# QUANTUM-CHEMICAL ESTIMATE OF DIPOLE
# MOMENTS OF TROPONES AND TROPOLONES

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*Data on the experimental dipole moments of tropones and tropolones including natural compounds and their substitution products and analogs were systematized. Dipole moments ($\mu$) of 28 tropones and 34 tropolones were calculated using MNDO, AM1, and PM3. The capabilities of these bonding schemes to estimate the $\mu$ values were found. Correlations $\mu_{exp} = b\mu_{theor}$ were found. The electronic structure of parent molecules of these compounds was studied using the ab initio (RHF/6-31G$^{**}$) method. It has been found that the regioselectivity of electrophilic reactions of troponoids is consistent with the distribution of electron density in the molecules that was found using semi-empirical MNDO, AM1, PM3 and ab initio methods.*

**Key words:** tropones, tropolones, natural compounds, dipole moment, quantum-chemical estimate, theory—experiment correlation, electronic structure.

Tropones and tropolones comprise many natural compounds and interesting structures [1-15] that combine the properties of nonbenzene aromatic and unsaturated compounds. In certain instances, the tropone acts as a ketone; tropolone, as a vinyl analog of a carboxyl.

The tropolone moiety appears in $\alpha$-, $\beta$-, and $\gamma$-thujaplicins (3-, 4-, and 5-isopropyltropolones, respectively), which are isolated from wood of the Western red cedar (*Thuja plicata* D. Don.). These and other terpene tropolones, e.g., 7-hydroxy-$\beta$-thujaplicin, $\beta$-dolabrin (4-isopropenyltropolone), and nutcatin, occur in the wood and essential oils of the cypress (Cupressaceae) family. $\beta$-Thujaplicin (hinokitiol) was isolated from the fragrant oil of Taiwan cedar (*Chamaecyparis taiwanensis* Mas. et Suz.). Stipitatic, stipitatonic, puberulic, and puberulonic acids are metabolites of various mold species. Purpurogallin was found in certain nut galls as a glycoside. Colchicine is an alkaloid of Autumn crocus (*Colchicum autumnale* L.) [3-5].

Troponoids exhibit an antimitotic effect; possess bacteriostatic, bactericidal, fungistatic, and fungicidal activities; and are used as antibiotics [1-3, 6-8]. Tropolones may be intermediates in the biogenesis of alkaloids [2-5]. Liquid crystals, ionophores, J-aggregated dyes, and other modern materials are based on troponoids [9].

Molecular recognition, the interaction of biologically active substances with biosubstrate receptors, is determined by the electrostatic properties of chemical compounds ([10-13] etc.). The dipole moment is an important characteristic of the electrical properties of a molecule the measures its electrostatic (ion—dipole, dipole—dipole) interaction with other molecular systems. In addition to explaining the biological activity, data on dipole moments are necessary for studying the mutual influence of atoms, electronic effects in molecules, intermolecular interactions, H-bonds, tautomeric transformations, and solvation in order to solve various chemical and physicochemical problems [14, 15].

Dipole moments cannot always be measured because existing methods have serious limitations [14, 15]. Theoretical estimates must be made. Vector-additive schemes are widely employed to calculate dipole moments [14-16]. However, the determination of absolute values and directions of bonded and group moments and the calculation of homeopolar dipoles and moments of nonbonding electron pairs is an exceedingly difficult task.

Dipole moments of organic molecules are calculated by the semi-empirical quantum-mechanical methods MNDO, AM1, and PM3 with absolute uncertainties of 0.30-0.45, 0.24-0.35, and 0.38-0.40 D, respectively ([17-20] etc.).

TABLE 1. Dipole Moments of Tropones and Tropolones Measured in Benzene by Debye's Second Method [2-5, 16, 26-31] and Calculated

| Compound | $\mu_{exp}$, D | Temperature, K | $\mu_{theor}$, D | | |
|---|---|---|---|---|---|
| | | | MNDO | AM1 | PM3 |
| Tropones | | | | | |
| Tropone (2,4,6-Cycloheptatrien-1-one) | 4.1* | Room | 3.58 | 4.02 | 3.76 |
| 2-Phenyltropone | 3.82 | 298 | 2.86 | 2.99 | 2.90 |
| 2-$p$-Methoxyphenyltropone | 3.63 | 298 | 1.98 | 4.14 | 3.44 |
| 2-Aminotropone | 3.78 | 298 | 2.42 | 2.34 | 2.21 |
| 4-Hydroxytropone | 5.9 | 298 | 2.73 | 3.16 | 2.94 |
| 2-Methoxytropone | 4.72 | 298 | 3.62 | 4.23 | 3.60 |
| 2-Methoxy-3-isopropyltropone | 4.11 | 298 | 3.50 | 2.07 | 4.00 |
| 2-Methoxy-6-methyltropone | 5.06 | 298 | 2.77 | 4.03 | 3.60 |
| 2-Mercaptotropone | 4.36 | 298 | 3.39 | 3.21 | 2.59 |
| 2-Methylmercaptotropone | 4.64 | 298 | 3.76 | 2.09 | 1.73 |
| 2-Bromotropone | 4.94 | 303 | 4.38 | 4.79 | 4.34 |
| 3-Bromo-2-methoxytropone | 3.31 | 298 | 3.54 | 1.76 | 2.28 |
| 4-Bromo-2-phenyltropone | 2.73 | 298 | 2.36 | 2.52 | 2.56 |
| 7-Bromo-2-methoxytropone | 5.51 | 298 | 3.52 | 4.43 | 4.43 |
| 2,7-Dibromotropone | 5.27 | 298 | 4.01 | 4.08 | 4.67 |
| 3,7-Dibromo-2-phenyltropone | 3.67 | 298 | 2.30 | 2.39 | 2.90 |
| 2,3-Benzotropone | 3.61 | 298 | 2.95 | 3.23 | 2.98 |
| 4,5-Benzotropone | 4.70 | 298 | 4.17 | 4.48 | 4.16 |
| 2-Methyl-4,5-benzotropone | 4.25 | 298 | 4.05 | 4.04 | 3.76 |
| 2,7-Dimethyl-4,5-benzotropone | 3.66 | 298 | 3.94 | 3.61 | 3.38 |
| 2,7-Diethyl-4,5-benzotropone | 3.47 | 298 | 3.64 | 3.65 | 3.26 |
| 2,7-Dipropyl-4,5-benzotropone | 3.50 | 298 | 4.01 | 3.47 | 3.34 |
| 2,7-Diisopropyl-4,5-benzotropone | 3.16 | 298 | 3.05 | 2.78 | 2.55 |
| 2,7-Di-$t$-butyl-4,5-benzotropone | 2.32 | 298 | 3.00 | 2.49 | 2.62 |
| 2,7-Dihexyl-4,5-benzotropone | 2.08** | 298 | 2.88 | 2.66 | 2.63 |
| 2,7-Pentamethylen-4,5-benzotropone | 3.09 | 298 | 2.78 | 3.00 | 2.85 |
| 2,7-Dodecamethylen-4,5-benzotropone | 3.46 | 298 | 2.96 | 3.02 | 2.80 |
| 2,7-Diphenyl-4,5-benzotropone | 3.69 | 298 | 2.68 | 2.59 | 2.62 |
| Tropolones | | | | | |
| Tropolone (2-Hydroxy-2,4,6-cycloheptatrien-1-one, Purpurocatechin) | 3.53 | 298 | 2.64*** | 3.34 | 3.12 |
| 3-Methyltropolone[+] | 3.27 | 298 | 1.88 | 3.41 | 3.21 |
| 3-Isopropyltropolone ($\alpha$-Thujaplicin)[++] | 3.37 | 298 | 1.84 | 3.35 | 3.15 |
| 4-Methyltropolone[+], 4-Isopropyltropolone | 3.88 | 298 | 2.31 | 3.68 | 3.42 |
| ($\beta$-Thujaplicin, Hinokitiol)[++] | 3.93 | 298 | 2.82 | 3.76 | 3.45 |
| 5-Methyltropolone[+] | 3.94 | 298 | 2.04 | 3.69 | 3.46 |
| 7-Isopropyltropolone[+] | 3.37 | 298 | 1.70 | 2.96 | 2.87 |
| 3-Nitrohinokitiol[+++] | 6.19 | 298 | 4.85 | 5.13 | 4.63 |
| 3,5-Dinitrohinokitiol[+++] | 4.63 | 293 | 4.15 | 3.22 | 4.01 |
| 5,7-Dinitrohinokitiol[+++] | 4.79 | 298 | 5.45 | 5.96 | 5.81 |
| 3-Chlorohinokitiol[+++] | 4.74 | 298 | 2.27 | 3.16 | 2.33 |
| 5-Chlorohinokitiol[+++] | 2.70 | 298 | 1.16 | 2.46 | 2.42 |
| 7-Chlorohinokitiol[+++] | 4.38 | 298 | 2.71 | 4.26 | 3.67 |
| 3,7-Dichlorohinokitiol[+++] | 4.46 | 298 | 2.07 | 2.94 | 2.34 |

TABLE 1. (continued)

| Compound | $\mu_{exp}$, D | Temperature, K | $\mu_{theor}$, D | | |
|---|---|---|---|---|---|
| | | | MNDO | AM1 | PM3 |
| Tropolones | | | | | |
| 3-Bromotropolone | 3.91 | 298 | 2.64 | 3.36 | 2.86 |
| 3-Bromo-4-methyltropolone[+] | 4.42 | 298 | 2.05 | 2.90 | 3.11 |
| 3-Bromohinokitiol[+++] | 4.40 | 298 | 1.96 | 2.86 | 2.41 |
| 3-Bromo-5-methyltropolone[+] | 4.51 | 298 | 2.11 | 3.74 | 3.25 |
| 5-Bromotropolone | 2.07 | 298 | 1.15 | 1.78 | 1.74 |
| 5-Bromo-3-methyltropolone[+] | 1.95 | 298 | 1.25 | 1.92 | 1.86 |
| 5-Bromo-4-methyltropolone[+] | 2.68 | 298 | 1.39 | 2.30 | 2.19 |
| 7-Bromo-3-methyltropolone[+] | 4.05 | 303 | 2.11 | 3.22 | 3.53 |
| 7-Bromohinokitiol[+++] | 4.40 | 298 | 2.41 | 4.35 | 3.68 |
| 3,5-Dibromohinokitiol[+++] | 4.27 | 306 | 1.02 | 1.27 | 1.35 |
| 3,7-Dibromotropolone | 3.57 | 303 | 1.81 | 2.53 | 2.84 |
| 3,7-Dibromo-4-methyltropolone[+] | 4.19 | 298 | 1.80 | 2.58 | 3.19 |
| 3,7-Dibromohinokitiol[+++] | 4.27 | 306 | 1.78 | 2.61 | 2.90 |
| 3,7-Dibromo-5-methyltropolone[+] | 4.27 | 298 | 1.79 | 2.84 | 3.25 |
| 5,7-Dibromo-$\alpha$-thujaplicin[+++] | 2.82 | 298 | 1.56 | 2.25 | 2.36 |
| 5,7-Dibromohinokitiol[+++] | 3.14 | 293 | 1.67 | 3.27 | 2.66 |
| 3,5,7-Tribromotropolone | 1.83 | 298 | 0.851 | 1.20 | 1.67 |
| 3,5,7-Tribromo-4-methyltropolone[+] | 3.02 | 298 | 0.681 | 1.26 | 1.91 |
| 3,5,7-Tribromohinokitiol[+++] | 3.05 | 298 | 0.643 | 1.24 | 1.74 |
| 3,5'-Ditropolonyl | 4.85[^] | 298 | 2.02 | 4.33 | 4.60 |

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*Microwave spectroscopy; **in cyclohexane; ***according to MNDO method, energetically slightly more ($\Delta\Delta H_f$ 5.63 kJ/mol, $\Delta\Delta G_f$ 5.04 kJ/mol) favorable nonplanar conformer with dipole moment 2.13 D, which is an artifact of the MNDO method; [+]analogs of natural compounds; [++]natural compounds; [+++]substituted natural compounds; [^]in dioxane.

Our goal was to calculated by MNDO [17], AM1 [18], and PM3 [20] methods the dipole moments of tropone, tropolone, and their derivatives (including natural compounds and their substituted analogs) and to establish a correlation of the calculated and experimental values.

Semi-empirical calculations were performed using the MOPAC program set [21, 22] with full optimization of the geometry (Broyden—Fletcher—Goldfarb—Shanno procedure [23]) and application of the Thiel rapid minimization algorithm [24]. Preliminary minimization was achieved by molecular mechanics (MMX procedure) using the PCMODEL program set [25]. The condition for which the gradient norm was less than 0.084 kJ/(mol·Å) was imposed for the quantum-chemical calculations. In some instances the gradient norms were decreased by not using Thiel rapid minimization (the keyword NOTHIEL of the MOPAC set was used), by optimization using the Davidon—Fletcher—Powell (keyword DFP) method [23], and by combining the approaches symbolized by the keywords NOTHIEL and DFP.

Ab initio (RHF/6-31G**) calculations used the HyperChem program set [HyperChem™, Hypercube, Inc., 1115 NW 4th St., Gainesville, FL 32601, USA) with full optimization of the geometry and use of the Polak—Ribiere algorithm [23]. Preliminary optimization was performed by the PM3 method. A gradient norm less than 0.084 kJ/(mol·Å) was the target.

Table 1 systematizes the various experimental data and the results of our semi-empirical quantum-chemical calculations according to dipole moments of troponoids (including natural compounds and their derivatives and analogs).

We established previously that the MNDO, AM1, and PM3 methods reproduce correctly the most important thermodynamic and molecular characteristics ([32-42] etc.), electronegativity, and inductive and mesomeric parameters of atomic groups [43, 44] in series of organic compounds of various classes with various functional groups.

The semi-empirical approach is preferred over the ab-initio one owing to the simplicity of producing quantitative relationships of the required accuracy.

The fundamental correctness (disregarding several substantial deviations of $\mu_{theor}$ and $\mu_{exp}$ values) of quantum-chemical calculations of molecular electronic structures can be seen in the experimental and calculated standard gas-phase heats of formation of tropolone (kJ/mol):

| Experiment [75] | MNDO | AM1 | PM3 |
|---|---|---|---|
| -155.77 | -161.73 | -137.53 | -129.66 |

Furthermore, the AM1 and PM3 methods confirm the conclusion that tropolone contains an intramolecular H-bond (IHB) [2-5, 9, 45-50]. The IHB enthalpy ($\Delta H_{IHB}$) was calculated as the difference of the heats of formation of planar conformers A and B, which differ in the torsion angle of the O–H bond around the C–O bond by $180°$. The justification of such an approach for estimating the IHB energy was noted in a review [51] and an original article [52].
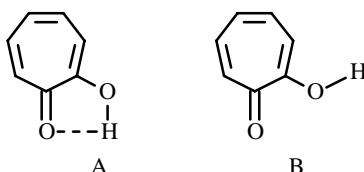


The $\Delta H_{IHB}$ values obtained by the AM1 and PM3 methods are negative. This corresponds to the presence of an IHB. However, the employed semi-empirical methods produce unsuccessfully numerical values for the IHB enthalpy of formation. The MNDO, AM1, and PM3 methods produce values of 4.37, -17.2, and -5.94 kJ/mol, respectively. The AM1 results are best.

The value -29.3 kJ/mol was proposed as the experimental estimate of the IHB energy in tropolone according to IR spectroscopy [46]. Later [45] thermochemical considerations established that the IHB energy lies in the range -20.9 to -29.3 kJ/mol, with -29.3 kJ/mol being the overestimated value. On the other hand, the total energy of molecule B according to Hartree—Fock ab initio calculations using 6-31G and 6-31G* basis sets is 48.99 and 42.76 kJ/mol, respectively, greater than these values for H-bonded conformer A [50]. It may be that the discrepancy with the experiments is due to unaccounted correlational uncertainties [22].

The dipole moment determines the electron-density distribution in a molecule. The Fockian matrix elements of the MNDO, AM1, and PM3 methods, in turn, are expressed as electron-density matrix elements, integrals $V\mu\nu^B$ that describe the coulombic interaction of atomic orbitals $\mu$ and $\nu$ of atom A with the shell of atom B, and two-electron integrals. The two-electron integrals appear in the expression for the repulsion energy of the shells. Resonance integrals, overlap integrals, and repulsion energies of the shells depend (like the charge distribution) on the internuclear distances.

Thus, the reproducibility of heats of formation is direct confirmation of the correctness of the dipole-moment calculations. Nevertheless, an unsatisfactory description of the IHB is a source of uncertainties in the estimate of both the energy characteristics and the dipole moments although the AM1 and PM3 methods are parametrized for the study of H-bonds.

The adequacy of the electron-density distribution found by quantum calculations and, therefore, of the dipole moments, is also demonstrated by a correlation of the regioselectivity of electrophilic-substitution reactions in series of tropones and tropolones with the Mulliken charges on the atoms. These are given below as an example for C atoms in parent molecules of representatives of these series of compounds:
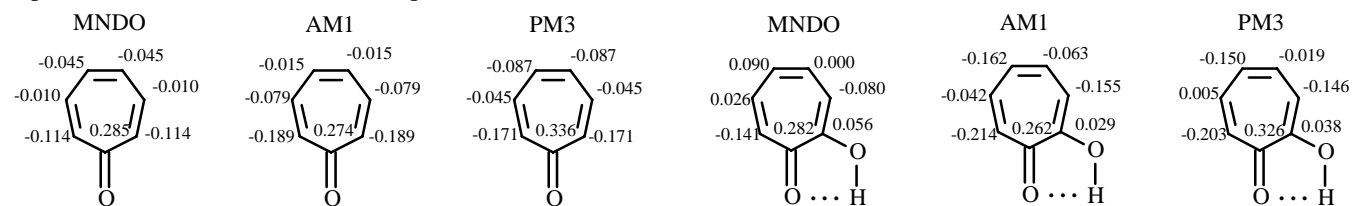


The values of the charges are consistent with electrophilic reactions of tropones at the 2- and 7-positions of the seven-membered ring, azo-coupling processes, nitrosation, nitration, sulfination, halogenation, hydroxylation, and hydroxymethylation of tropolones involving the 3-, 5-, and 7-positions of the ring [1-5].

According to non-empirical Hartree—Fock calculations using the 6-31G$^{**}$ basis set, the charge distribution in tropone and tropolone is qualitatively analogous to that obtained by semi-empirical calculations. However, it has a slightly greater charge polarization:
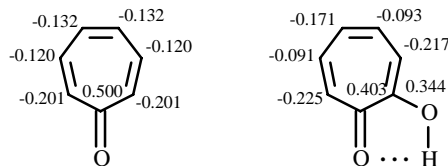


The dipole moments of tropone and tropolone according to the RHF/6-31G$^{**}$ calculations are 4.58 and 3.75 D, respectively. These values agree well with the experimental ones (Table 1).

As a rule, the MNDO, AM1, and PM3 methods give lower dipole moments for tropones and tropolones than experiments. The condition $\mu_{theor} > \mu_{exp}$ is observed only for 17 of the 186 instances. This is 9.14% of the total data (Table 1).

The absolute uncertainty of $\mu_{theor}$ - $\mu_{exp}$ (D) has the following values:

| Compound | MNDO | AM1 | PM3 |
|---|---|---|---|
| Tropones | from -3.17 to 0.68 | from -2.74 to 0.58 | from -2.96 to 0.55 |
| Tropolones | from -3.25 to -0.48 | from -3.00 to 0.39 | from -2.92 to 0.08 |

The condition $\mu_{exp} > \mu_{theor}$ could be met by charge separation resulting from polarization of the C=O bond, which is inadequately considered in the semi-empirical approach. However, our calculations indicate that a more substantial shift of electron density to the carbonyl C in tropone and tropolone is slightly exaggerated compared with other ketones with an exocyclic carbonyl (expressed in terms of resonance theory as a signinficant contribution of a bipolar tropyl structure [3-5] to the electronic structure of troponoids).
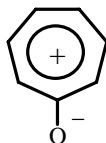


In order to prove this, we calculated the electronic structure of saturated ketones with a seven-membered ring, cycloheptanone (suberone) and its 2-hydroxy derivative, in addition to molecules of compounds analogous to tropone and tropolone that have a carbonyl with two neighboring double bonds. The latter include 4,5-dihydrotropone and 4,5-dihydrotropolone (differing little in structure from tropone and tropolone, respectively, but, in contrast with them, having nonplanar structures) and fluorone and 2-hydroxyfluorone (more distant analogs of troponoids that are, however, planar). Justification for comparing the electronic properties of troponoids and their more saturated seven-membered analogs derives from the similarity of the geometric parameters for the carbonyl C (Table 2). The charges on the atoms and the bond orders show that the charge polarization between the ring and carbonyl O is noticeably greater for troponoids than for the other molecules. The difference between the charges on the carbonyl O of the troponoids and those of the fluorene systems is more significant, which may be due to a substantially different geometry for the carbonyl group.

One of the reasons for the increased $\mu_{exp}$ may be the formation of donor—acceptor complexes of tropones and tropolones with the solvent in which the dipole moments are measured (most often benzene). Such a phenomenon is observed for quinones. The free molecules of 1,4-benzoquinone, 2,3,5,6-tetrachloro-1,4-benzoquinone, and 9,10-anthraquinone are nonpolar. In benzene, mesitylene, 1,4-dioxane, and $CCl_4$, their polarity is due to complexation with solvent molecules [53].

We note in support of this:

1. The dipole moment of 2,7-dihexyl-4,5-benzotropone was measured in cyclohexane, complexation with which is impossible. The $\mu_{exp}$ and $\mu_{theor}$ values agree well with each other and $\mu_{exp} < \mu_{theor}$ for all methods (Table 1).

2. Experimental (in benzene) dipole moments of 2,7-dialkyl-4,5-benzotropones (2.32-3.66 D) and 2,7-diphenyl-4,5-benzotropone (3.69 D) are noticeably less than those of 4,5-benzotropone (4.70 D) (Table 1). 2,7-Di-*t*-butyl-4,5-benzotropone has the highest dipole moment (2.32 D) among these molecules. Alkyl and phenyl groups are slightly polar. Their electronic effects are unclear [43, 44, 54-57]. Therefore, the trend in the change of dipole moments in the 4,5-benzotropone series is explained by steric hindrance to complexation with benzene. The electron-donor (although weak) properties of alkyl and phenyl substituents [43, 44, 54-57] may also prevent complexation.

TABLE 2. Certain Parameters of the Electronic Structure of Troponoids and Their Analogs

| Results of semi-empirical calculations | | | |
|---|---|---|---|
| Method | Charge on carbonyl oxygen | C=O bond order | C–CO–C angle, deg |
| Tropone (-0.583; 122.43) | | | |
| MNDO | -0.313 | 1.873 | 122.46 |
| AM1 | -0.320 | 1.820 | 122.65 |
| PM3 | -0.342 | 1.840 | 125.23 |
| Tropolone (-0.634; 123.36) | | | |
| MNDO | -0.302 | 1.900 | 118.51 |
| AM1 | -0.343 | 1.782 | 122.86 |
| PM3 | -0.372 | 1.781 | 124.34 |
| 4,5-Dihydrotropone (-0.555; 124.00) | | | |
| MNDO | -0.288 | 1.921 | 118.44 |
| AM1 | -0.290 | 1.880 | 118.90 |
| PM3 | -0.311 | 1.902 | 117.89 |
| 4,5-Dihydrotropolone (-0.585; 124.92) | | | |
| MNDO | -0.290 | 1.926 | 116.06 |
| AM1 | -0.305 | 1.855 | 121.72 |
| PM3 | -0.316 | 1.894 | 118.39 |
| Cycloheptanone (suberone) (-0.536; 120.08) | | | |
| MNDO | -0.291 | 1.944 | 121.75 |
| AM1 | -0.303 | 1.901 | 119.05 |
| PM3 | -0.326 | 1.914 | 119.67 |
| 2-Hydroxysuberone (-0.563; 121.59) | | | |
| MNDO | -0.285 | 1.951 | 119.82 |
| AM1 | -0.290 | 1.910 | 116.27 |
| PM3 | -0.303 | 1.929 | 116.37 |
| Fluorone (-0.512; 105.50) | | | |
| MNDO | -0.252 | 1.947 | 104.43 |
| AM1 | -0.237 | 1.930 | 104.68 |
| PM3 | -0.259 | 1.940 | 104.65 |
| 2-Hydroxyfluorone (-0.538; 105.67) | | | |
| MNDO | -0.258 | 1.947 | 103.86 |
| AM1 | -0.244 | 1.926 | 103.98 |
| PM3 | -0.268 | 1.937 | 103.81 |

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Results of RHF/6-31G** calculations (charge on carbonyl oxygen, C–CO–C angle, deg) are given in parentheses.

However, complexation with solvent can hardly increase the dipole moments of tropones and tropolones by more than 1.1 D [53]. Therefore, the principal reason for generating uncertainties upon reproducing dipole moments of troponoids lies in the deficiencies of the MNDO, AM1, and PM3 methods themselves. Furthermore, as mentioned above, the non-empirical RHF/6-31G$^{**}$ method gives good agreement for tropone and tropolone of the calculated dipole moments with the experimental values with $\mu_{exp} < \mu_{theor}$. The deficiencies of the MNDO, AM1, and PM3 methods may be due to: 1) The set of molecular systems used for the parametrization methods did not include "nonclassical" objects with nonbenzenoid aromatic compounds. In other words, the MNDO, AM1, and PM3 methods consider correlation effects in parameters that were not selected for this class of molecules. 2) The IHB enthalpy was not considered satisfactorily (for AM1 and PM3).

TABLE 3. Coefficients **b** and Correlation Coefficients **r** for Equations $\mu_{exp} = b\mu_{theor}$

| Method | Number of compounds | b | r |
|---|---|---|---|
| Compounds for which $\Delta = \mu_{exp} - \mu_{theor} > 1.8$ D are excluded | | | |
| Tropones | | | |
| MNDO | 25 | 1.1325±0.0866 | 0.5775 |
| AM1 | 25 | 1.1239±0.0771 | 0.7402 |
| PM3 | 26 | 1.1768±0.0696 | 0.7684 |
| Tropolones | | | |
| MNDO | 19 | 1.3387±0.1771 | 0.8984 |
| AM1 | 31 | 1.1566±0.0831 | 0.7488 |
| PM3 | 30 | 1.1731±0.0673 | 0.8500 |
| Combined set | | | |
| MNDO | 44 | 1.1983±0.0863 | 0.7606 |
| AM1 | 56 | 1.1415±0.0557 | 0.7428 |
| PM3 | 56 | 1.1749±0.0468 | 0.8187 |
| Compounds for which $\Delta = \mu_{exp} - \mu_{theor} > 1.5$ D are excluded | | | |
| Tropones | | | |
| MNDO | 24 | 1.1225±0.0816 | 0.6176 |
| AM1 | 24 | 1.1160±0.0719 | 0.7613 |
| PM3 | 25 | 1.1646±0.0638 | 0.8127 |
| Tropolones | | | |
| MNDO | 13 | 1.2374±0.1900 | 0.9277 |
| AM1 | 25 | 1.0923±0.0705 | 0.8624 |
| PM3 | 29 | 1.1610±0.0688 | 0.8412 |
| Combined set | | | |
| MNDO | 37 | 1.1547±0.0785 | 0.7998 |
| AM1 | 49 | 1.1041±0.0486 | 0.8221 |
| PM3 | 54 | 1.1627±0.0456 | 0.8256 |

Despite these limitations, semi-empirical quantum-chemical methods are suitable for establishing relationships even if they are semi-quantitative with the ability to predict dipole moments of tropones and tropolones. In analogy to literature investigations [32-42], we studied the function $\mu_{exp} = b\mu_{theor}$ (Table 3). Linear regression gave a confidence probability 0.95. We excluded from the correlations compounds for which the difference $\Delta = \mu_{exp} - \mu_{theor}$ exceeded 1.8 D in one instance [32, 33, 36] and 1.5 D in the other.

For $\Delta > 1.5$ D, the correlation coefficient **r**, as a rule, is greater than that for $\Delta > 1.8$ D, except for tropolone dipole moments calculated by the PM3 method (the **r** value is slightly less). If the selection criterion $\Delta$ is decreased, the number of points in the linear regression is substantially decreased (in each instance by 6) only for tropolone dipole moments calculated by the MNDO and AM1 methods.

On going from $\Delta > 1.8$ D to $\Delta > 1.5$ D, **r** increases greatly for the results of the AM1 calculation (tropolones and the combined set). Thus, the equations $\mu_{exp} = b\mu_{theor}$ are more acceptable for apriori estimation of the dipole moments (Table 3).

In the other instances, decreasing $\Delta$ slightly increases **r** whereas it decreases slightly for the set {tropolones, PM3}. The correlations $\mu_{exp}$ vs. $\mu_{theor}$ (Table 3) are practically identically suitable for quantitative estimates with a small advantage in favor of the data in Table 3 (except for PM3 results for tropolones).

The functions $\mu_{exp} = b\mu_{theor}$ obtained from MNDO calculations for tropones are not recommended for predicting "experimental" dipole moments of this series of compounds.

TABLE 4. Dipole Moments of Tropones and Tropolones Unsuccessfully Reproduced by Semi-Empirical Quantum-Chemical Methods

| Compound | Method |
|---|---|
| With exclusion from correlation series of molecules for which $\mu_{exp}$ - $\mu_{theor}$ > 1.8 D | |
| 4-Hydroxytropone | MNDO, AM1, PM3 |
| 2-Methoxy-3-isopropyltropone | AM1 |
| 2-Methoxy-6-methyltropone | MNDO |
| 2-Methylmercaptotropone | AM1, PM3 |
| 7-Bromo-2-methoxytropone | MNDO |
| 5-Methyltropolone | MNDO |
| 3-Chlorohinokitiol | MNDO, PM3 |
| 3,7-Dichlorohinokitiol | MNDO, PM3 |
| 3-Bromo-4-methyltropolone | MNDO |
| 3-Bromohinokitiol | MNDO, PM3 |
| 3-Bromo-5-methyltropolone | MNDO |
| 7-Bromo-3-methyltropolone | MNDO |
| 7-Bromohinokitiol | MNDO |
| 3,5-Dibromohinokitiol | MNDO, AM1, PM3 |
| 3,7-Dibromotropolone | MNDO |
| 3,7-Dibromo-4-methyltropolone | MNDO |
| 3,7-Dibromohinokitiol | MNDO |
| 3,7-Dibromo-5-methyltropolone | MNDO |
| 3,5,7-Tribromo-4-methyltropolone | MNDO, AM1 |
| 3,5,7-Tribromohinokitiol | MNDO, AM1 |
| 3,5′-Ditropolonyl | MNDO |
| With exclusion of results with $\mu_{exp}$ - $\mu_{theor}$ > 1.5 D, reproducibility of dipole moments for the following molecules was considered unsuccessful: | |
| 2-*p*-Methoxyphenyltropone | MNDO |
| 2-Mercaptotropone | PM3 |
| 3-Bromo-2-methoxytropone | AM1 |
| 3-Isopropyltropolone (α-Thujaplicin) | MNDO |
| 4-Methyltropolone | MNDO |
| 7-Isopropyltropolone | MNDO |
| 3-Nitrohinokitiol | PM3 |
| 3-Chlorohinokitiol | AM1 |
| 5-Chlorohinokitiol | MNDO |
| 7-Chlorohinokitiol | MNDO |
| 3,7-Dichlorohinokitiol | AM1 |
| 3-Bromo-4-methyltropolone | AM1 |
| 3-Bromohinokitiol | AM1 |
| 3,7-Dibromotropolone | AM1 |
| 3,7-Dibromo-4-methyltropolone | AM1 |
| 3,7-Dibromohinokitiol | AM1 |

The **r** values for the other functions $\mu_{exp}$ = **b**$\mu_{theor}$ are not as large as for the quantitative predictive relationships ([32-42] etc.). This is due to the aforementioned methodical uncertainties of the semi-empirical calculations as applied to such a unique structural system as the troponoids. However, these relationships can be used for a semi-quantitative apriori estimate of dipole moments of tropones and tropolones, including natural compounds of these series.

Table 4 lists compounds for which the calculation of dipole moments by one method or another gives incorrect results. The corresponding values are excluded from the correlation series.

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