ELSEVIER

Journal of Molecular Structure (Theochem) 504 (2000) 119–126

THEO CHEM

www.elsevier.nl/locate/theochem

Interactions that define the alkylamine side-chain conformation in phenylalkylamine hallucinogens: an ab initio study

O.E. Taurian[a,*], R.H. Contreras[b,1]

[a]*Departamento de Química y Física, Facultad de Ciencias Exactas, Físico-químicas y Naturales, Universidad Nacional de Río Cuarto, Ruta Nac. 36, Km 601, 5800 Río Cuarto, Argentina*

[b]*Departamento de Física, FCEyN, Universidad de Buenos Aires, Buenos Aires, Argentina*

Abstract

Different interactions that define the alkylamino side chain conformation in phenylalkylamine hallucinogen compounds are studied with HF/6-31G* ab initio calculations and natural bond orbital, NBO, analyses. These studies were performed on three model compounds, namely, 2,3,4-trimethoxyphenethylamine (IM) **I**, 3,4,5-trimethoxy-phenethyl-amine (mescaline), **II**, and 2-methyl-2,5-dimethoxy-amphe-tamine (DOM) III. It was found that the three of them present three alkylamino rotamers which can be classified as *gauche-1*, *gauche-2* and *trans* according to the C–NH_2 orientation with respect to the C_α–C_β bond. Although in all cases the *gauche-1* conformer is the preferential one, its relative stability with respect to the *trans* one was found to decrease when increasing the hallucinogen potency. A variety of interactions could be identified and their role played in that behavior are discussed.

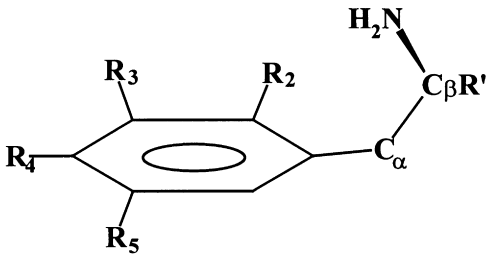
Keywords: Natural bond orbital; 2-Methyl-2,5-dimethoxy-amphe-tamine; Ab initio

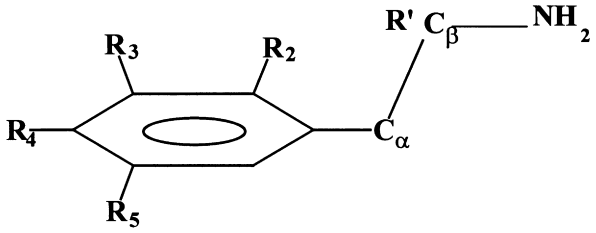
1. Introduction

Different properties of phenylalkylamine derivatives were being studied for a long time with different approaches [1–9] and at present many of such compounds are known to have hallucinogenic properties. When comparing their potency, one of the most conspicuous features that is observed, is the broad range of values that such property can take and that in most cases the phenyl group bears one or several methoxy groups as side-chains. The biological activity strongly depends on the phenyl substitution pattern [2,7] of those methoxy groups. It is interesting to note that other compounds presenting different types of biological activity such as antitumoral, antiviral or antibacterial, have also methoxy groups as substituents on an aromatic ring, as, for instance, 2,4-diamino-5(3′,4′,5′-trimethoxy-benzyl)pyrimidine (trimethoprim) [10], 2,4-diamino-6-(2,5-dimethoxybenzyl)-5-methyl-pyrido[2,3-d]pyrimidine (piritrexim) [11] and (2,4-diamino-methyl-6-[(3,4,5-trimethoxyanilino)methyl]-quinazoline) (trimetrexate) [12] and also their substitution pattern plays also an important role in defining the potency of a given compound [13–15]. Such observation suggests that the interactions between the methoxy groups and the aromatic ring are important in defining the role played by the "pharmacophoric moiety". In phenylalkylamine hallucinogens it can be expected that the role of "pharmacophoric moiety" is played mainly by the alkylamine side-chain group.

* Corresponding author.
E-mail address: otaurian@cdc.unrc.edu.ar (O.E. Taurian).
[1] Member of Carrera del Investigador (CONICET).

0166-1280/00/$ - see front matter
PII: S0166-1280(00)00359-6





Compound	R_2	R_3	R_4	R_5	R´
I	OMe	OMe	OMe	H	H_2
II	H	OMe	OMe	OMe	H_2
III	OMe	H	CH_3	OMe	CH_3

Scheme 1.

Interactions that define the methoxy group conformation in unsaturated methyl ethers were studied extensively during the last two decades [16–28]. A brief account of the main features of such interactions is as follows. In anisole derivatives the OMe group adopts a heavy atom planar conformation [29–33] unless it is flanked by two *ortho* substituents [34,35]. In some cases an unhindered methoxy group adopts as preferential one of the two possible planar conformations like, for instance, in 3-NO_2-4-NH_2-anisole [36]. Similar behavior was also observed in other aryl and heteroaryl compounds like 2-OMe-pyridine [37,38], 2-methoxy phenazyne [39,40] and 3-fluoroanisole [41]. This seems to indicate that the preferential OMe conformation is *cis* to the adjacent bond with the larger π-mobile bond order [42–44]. However, there are two known cases which show that such trend is not general, namely, *o*-dimethoxy benzene which is known that in gas phase the preferential conformation is non-planar [45,46], and *p*-dimethoxy benzene where the conformation with the methoxy groups opposite to each other was calculated to be more preferential than that with both groups *cis* to the alternating aromatic bonds [47]. These observations suggest that in the last two cases, an OMe conformation *cis* to the aromatic bond with larger π-mobile bond order renders a destabilizing interaction. A good probe to detect the OMe conformation in

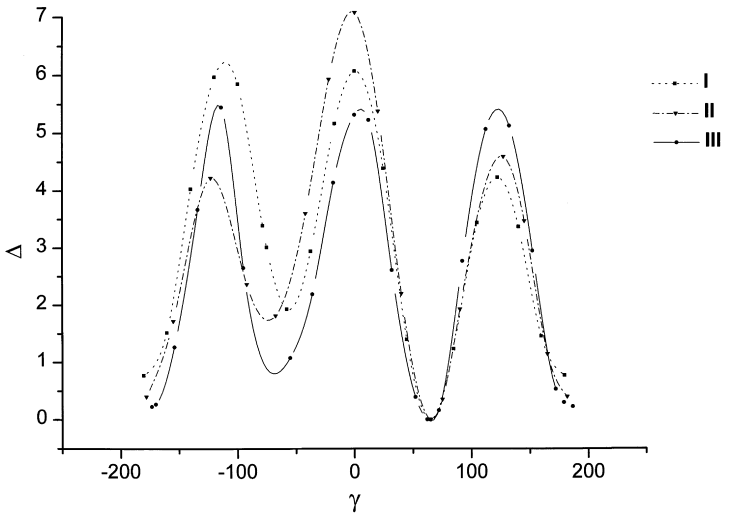


Fig. 1. Barrier to inner rotation around the C_α–C_β bond for compounds **I**–**III**. In all three cases the energy, ΔE (in kcal/mol), is referenced to that of the *gauche-1* rotamer,. The torsion angle C_{ipso}–C_α–C_β–N, γ (in degrees), is referenced to the *cis* conformation between the C_{ipso} and N atoms.

aryl methyl ethers is NMR spectroscopy. For instance, in anisole derivatives the ^{13}C substituent chemical shifts, SCS, are different for the *cis–ortho* and *trans–ortho* orientations, being the former a larger shielding effect of about 7 ppm than the latter [16,48]. The *trans–ortho* SCS, is not far from the *para*-OMe SCS and this suggests that it is mainly determined by the mesomeric interaction. Recently, [49] all these observations were rationalized as follows. The O–CH_3 moiety is a highly polar group and if there is one OMe group placed proximate to a π-type bond, which is highly polarizable, an opposite dipole is induced in the latter, and both dipoles yield a stabilizing interaction which was dubbed the "polar bond-polarizable bond", PB–PzB, interaction [50,51], and an idea of its strength can be obtained measuring the difference in ^{13}C SCSs of the *cis–* and *trans–ortho* carbon atoms. The known deshielding effect of the OMe ^{13}C chemical shift for an out-of-plane conformation [52] was interpreted on similar grounds [53], i.e. as an inhibition of the PB–PzB interaction.

From the above rationalization in terms of the PB–PzB interaction it can be expected that the π aromatic system around the aryl carbon placed *cis–ortho* to a planar OMe group, should be notably polarized and it should have the capability of interacting with other side-chain groups attached to the same aryl ring. In the case under consideration a polarized π aromatic system could be important in defining the alkylamine side-chain conformation in phenylalkyl hallucinogens. In order to study such possibility, in this work the alkylamine preferential conformations are studied in three model compounds, 2,3,4-trimethoxyphenethylamine (IM) **I**, 3,4,5-trimethoxy-phenethylamine (mescaline), **II**, and 2-methyl-2,5-dimethoxyamphetamine (DOM) **III**. The first one is known to be inactive [2], the second one is taken as reference for comparing hallocinogenic potency [2,7], and the third one has a potency much larger than **II** [2,7]. In order to acquire an insight into the interactions that define the alkylamino group conformation, NBO, Natural Bond Orbital, [54] analysis were performed for the three lowest energy conformations.

2. Computational details

In **I**–**III** the alkylamine side-chain stable conformations were sought studying the respective barriers to inner rotation around the C_α–C_β bond. In all three compounds, three stable conformers were thus found which are hereafter dubbed as *gauche-1*, *gauche-2* and *trans* rotamers (see Scheme 1 for *Gauche-1* and *trans* rotamers for compounds **I**–**III)**; the first one corresponds to the gauche conformation with the NH_2 moiety close to ring position 6, while the second

Table 1
C_{ipso}–C_α–C_β–N torsion angles for *gauche-1*; *gauche-2* and *trans* rotamers referenced to the *cis* conformation between the C_{ipso} and N atoms; their respective differences (in degrees); and their relative energies respect to that of the *gauche-1* rotamer (in kcal/mol) in compounds **I**–**III**

Compound	**I**	**II**	**III**
γ-*gauche-1*	64.53	65.08	61.97
γ-*gauche-2*	−55.90	−75.62	−57.00
γ-trans	179.45	181.76	186.06
Δγ-1	114.92	116.68	124.09
Δγ-2	124.65	102.62	116.94
ΔE_{trans}	0.77	0.40	0.23
$\Delta E_{gauche\text{-}2}$	1.90	1.63	1.06

one corresponds to that with the NH_2 moiety close to ring position 2. Natural Bond Orbitals [55], NBO, analysis were performed for those three rotamers of each compound. All calculations were carried out at the HF/6-31G* level, using the GAUSSIAN 94 package of programs [56].

3. Results and discussion

The comparison of several parameters of the full optimized geometries in the *gauche* and *trans* conformations of the amino group for compounds **I**–**III** show several peculiarities which are worth noting. In all of them the most stable rotamer is the *gauche-1* one, and the next two energy minima correspond to the *trans* and *gauche-2* rotamers, respectively. The barriers to inner rotation around the C_α–C_β bond for **I** and **III** are shown in Fig.1 while the relative energy to that of the *gauche-1* rotamers for the *trans* and *gauche-2* ones are displayed in Table 1 where it is observed both of them decrease from **I**–**III**. This observation suggests that the alkylamine side chain conformation could be an important factor in defining the potency of the hallucinogenic effect in these compounds. Therefore, it seems interesting to analyze which interactions define the alkylamine group conformation. Some of them seem to depend on the atomic charges placed at the aromatic **1**, **2** and **6** ring positions; the respective NBO values are displayed in Fig. 2. A brief account of the most evident interactions defining the alkylamine group conformation is as follows.

3.1. Conspicuous interactions present in the gauche-1 rotamers

Four main interactions are recognized for this conformer:

1. An N–H$\cdots\pi$ hydrogen bond interaction with the aromatic electronic system, as gauged by an amino H proton to the C_6 carbon atom distance. Such interatomic distances for compounds **I** to **III** are displayed in Table 2 where a shortening of the N–H$\cdots\pi$ distance along the series **I** to **III** is observed which seems to indicate that this interaction increases accordingly. According to the NBO analyses carried out on these three compounds, no charge transfer either of type (N–H) $\rightarrow \pi^*$ or $\pi \rightarrow$ (N–H)* takes place (the respective second order perturbation energies [54] are smaller than 0.50 kcal/mol). This indicates that its origin is mainly electrostatic and, according to Hobza et al. [57] they can be called “anti-hydrogen bonds”. As studied in previous papers [58–60], in hydrogen bonds dominated by an electrostatic interaction the X–H bond of the proton donor is slightly shortened. In the present case, it is difficult to identify a bond length shortening of this type owing to the N–H delocalization interactions involving a vicinal bond (or antibond) belonging to the same alkylamino moiety.
2. The strengths of the $(C_{ipso}\text{–}C_\alpha) \rightarrow (C_\beta\text{–}H_{\beta1})^*$ and $(C_\beta\text{–}H_{\beta1}) \rightarrow (C_{ipso}\text{–}C_\alpha)^*$ interactions (σ conjugation) [61] are shown in Table 3. While in compounds **I** and **II** the sum of these two interactions is practically the same, in **III** the sum of these two interactions is somewhat larger than in the former two, in accordance with the well known trends given by the simple PMO theory (Perturbed Molecular Orbitals) [62,63] since in **III** a methyl group is bonded to the C_β atom.
3. There is also a destabilizing interaction which is present in all three compounds, although their strengths could be quite different, i.e. there is a large and negative charge at the N atom and it is close to the C_6 atom which bears also an important negative charge, as shown in Table 2.
4. In **I** and **III** there are close contacts of type C–H$\cdots$O between an alkylamino C–H bond and the

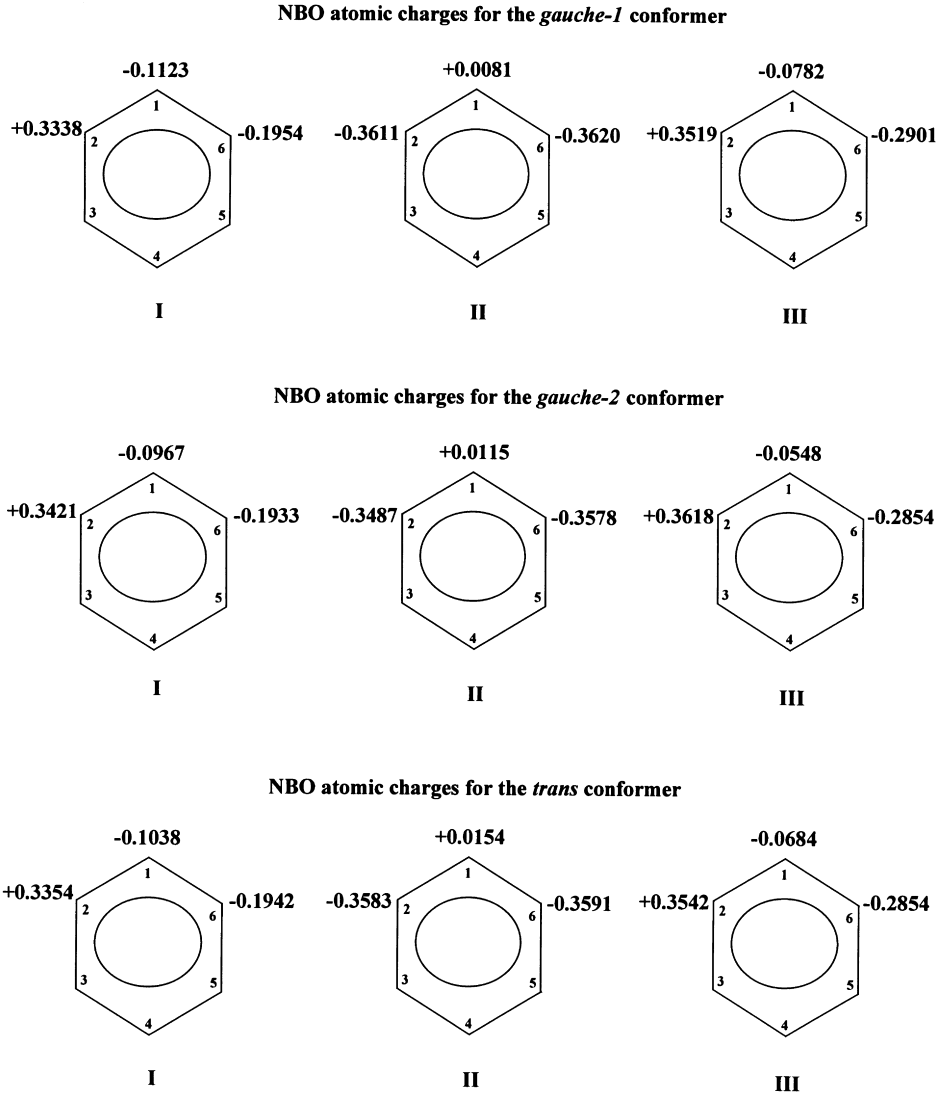


Fig. 2. C_1; C_2 and C_6 NBO atomic charges for the *gauche-1*, *gauche-2* and *trans* rotamers of compounds **I**–**III** (in a.u.).

O atom of the methoxy group attached to the ring position 2. Close contacts of this type are now well known to be important enough to define preferential conformations in many organic and biological compounds [62,63]. In **I** there is a $C_\beta-H_{\beta2}\cdots O$ contact where the $H_{\beta2}\cdots O$ distance is only 2.8179 Å, and in **III**, there is a methyl $C-H\cdots O$ contact where the corresponding $H\cdots O$ distance is 2.9602 Å. In both cases such proximate interactions favor the *gauche-1* conformer.

3.2. Conspicuous interactions present in the gauche-2 rotamers

The main interaction that defines the *gauche-2* conformer in all three compound seems to be the $(C_{ipso}-C_\alpha) \rightarrow (C_\beta-X)^*$ and $(C_\beta-X) \rightarrow (C_{ipso}-C_\alpha)^*$

Table 2
Selected electron delocalization $\Delta E^{(2)}$ energies [52] (in kcal/mol); non-bonded interatomic distances, d (in Å); and net atomic charges as calculated with the NBO approach, q (in a.u.) for *gauche-1* rotamers of **I**–**III**

	I	**II**	**III**
$(C_{ipso}–C_\alpha) \rightarrow (C_\beta–H_{\beta 1})$	1.68	1.70	1.43
$(C_\beta–H_{\beta 1}) \rightarrow (C_{ipso}–C_\alpha)$	4.66	4.57	5.10
$d(N–H\cdots C_1)$	2.7696	2.7753	2.8175
$d(N–H\cdots C_6)$	2.9317	2.8596	2.7886
$d(N\cdots C_6)$	3.4049	3.3469	3.2194
$q(N)$	−0.9251	−0.9240	−0.9253
$q(C_6)$	−0.1954	−0.3620	−0.2901

($X = H$ in **I** and **II** and C_{Me} in **III**) electron delocalizations that causes the $C_\beta–X$ bond to adopt a *trans* configuration with respect to the $C_{ipso}–C_\alpha$ bond, Table 3. These two interactions are more stabilizing in **I** than in **III**. This interpretation is reinforced by noticing that for these last two compounds there are interactions that arise from the close proximity between the NH_2 moiety and the oxygen atom of the OMe(2) group; some relevant interatomic distances are also shown in Table 3, which are absent in compound **II**. In spite of this, all the three compounds display the practically identical configuration for the *trans* rotamers.

3.3. Conspicuous interactions present in the trans rotamers

The main interactions within the alkylamine group

Table 3
Selected electron delocalization $\Delta E^{(2)}$ energies [52] (in kcal/mol); non-bonded interatomic distances, d (in Å); and net atomic charge as calculated with the NBO approach, q (in a.u.) for *gauche-2* rotamers of **I**–**III**

	I	**II**	**III**
$(C_{ipso}–C_\alpha) \rightarrow (C_\beta–X)$[a]	1.67	1.49	2.15
$(C_\beta–X) \rightarrow (C_{ipso}–C_\alpha)$[a]	4.66	4.08	2.96
$d(N–H\cdots O)$	2.6973	–[b]	2.7067
$d(N\cdots O)$	3.1845	–[b]	3.1982
$d(N\cdots C_1)$	2.9760	3.1828	2.9561
$q(C_1)$	−0.0967	+0.0115	−0.0541

[a] $X = H$ in I and II, and $X = C_{Me}$ in **III**.
[b] There is no OMe substituent *ortho* to the ehtylamino group in compound **II**.

Table 4
Selected electron delocalization $\Delta E^{(2)}$ energies [52] (in kcal/mol); non-bonded interatomic distances, d (in Å); and net atomic charges as calculated with the NBO approach, q (in a.u.) for *trans* rotamers of **I**–**III**

	I	**II**	**III**
$(C_{ipso}–C_\alpha) \rightarrow (C_\beta–N)$	2.44	2.46	2.16
$(C_\beta–N) \rightarrow (C_{ipso}–C_\alpha)$	2.35	2.29	2.63
$\pi \rightarrow (C_\beta–N)$	0.61	0.63	0.58
$d(N\cdots C_6)$	3.4049	3.3469	3.2194
$q(N)$	−0.9251	−0.9240	−0.9253
$q(C_6)$	−0.1954	−0.3620	−0.2901

that seem to determine its *trans* conformation are the $(C_{ipso}–C_\alpha) \rightarrow (C_\beta–N)^*$ and $(C_\beta–N) \rightarrow (C_{ipso}–C_\alpha)^*$ electron delocalizations, as expected from the simple PMO theory [59]. They are compared in Table 4 for compounds **I**–**III**, where it is observed that their sum differ only slightly from one compound to the other.

A survey of all interactions quoted above shows that for the *trans* rotamers there are only very slight differences among the three compounds. Therefore, their differences in $\Delta E_{t-g1} = E_{trans} - E_{gauche-1}$ seem to arise mainly from differences in interactions operating in the *gauche-1* rotamers. Their comparison shows that, interactions of types (1) and (2) have almost the same strength in all three compounds, and whence they cannot account for the ΔE_{t-g1} differences shown in Table 1. It seems that such differences arise from interactions of type 3, which destabilize the *gauche-1* conformation in compounds **II** and **III**. Why interaction (3) seems to be so different in these model compounds? Apparently, they originate in the large polarization of the aromatic π electronic system. This polarization can be assessed comparing the NBO atomic charges at the ring position 6 for the different compounds, Table 2. According to previous studies [49,51] this polarization arises from the conformation of the OMe placed at ring position 5, i.e. the C_6 atom is placed *ortho–cis* to the methyl moiety. There is a further destabilizing effect due to such polarization of the π electronic system for the *gauche-1* rotamers; in fact, since the C–N bond is a single one and therefore a rapid rotation of the NH_2 around such bond can be expected. Such a rotation would cause the N lone pair to face the negatively charged C_6 carbon atom, and therefore it would increase their repulsion. This destabilizing effect is

expected to be stronger in **II** and **III** than in **I** owing to the different charge at the C_6 carbon atom (see Table 4).

The smaller ΔE_{t-g1} value in **III** than in **II** can be rationalized on similar grounds, since there is a close contact between an N methyl C–H bond and the OMe(2) oxygen atom. This interaction, although at first sight stabilizing, becomes destabilizing as soon as that methyl group rotates away from its equilibrium position.

4. Conclusions

In the three model compounds studied in this paper, it was found that the ΔE_{t-g1} energy is smaller the larger is the hallucinogen activity. The ΔE_{t-g1} trend can be expressed by saying that in **II** and **III** their *trans* rotamers are more favored than in compound **I**. Since the former two compounds are known to have hallucinogen properties, in a somewhat speculative way, it can be thought that an alkylamino group in a *trans* conformation favors an N–H hydrogen bond interaction with the receptor. Therefore, the dependence of the potency of a phenylalkylamine hallucinogen compound upon the substitution pattern on the aromatic ring seems to originate in side-chain interactions that cause a destabilizing effect on the *gauche-1* alkylamine conformation. Such side-chain interactions are found to work in two different ways, namely, a direct one like the close C–H contacts with an electronegative group, and an indirect one through the polarization of the aromatic π electronic system.

Acknowledgements

Economic supports from UBACyT, CONICET, ANPCyT (BID 802/OC-AR-PICT # 00604), Córdoba Research Council, CONICOR, and University of Río Cuarto SECyT are gratefully acknowledged. O.E.T. is very grateful to Prof. D.E. Nichols for interesting comments. The services and computer time made available by the Faculty of Chemistry, Biochemistry and Pharmacy of the University of San Luis and the University of Río Cuarto Computer Center are gratefully acknowledged.

References

[1] U. Braun, P. Jacob, D.E. Nichols, A.T. Shulgin, in: G. Barnett, M. Trsic, R. Willette (Eds.), Quantitative Structure Activity Relationships of Analgesics, Narcotic Antagonists and Hallucinogens, Research Monograph 22National Institute on Drug Abuse, Washington, DC, 1978, p. 27.
[2] J.J. Knittel, A. Makriyannis, J. Med. Chem. 24 (1981) 906.
[3] T. Shulgin, in: L.L. Iversen, S.D. Iversen, S.H. Snyder (Eds.), Handbook of Psychopharmacology, vol. 11, Plenum Press, New York, 1978 (243pp.).
[4] T. Shulgin, in: M.E. Wolff (Ed.), Burger's Medicinal Chemistry, 4th ed., Wiley, New York, 1981 (1109pp.).
[5] t. Shulgin, in: F. Hoffmeister, G. Stille (Eds.), Handbook of Experimental Pharmacology, vol. 55, no. 3, Springer, Berlin, 1981, p. 3.
[6] A. Shulgin, A. Shulgin, PiHKAL, Part. 2. A Chemical Love Story, Transform Press, Berkeley, USA, 1991.
[7] P. Jacob III, A.T. Shulgin, in: G.C. Lin, R.A. Glennon (Eds.), Hallucinogens: an Update, Research Monograph 146National Institute on Drug Abuse, Washington, DC, 1994, p. 74.
[8] B.W. Clare, J. Mol. Struct. (Theochem) 337 (1995) 139.
[9] B.W. Clare, J. Med. Chem. 41 (1998) 3845.
[10] B. Roth, E.A. Falco, G.H. Hitchings, S.R.M. Bushby, J. Med. Pharm. Chem. 5 (1962) 1103.
[11] E.M. Grivsky, S. Lee, C.W. Sigel, D.S. Duch, C.A. Nichol, J. Med. Chem. 23 (1980) 327.
[12] W.R. Leopold, D.D. Dykes, D.P. Griswold Jr., Proc. Annu. Meet. A, Assoc. Cancer Res. 27 (1986) 253.
[13] B. Roth, E. Aig, B.S. Rauckman, J.Z. Strelitz, A.P. Phillips, R. Ferone, S.R.M. Bushby, C.A. Sigel, J. Med. Chem. 24 (1981) 933.
[14] L.F. Kuyper, B. Roth, D.P. Baccanari, R. Ferone, C.R. Beddell, J.N. Champness, D.K. Stammers, J.G. Dann, F.E.a. Norrington, D.J. Baker, P.J. Goodford, J. Med. Chem. 25 (1982) 1120.
[15] B. Roth, E. Aig, J. Med. Chem. 30 (1987) 1998.
[16] P.W. Jardon, E.H. Vickery, L.F. Pahler, N. Pourahmady, G.J. Mains, E.J. Eisenbraun, J. Org. Chem. 49 (1984) 2130.
[17] A. Makriyannis, S. Fesik, J. Am. Chem. Soc. 104 (1982) 6462.
[18] L.I. Kruse, J.K. Cha, J. Chem. Soc., Chem. Commun. (1982) 1329.
[19] M.A. Natiello, R.H. Contreras, J.C. Facelli, D.G. de Kowalewski, J. Phys. Chem. 87 (1983) 2603.
[20] S.R. Salman, Spectrochim. Acta A 39 (1983) 1073.
[21] S.R. Salman, F.S. Kamounah, Magn. Reson. Chem. 25 (1987) 966.
[22] L.I. Kruse, C.W. DeBrosse, C.H. Kruse, J. Am. Chem. Soc. 107 (1985) 5435.
[23] D. Bond, P.v.R. Schleyer, J. Org. Chem. 55 (1990) 1003.
[24] I.I. Schuster, M. Parvez, A.J. Freyer, J. Org. Chem. 53 (1988) 5819.
[25] G.H. Penner, R.E. Wasylishen, Can. J. Chem. 67 (1989) 525.
[26] J. Joseph-Nathan, C. García, M.S. Morales Ríos, Magn. Reson. Chem. 28 (1990) 311.
[27] R.H. Contreras, R.R. Biekofsky, D.G. de Kowalewski, A.M. Orendt, J.C. Facelli, J. Phys. Chem. 97 (1993) 91.

[28] J.C. Facelli, A.M. Orendt, Y.J. Jiang, R.J. Pugmire, D.M. Grant, J. Phys. Chem. 100 (1996) 8268.
[29] V.M. Bzezovskii, G.A. Kalabin, I.A. Aliev, B.A. Trofimov, AN SSSR Ser. Khim. (1976) 1999.
[30] H. Konschin, H. Tylli, C. Grundfelt-Forsius, J. Mol. Struct. 77 (1981) 51.
[31] H. Konshin, J. Mol. Struct. 105 (1983) 213.
[32] T. Schaefer, S.R. Salman, T.A. Wildman, G.H. Penner, Can. J. Chem. 63 (1985) 782.
[33] T. Schaefer, R. Laatikainen, Can. J. Chem. 61 (1983) 224.
[34] I.I. Schuster, J. Org. Chem. 50 (1985) 1657.
[35] T. Schaefer, G.H. Penner, Can. J. Chem. 66 (1987) 1635.
[36] R.H. Contreras, D.G. de Kowalewski, J.C. Facelli, J. Mol. Struct. 81 (1982) 147.
[37] R.H. Contreras, J.C. Facelli, D.G. de Kowalewski, Org. Magn. Reson. 20 (1982) 40.
[38] W.J.P. Blonski, F.E. Hruska, T.A. Wildman, Org. Magn. Reson. 22 (1984) 505.
[39] A. Römer, Org. Magn. Reson. 19 (1982) 66.
[40] R.H. Contreras, M.A. Natiello, G.E. Scuseria, Magn. Reson. Rev. 9 (1985) 239.
[41] T. Schaefer, R. Sebastian, Can. J. Chem. 67 (1989) 1027.
[42] T. Schaefer, R. Sebastian, J. Magn. Reson. 73 (1987) 541.
[43] D.A. Forsyth, V.M. Osterman, J.R. DeMember, J. Am. Chem. Soc. 107 (1985) 818.
[44] W.J. Chazin, L.D. Colebrook, Can. J. Chem. 64 (1986) 2220.
[45] G.M. Anderson III, P.A. Kollman, L.N. Domelsmith, K.N. Houk, J. Am. Chem. Soc. 101 (1979) 2344.
[46] O. Exner, V. Jehlicka, Coll. Czech. Chem. Commun. 48 (1983) 1030.
[47] J.C. Facelli, J. Mol. Struct. (Theochem) 276 (1992) 307.
[48] R.R. Biekofsky, A.B. Pomilio, R.H. Contreras, D.G. de Kowalewski, J.C. Facelli, Magn. Reson. Chem. 27 (1989) 158.
[49] R.R. Biekofsky, A.B. Pomilio, R.A. Aristegui, R.H. Contreras, J. Mol. Struct. 344 (1995) 143.
[50] D.G. de Kowalewski, V.J. Kowalewski, E. Botek, R.H. Contreras, J.C. Facelli, Magn. Reson. Chem. 35 (1997) 351.
[51] J.E. Peralta, M.C. Ruiz de Azúa, R.H. Contreras, Int. J. Quantum Chem. 70 (1998) 105.
[52] K.S. Dhami, J.B. Stothers, Can. J. Chem. 44 (1966) 2855.
[53] A.L. Esteban, M.P. Galache, E. Diez, R.R. Biekofsky, R.H. Contreras, Magn. Reson. Chem. 32 (1994) 199.
[54] E. Reed, L.A. Curtiss, F. Weinhold, Chem. Rev. 88 (1988) 899.
[55] E.D. Glendening, A.E. Reed, J.E. Carpenter, F. Weinhold, NBO version 3.1.
[56] M.J. Frisch, G.W. Trucks, H.B. Schlegel, P.M.W. Gill, B.G. Johnson, M.A. Robb, J.R. Cheeseman, T. Keith, G.A. Petersson, J.A. Montgomery, K. Raghavachari, M.A. Al-Laham, V.G. Zakrzewski, J.V. Ortiz, J.B. Foresman, J. Cioslowski, B.B. Stefanov, A. Nanayakkara, M. Challacombe, C.Y. Peng, P.Y. Ayala, W. Chen, M.W. Wong, J.L. Andres, E.S. Replogle, R. Gomperts, R.L. Martin, D.J. Fox, J.S. Binkley, D.J. Defrees, J. Baker, J.P. Stewart. M. Head-Gordon, C. Gonzalez, J.A. Pople, GAUSSIAN 94, Revision D.4, Gaussian, Inc., Pittsburgh, PA, 1995.
[57] P. Hobza, V. Spirko, H.L. Selzle, E.W. Schlag, J. Phys. Chem. A 102 (1998) 2501.
[58] C.G. Giribet, C.V. Vizioli, M.C. Ruiz de Azúa, R.H. Contreras, J.J. Dannenberg, A. Masunov, J. Chem. Soc., Faraday Trans. 92 (1996) 3029.
[59] A.V. Afonin, C. Vizioli, M.C. Ruiz de Azúa, R.H. Contreras, Bull. Acad. Sci. Russia, Div. Chem. Sci. 45 (1996) 1362.
[60] M.J.S. Dewar, J. Am. Chem. Soc. 106 (1984) 669.
[61] M.J.S. Dewar, R.C. Dougherty, The PMO Theory of Organic Chemistry, Plenum, New York, 1975.
[62] T. Steiner, Cryst. Rev. 6 (1996) 1.
[63] T. Steiner, J. Chem. Soc., Chem. Commun. (1997) 727.