In the chair as well as the boat conformations of this family of molecules, the general feature of the bond angles at the quaternary C atom being smaller than those of the unsubstituted cyclohexane is observed without exception (cf. table 2, set III). Also, the C_q-C-C bond angles at both α-positions are larger than those in cyclohexane itself. According to the torsional angles, **9** is the only compound, where the structure of ring E is best described by a twist conformation. Analysis of the bond angles at C_q and at both α-positions of this structure reveals no exception to the general features described above ($\omega_{213} = 109.26°$, $\omega_{415} = 110.88°$, $\omega_{146} = 113.0°$, $\omega_{157} = 109.92°$).

Gem.-Dimethyl Substituted Cyclopentanes

The pseudorotation of cyclopentanes requires to consider the envelope (C_s), **12**, and the twisted envelope (C_2), **13**, separately.[12] The gem.-dimethyl groups might be located in each of the three topologically different positions A, B and C of the frozen conformations. The bond and torsional angles of cyclopentane used as refe-



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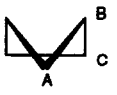

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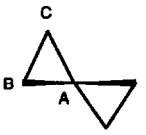

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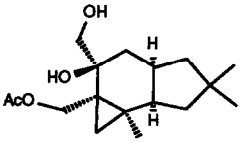

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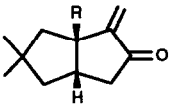

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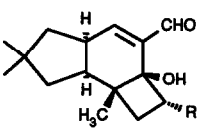
R = -CH_2CH=$CHS(O)$-p -tol.



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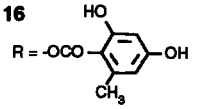

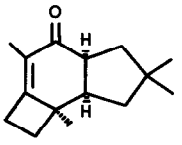

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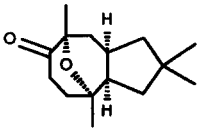

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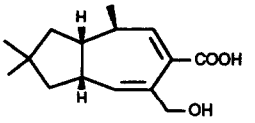

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rence (cf. table 1 and formulae **12** and **13**), have to be defined accordingly. 16 Compounds containing a total of 19 gem.-dimethyl cyclopentanes have been found. According to the torsional angles 10 cyclopentane rings have approximately C_S symmetry with the gem.-dimethyl groups in position A, B and C respectively. In the twisted envelope (C_2) form, the gem.-dimethyl groups are found to be located in all three positions A, B and C. Typical examples for each of these different structures are given by **14-19**.

Analysis of the bond angles at the quaternary C atom group revealed, that the bond angle CH_3-C_q-CH_3 is 108.6°-110.2° in the C_S- as well as in the C_2-form and independent of the location of the gem.-dimethyl groups (table 3). The opposite internal bond angle is very close to that found for the appropriate C atom in the electron diffraction analysis of unsubstituted cyclopentane (cf. table 1). In view of the few structures found for all six structural possibilities, an analysis of the other bond and torsional angles is not feasable.

Table 3. Average Bond Angles ω[°] for Cyclopentanes with Gem.-Dimethyl Groups of C_S-Symmetry (**a**) and C_2-Symmetry (**b**); A, B and C are the Different Positions in C_S- and C_2-Conformation of Cyclopentane (cf. **11** - **13**)

	a				**b**		
ω	A(6)*	B(1)*	C(4)*	ω	A(2)*	B(3)*	C(3)*
123	109.718±1.06	108.64	109.16±2.47	213	110.20±1.34	108.56	109.19±1.24
415	101.059±1.06	102.71	104.45±1.57	415	105.43±0.16	104.37±1.40	101.06±0.46
146 } av. 415 }	105.583±1.55	106.70	105.64±0.89 107.72±1.81	146 157	104.78±0.50 106.08±0.46	106.08±1.65 104.78±0.80	107.94±1.20 104.81±0.19
467 } av. 576 }	105.341	104.24	103.26±0.24 103.81±2.16	467 576	103.18±0.20 102.11±0.43	107.02±3.40 102.08±2.59	103.06±2.04 105.14±1.15

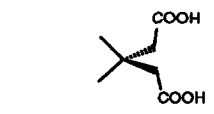
* number of structures found

Nevertheless, the data suggest that the bond angles in α-position are slightly larger than their reference values. Also, comparison of the number of gem.-dimethyl substituted cyclopentanes found in each structural class may indicate that the envelope (C_S)-form with two methyl groups in the 1-position is preferred. Although the number of examples is rather small, a scissor-like deformation of the angle between the gem.-dimethyl group as a consequence of the small internal bond angle cannot be observed.

Substituted n-Alkanes

Only 3,3-dimethylglutaric acid[17] **20** and 2,2,4,4-tetramethyl adipic acid[18] **21** qualify as n-alkanes with gem.-dimethyl groups. Like **22** and **23**,[19] which contain heteroatoms in the β-positions of the quaternary carbon center, their X-ray structures reveal (+)sc/(-)sc-conformations. The compound[20] **24** being unsymmetrical with respect to the substitution pattern in β-position to C_q is the only compound found with an ap/ap-conformation and will not be considered here. In **20** and **21**, the average CH_3-C-CH_3 bond angle is 109° (cf. table 4). The opposite bond angles at the central quaternary C atom are 114° whereas the remaining 4 bond angles at the C_q are close to 109°. This is in strong contrast to the 112° C-C-C bond angles found in small n-alkanes (cf.

table 1), but very close to the 114.8° found for the bond angle -H_2C-CβH_2-CH_2- in the X-ray structure analysis of unsubstituted adipic acid.[21] The 109.6° average CH_3-C_q-CH_3 bond angle of **20/21** H-Cβ-H is certainly larger than the 94° found for the H-C_b-H in adipic acid,[21] but this is not transformed into a scissor-like opening of the opposite bond angle at C_q in **20**.



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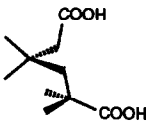

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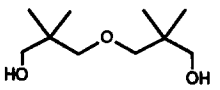

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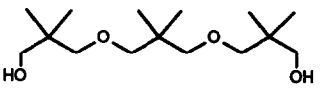

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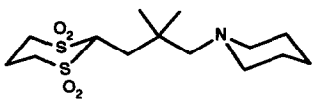

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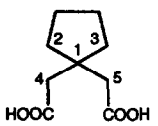

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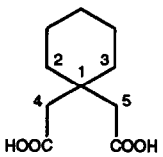

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Table 4. Average Bond Angles ω[°] of **20**[17], **21**[18] and **22**, **23**[19] with +sc, -sc-Conformation.

	20, 21	**22, 23**
213	109.55±0.12	109.91±0.89
415	114.50±0.01	110.41±0.29
146	120.45±3.29	111.13±2.18
157	116.92±1.79	111.26±1.69
214,215 }	108.19±2.35	
314,315 }		

Also, it may be noted, that the bond angles in α-position to the quaternary C atom and the COOH group of **20** are larger by 2° than the corresponding one found in unsubstituted adipic acid.[21] This fact, noticed by Benedetti and Pedone has been attributed to "steric hindrance of the substitutents in 3,3-position" of 3,3-dimethylglutaric acid.[17] Not unexpected for **21**, the bond angle at the CH_2 group by which the two quaternary C atoms are connected is larger than that at the other CH_2 group. Specifically, this interaction must be attributed to the well known gauche effect.

In the compounds **22** and **23**, which have O atoms in all β-positions, the bond angle between the gem.-dimethyl groups is 109.9° and thus close to that found in all structures investigated. In contrast to **20** and **21**, the opposite bond angle -H_2C-C_q-CH_2- is only 110.4°. Whether this is a general feature of such structures, is

unclear. In further search for compounds, which may be considered derivatives of glutaric acid, the structures **25** and **26** have been analyzed.[17, 22]

Table 5. Selected Bond Angles in **25** and **26**

	25	**26**
ω_{213}	104.8°	108.4°
ω_{415}	112.9°	112.7°
ω_{146}	115.9°	117.6°
ω_{157}	116.3°	118.0°

It is apparent, that the bond angle between the geminal acetic acid substituents at C_q in **25** and **26** is larger than that between the gem.-dimethyl groups of general structure **11** (cf. table 3a, b) respectively. More important is the structural feature, that the bond angles at the external CH_2 groups are larger than those in glutaric acid and similar to that found in **20** and **21**. This may be taken as further evidence for a strong gauche effect between the CH_2 groups located in α-position of the ring and the carboxylic acid groups.

CONCLUSION

The analysis of X-ray structures of three selected classes of compounds viz. **10**, **13** and **20** containing gem.-dimethyl groups has shown, that a scissoring deformation at the quaternary C atom is absent. Surprisingly, the C-C-C bond angles at the CH_2 groups in α-position to the quaternary C atom are larger by at least 2° than the standard values in the unsubstituted rings or alkane chains. This structural change in the presence of gem.-dimethyl groups is due to gauche interactions. It is highly unlikely, that the structure-reactivity relationship, which Thorpe and Ingold have observed is due to a static scissor like deformation, which would tie the reactive groups together.

DATA

Identification of the Structures Analyzed

The structures for the tables are listed according to their Cambridge Structural Database identifier and the number of the formula, if given. "# molecules" means the number of independent molecules in one crystallographic unit cell. "# fragments" means the number of independent parts of the molecule that have the investigated structure.

Set I (table 2): AMZTCE11 (2 molecules); BNCYHO; BOCRIU; BOCROA; BOXJON (2 fragments); BRTCBN; BTNPOC; BURWAM (2 molecules); BUYHEI; CAIPIP (2 fragments); CETMCD; CIYLUR (2 molecules); CIYLUR; CMCHXO; CMDECO; COZZAS; CPMCHX; CURFOK; CURKIJ; DEFKEE; DENBED; DENBIH; DHBFZO; DIGYOH; DIMEDO01; DMCYHX; DMXTCD; DOKJUI; FAWDEM; FIFGUW; FIXXOZ; FOSDOG (4); FUJVUB; FUTFIJ; FUWSIZ; GAFTOW; GAJHII; HMBFUR; HMBFZO (1); HMPCIN; HMPNDT; MNBOCT (3);

MTTSPT; MXTDOA (2); OXSEAZ10; OXTHAZ; PMNBOX (6); SAPWAH (2 fragments); TMCHOX (2 fragments); TMPCHO; VAMKEZ (2 fragments); XTMDCO.

Set II (table 2): BNCYHO; BOXJON (2 fragments); CMDECO; CURKIJ; DENBED; DENBIH; FUTFIJ; FUWSIZ; MTTSPT; PMNBOX (6).

Set III (table 2): BIKCED; CERCEH; CMPANL01; ECHABL10; FASFIO; FAWXUW; FINTUR; FITVOT; FUGWEJ; HEDGEN; KADTOY; KAZLEC (2 molecules); KAZPAC; OLDABL; PLAGBL10; SARYEP (9).

Data in table 3a: AISMRS (14); BAYHEO; BENCUS; BEZSEE (one of two molecules, 16); COVPAE; CUXZAW (2 molecules); FITYEM (15); GAGFID; GIMYAC; HLAROS (one of two molecules).

Data in table 3b: BEZSEE (one of two molecules, 16); BUTKAC; CHMHAZ (19); DEKREQ (17); FOMANN; HLAROS (one of two molecules); TMODOD (18); XMOHAZ.

Data in table 4: DMGLUT10 (20); TMEAPI10 (21); GAPSUL (22); GAPTAS (23).

Data in table 5: CYPNAC10 (25); CYHDAC (26).

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