

Synthesis, structural and computational studies of a 3x3 isomer grid based on nine methyl-*N*-(pyridinyl) benzamides

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Supplementary Information

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1. Detailed description of synthesis procedures

The classical nucleophilic acyl substitution reactions (Schotten–Baumann) between the 4-, 3- or 2-aminopyridines and 4-, 3- or 2-toluoyl chlorides were used to produce a set of the nine methyl-*N*-(pyridinyl) benzamides (**Mxx**) (where **x** = *para*-/*meta*-/*ortho*-). Reactions were performed in anhydrous conditions in CH₂Cl₂ (under N₂), initially at 5°C and then at room temperature. A by-product was HCl, and Et₃N was employed, except in case of 2 to drive the reaction equilibrium towards the product; in total, one molar equivalent of Et₃N was added.

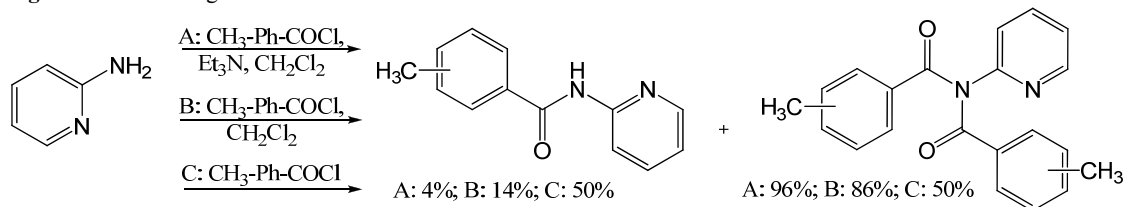
The 4-, 3- or 2-aminopyridine (0.9411 g, 10.0 mmol) were added to a 250 ml round bottom flask placed on an ice bath with stirring. Then, 30 ml of solvent (CH₂Cl₂) was added to the flask, followed by addition of Et₃N (1.5 ml, 10.76 mmol). Finally, the 4-, 3- or 2-toluoyl chlorides (~1.5 ml, 11.0 mmol) were added in excess directly into the solution mixture. The reaction mixture was allowed to warm to room temperature and stirred overnight.

The standard washing was the same for all groups of compounds: the organic reaction phase was washed with 30 ml of KHCO₃ (0.1 M) solution *ca.* 3-7 times. Then, 1.5 g of anhydrous MgSO₄ was added to the organic solutions for 20 minutes. The flask contents were filtered through a Büchner funnel (under vacuum) to remove MgSO₄. The filtrate was evaporated under vacuum and the product dissolved in minimal volumes of warm CHCl₃. A saturated solution was placed on ice and re-crystallization induced. The resulting product was dried overnight and weighed. Since the purity of 3-aminopyridine was poor, column chromatography was employed in case of the **Mxm** compounds with success. Silica was used as stationary phase and the mixture of CHCl₃, ethyl acetate and cyclohexane (4:2:1) was used as mobile phase.

This procedure was appropriate for the first six isomers (derivatives of 4-aminopyridine, **Mxp** and 3-aminopyridine, **Mxm**), however, if 2-aminopyridine was used the products were almost exclusively double amides, 4/3/2-methyl-*N*-(4/3/2-tolyl)-*N*-(pyridin-2-yl) benzamides (**Mxod**). Exclusion of the Et₃N improved formation of **Mxo** but not in sufficient ration (14% of **Mxo**). Finally, the **Mxo** compounds were sufficiently synthesized by performing the reaction without solvent and Et₃N by simple mixing of 2-aminopyridine and toluoyl chlorides in round bottom flask until a crude product is formed, containing 50% of **Mxo** and 50% **Mxod**. After the standard washing, the separation of the compounds was performed using above described column chromatography.

In most cases, yields were modest to good (19-70%), with the exception of **Mmp** (11%).

Fig. 1. Schematic diagram of the reactions



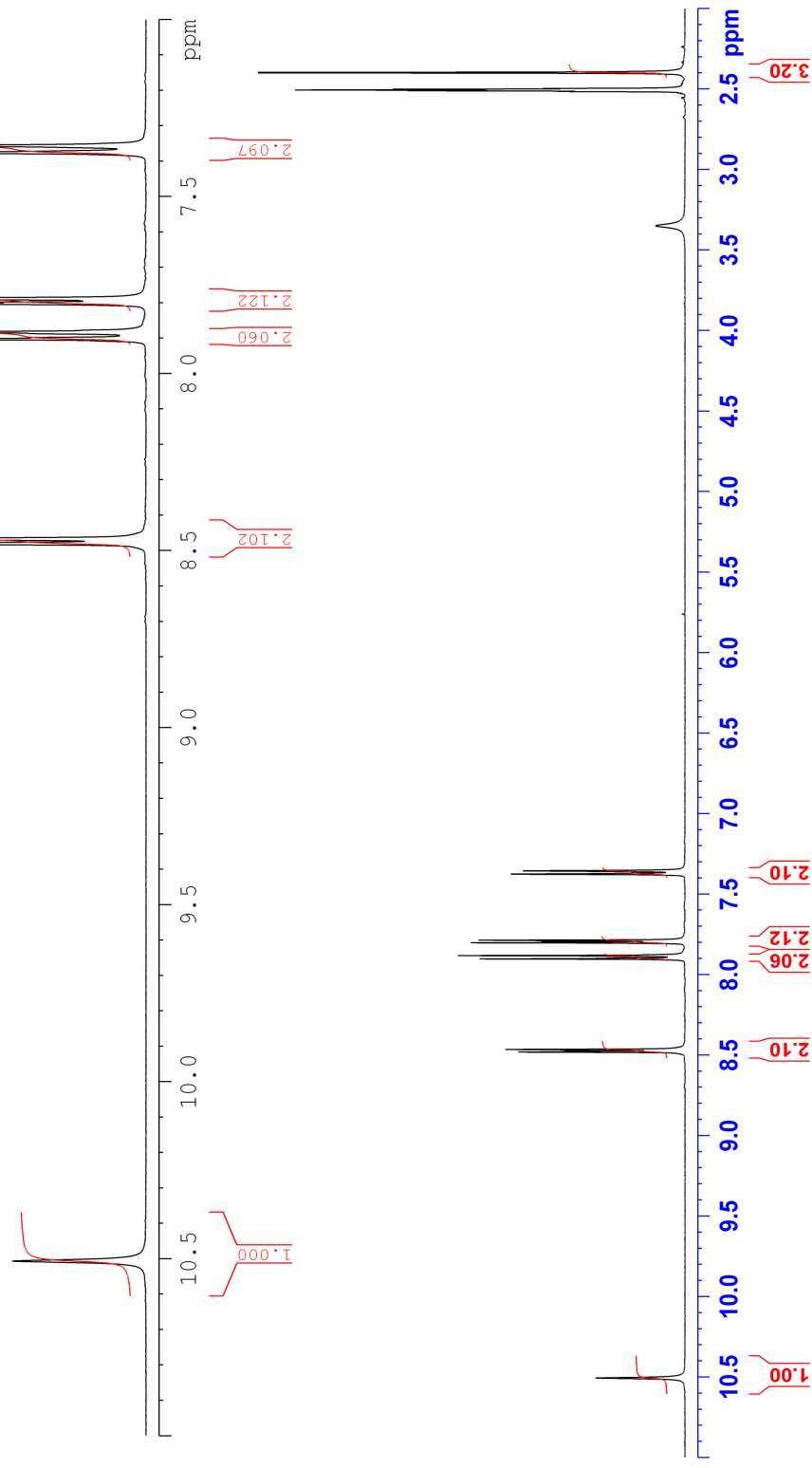
2. ¹H NMR data and spectra (400MHz, DMSO-d₆)
2.1. Mpp

H-NMR

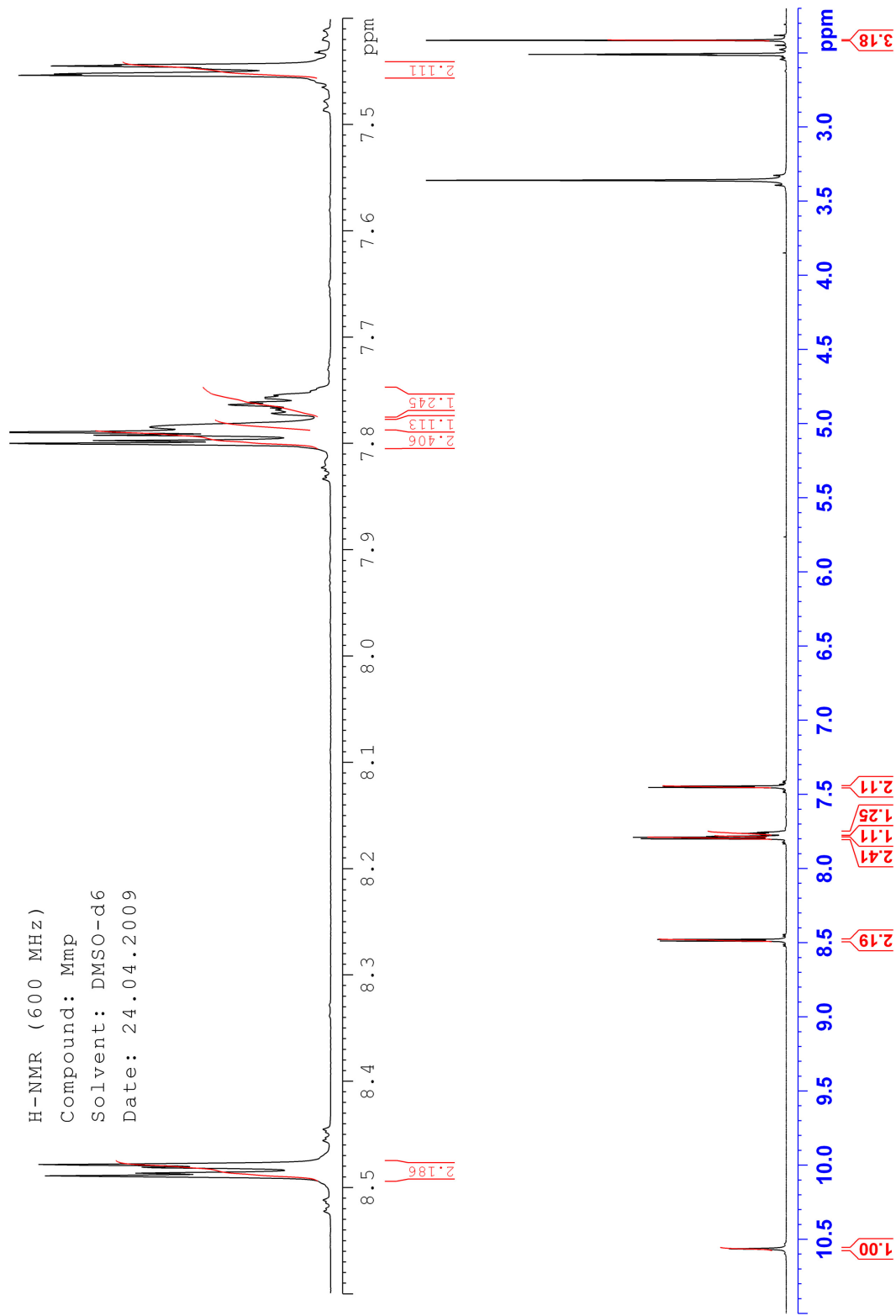
Compound: Mpp

Solvent: DMSO-d₆

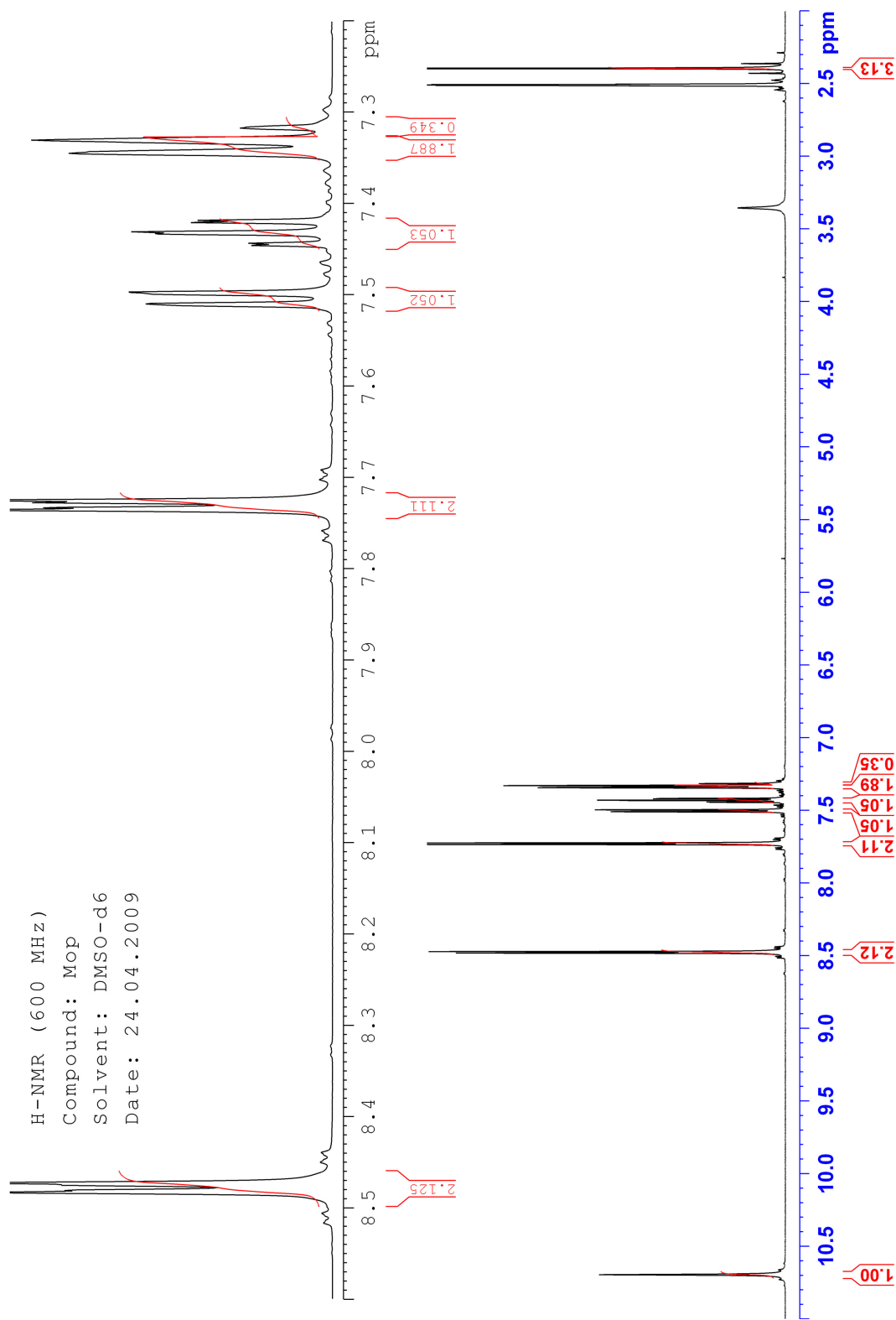
Date: 22.04.2009



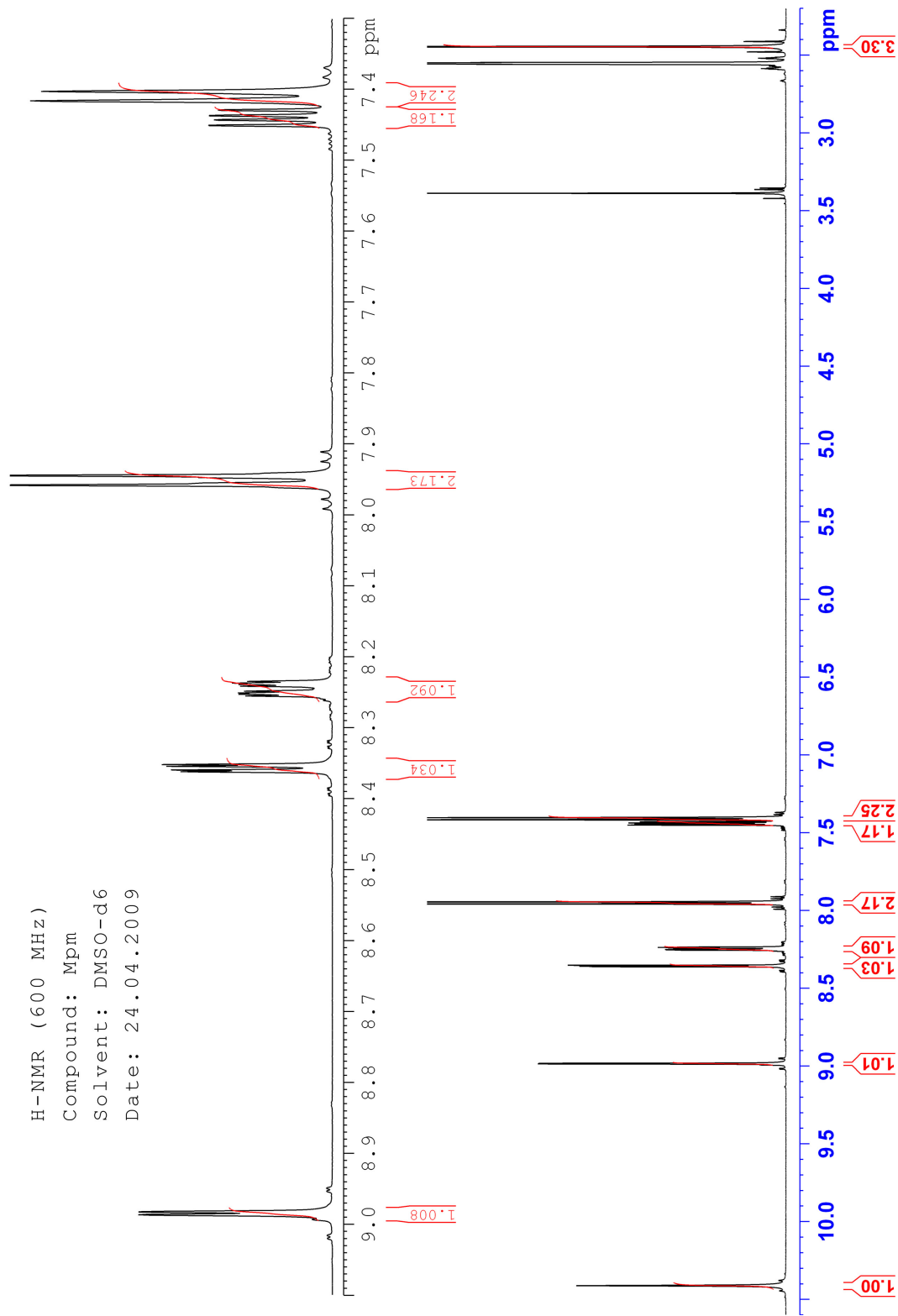
2.2. Mmp



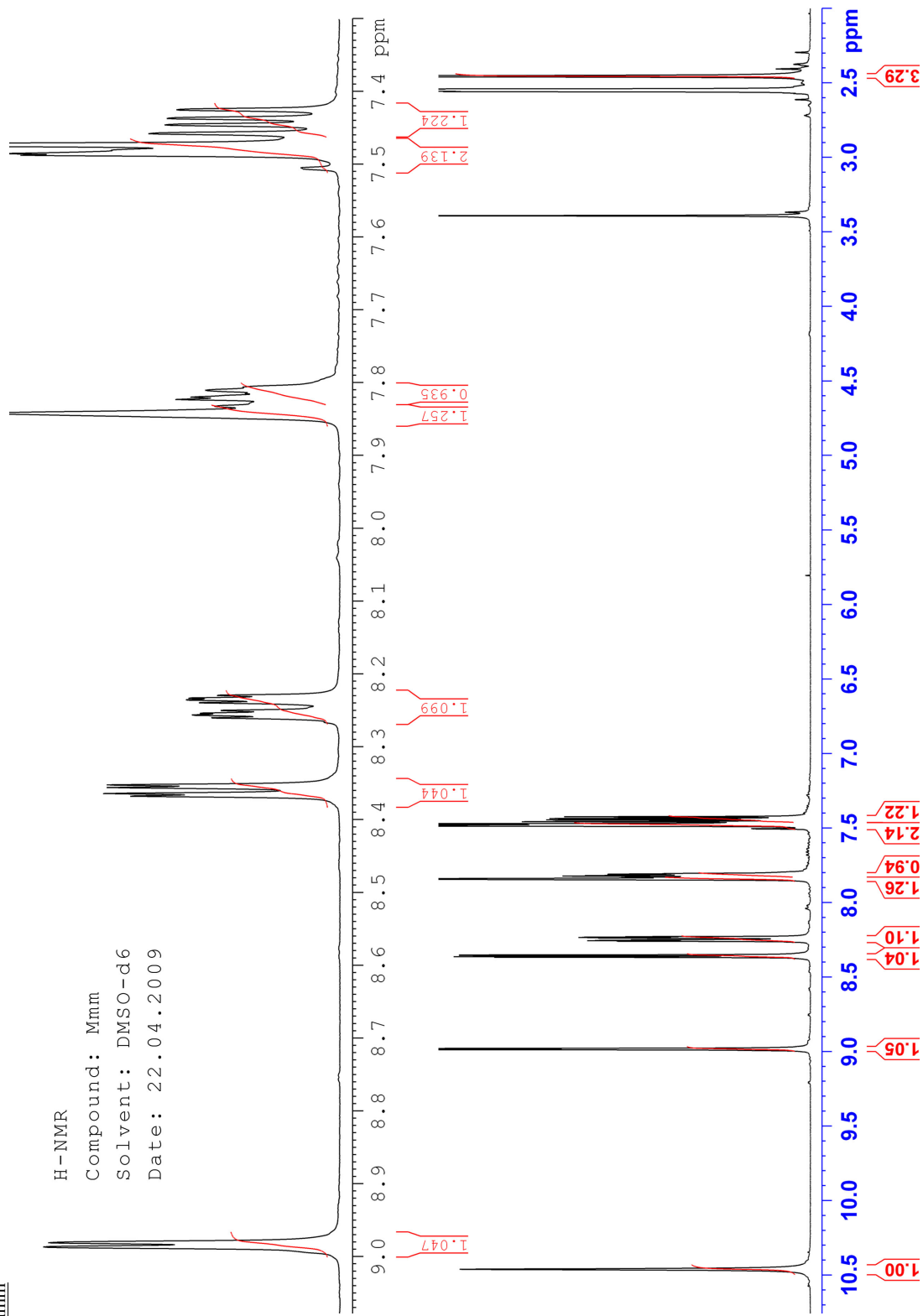
2.3. Mop



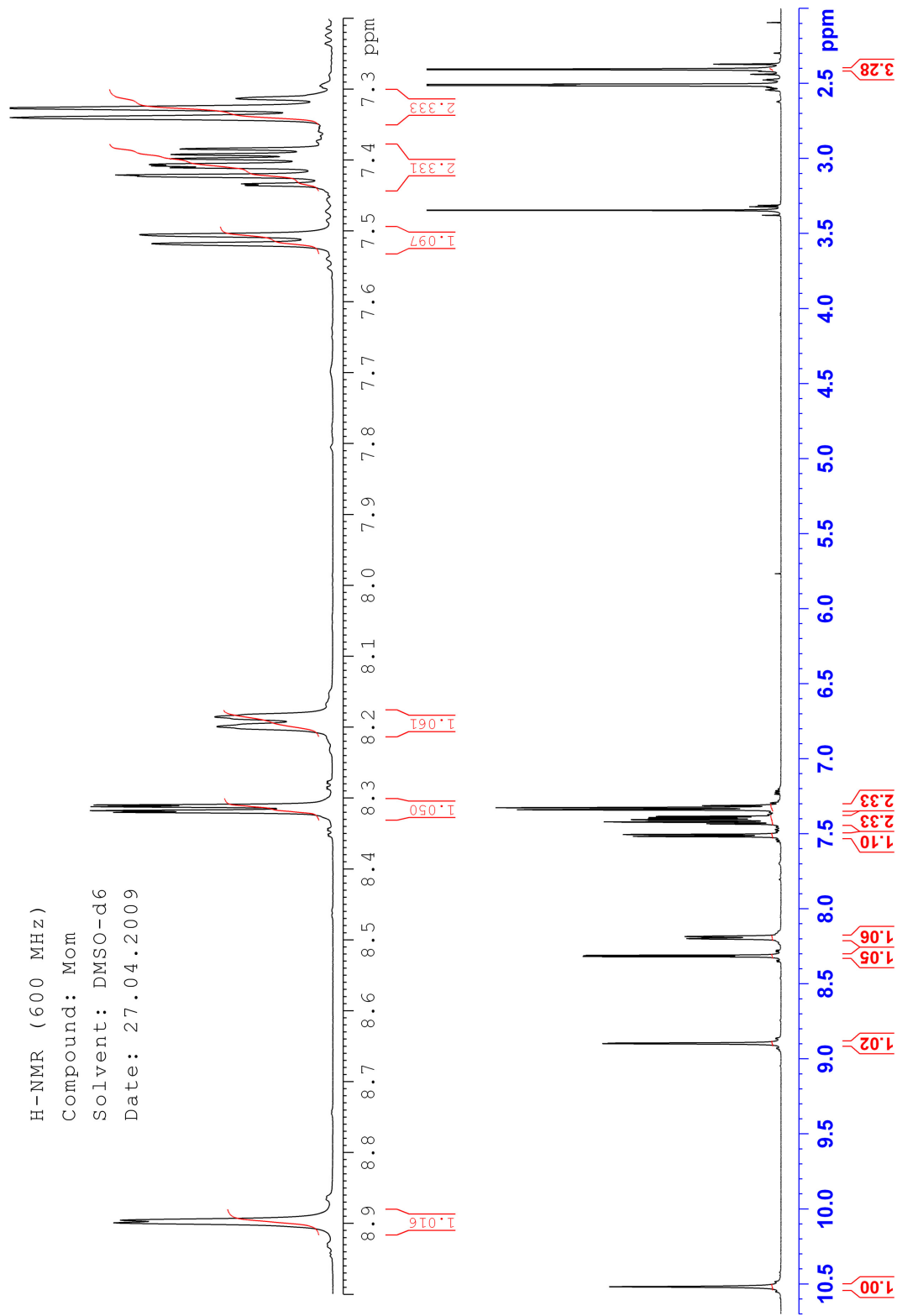
2.4. Mpm



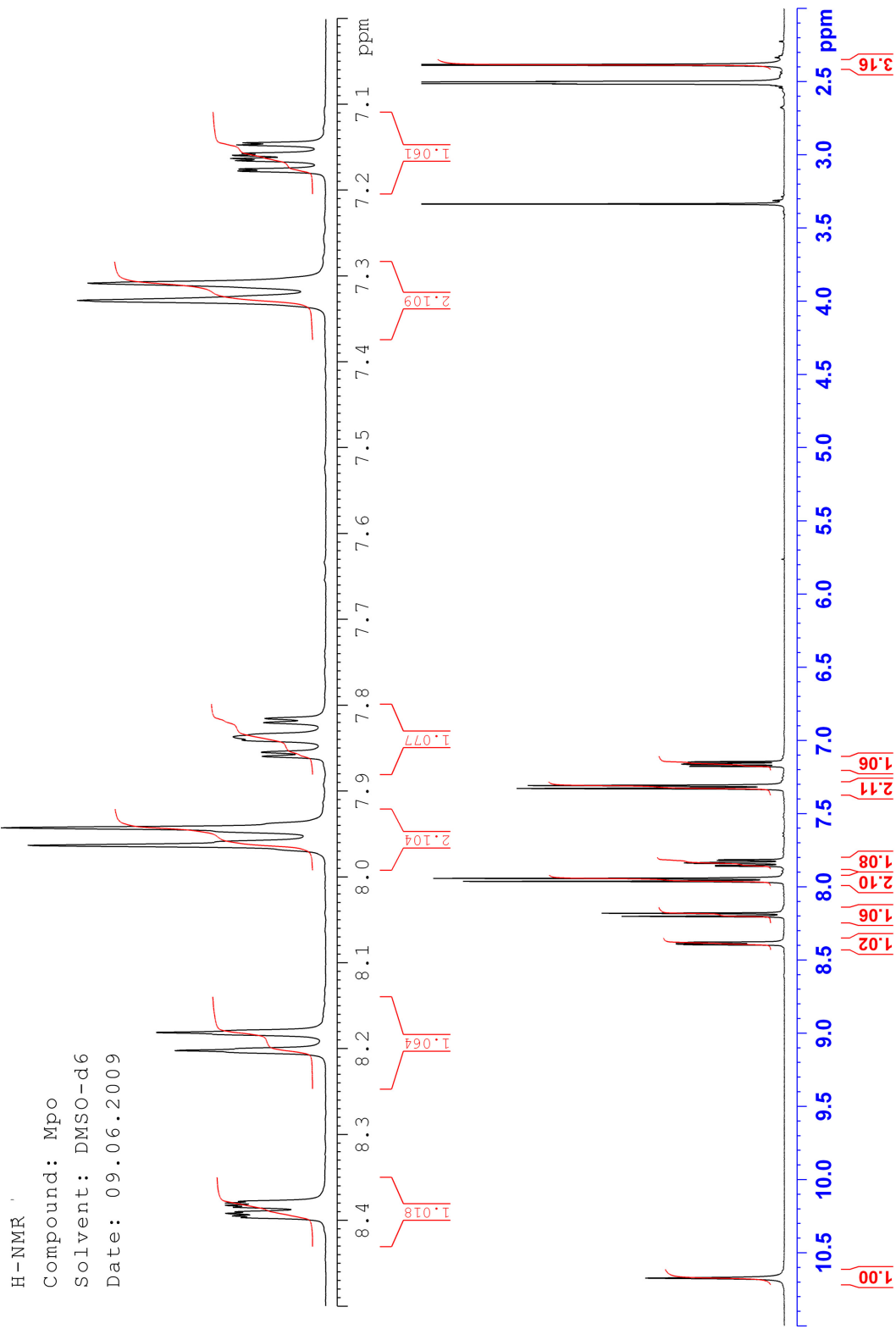
2.5. Mmm



2.6. Mom



2.7. Mpo



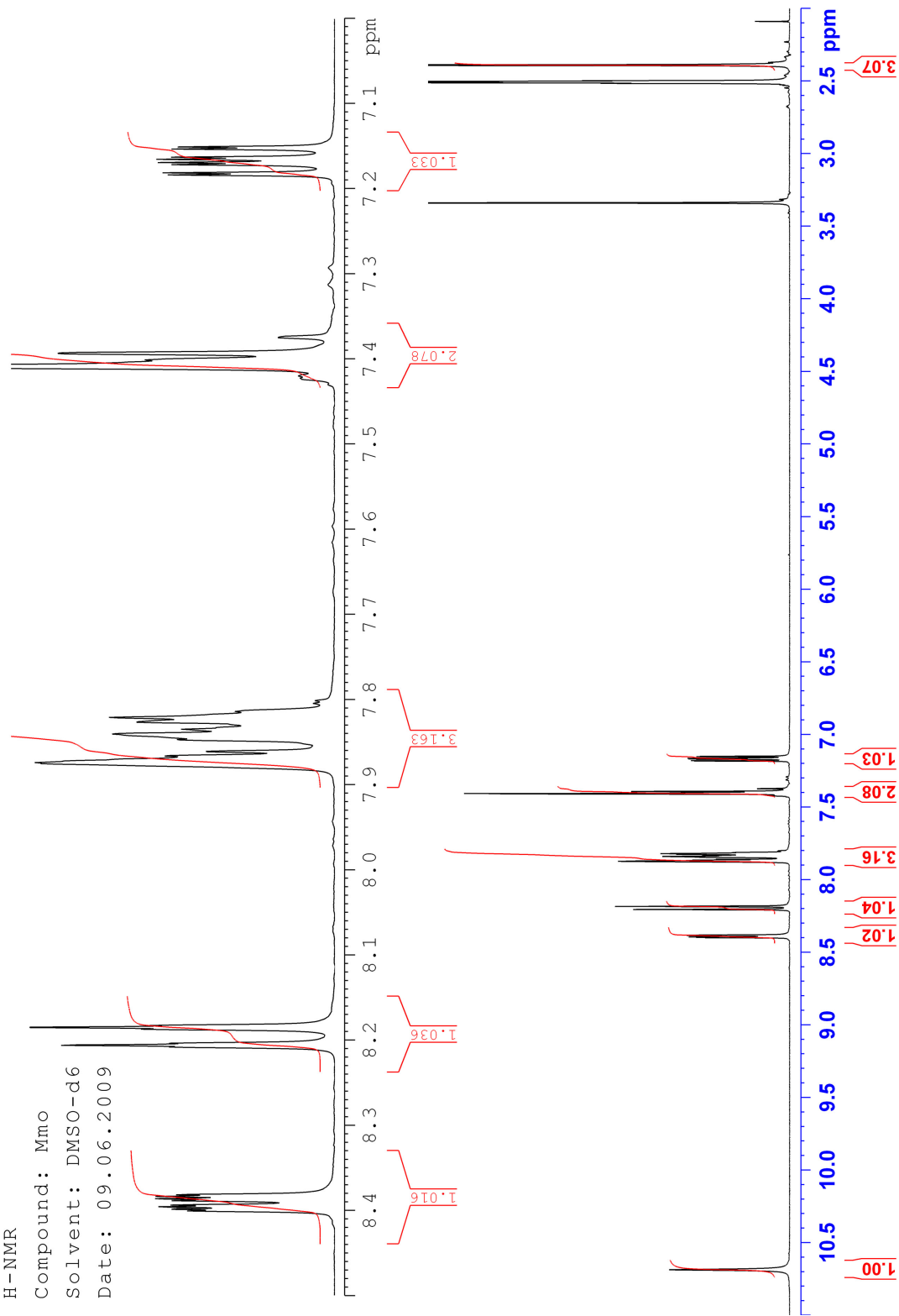
2.8. Mmo

H-NMR

Compound: Mmo

Solvent: DMSO-d6

Date: 09.06.2009



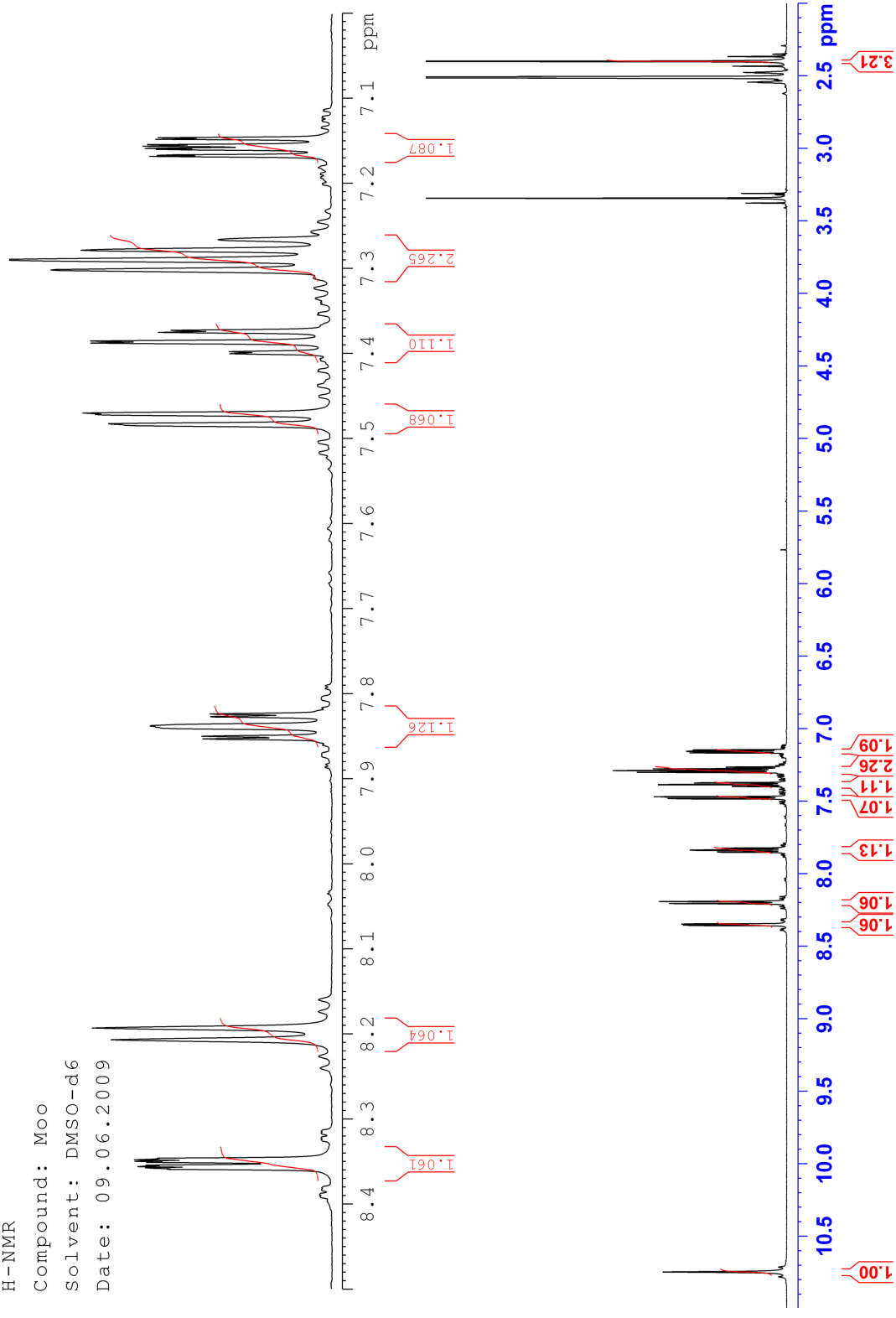
2.9. Moo

H-NMR

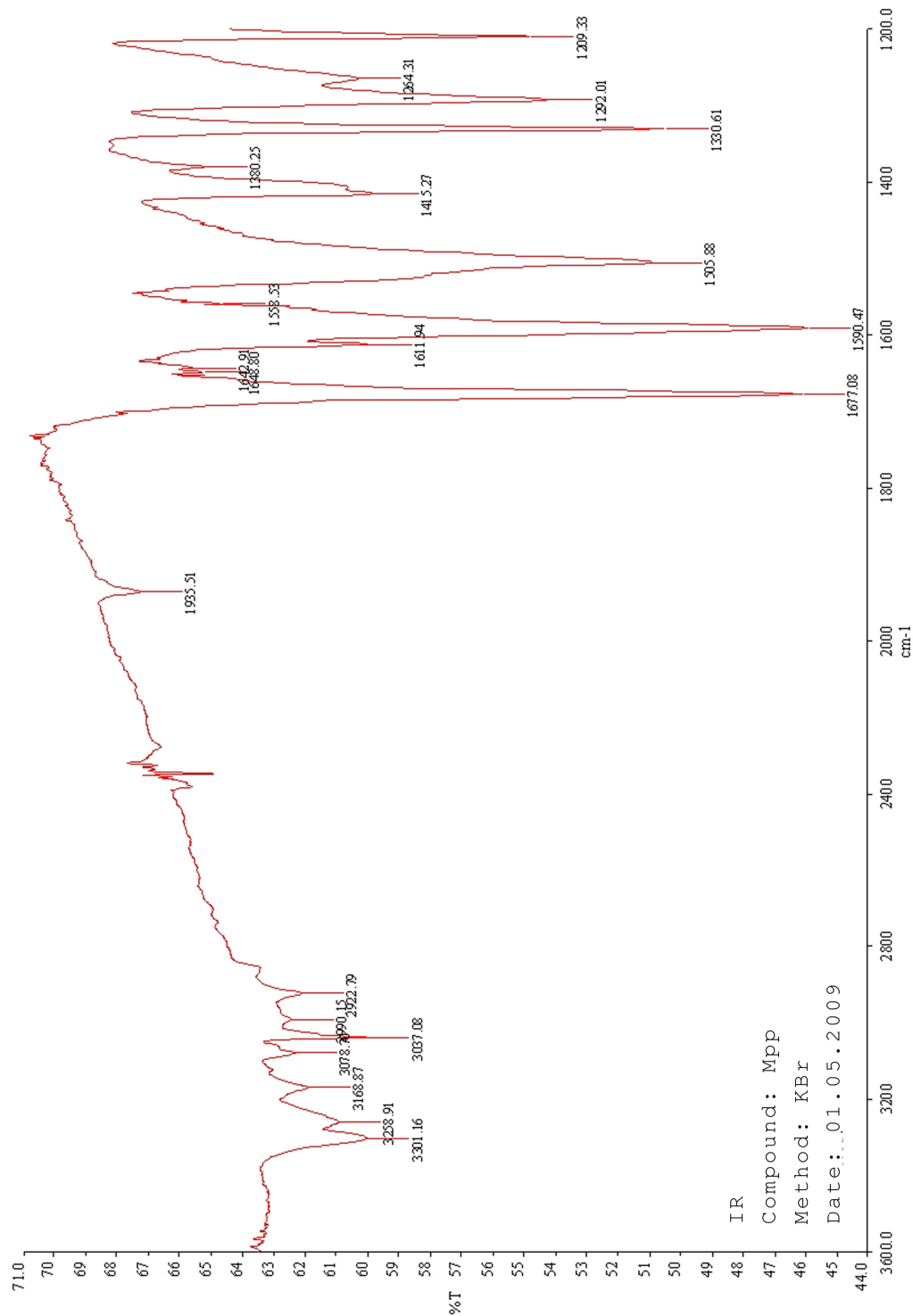
Compound: Moo

Solvent: DMSO-d6

Date: 09.06.2009

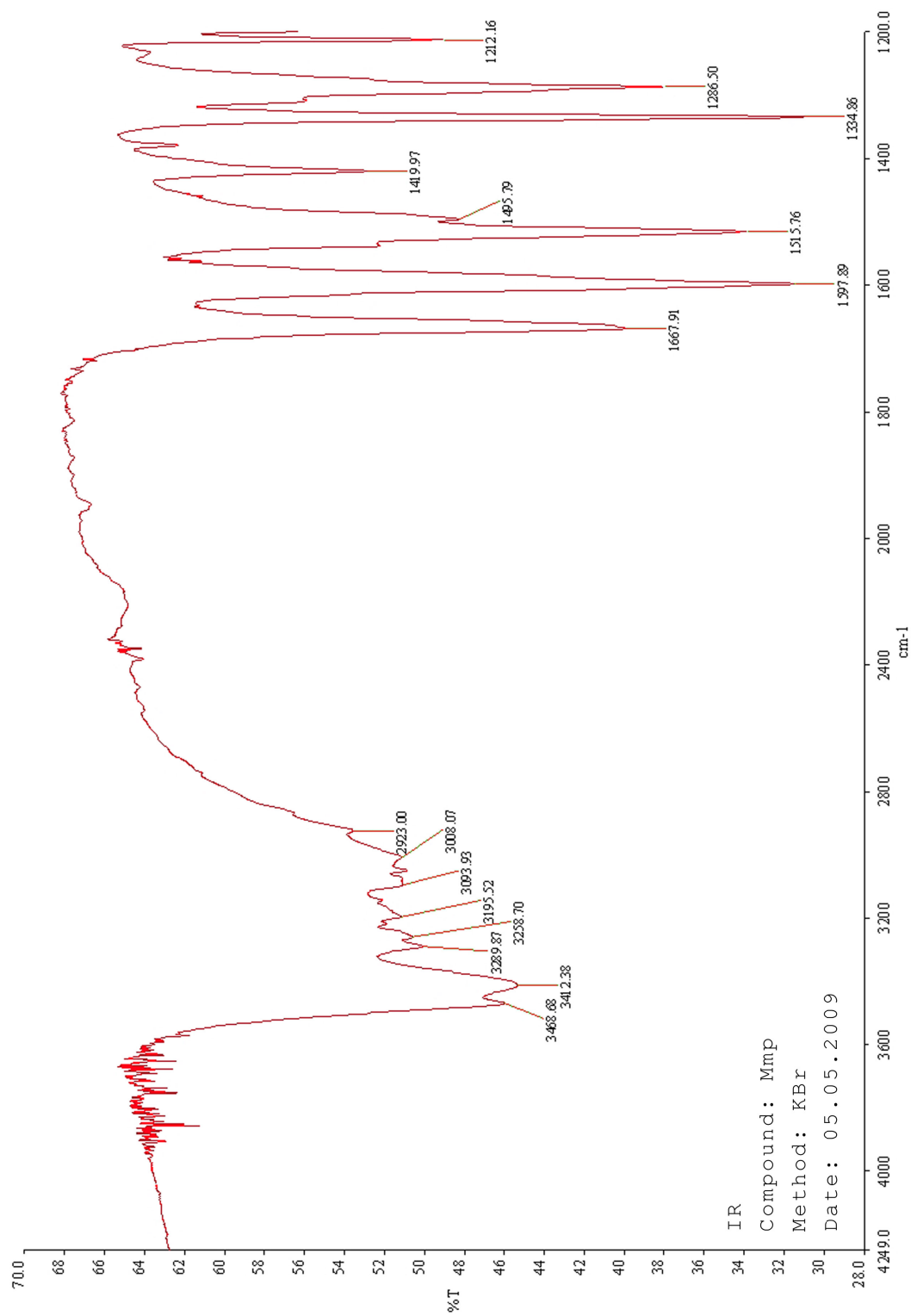


3. IR (KBr disc)
3.1. Mpp

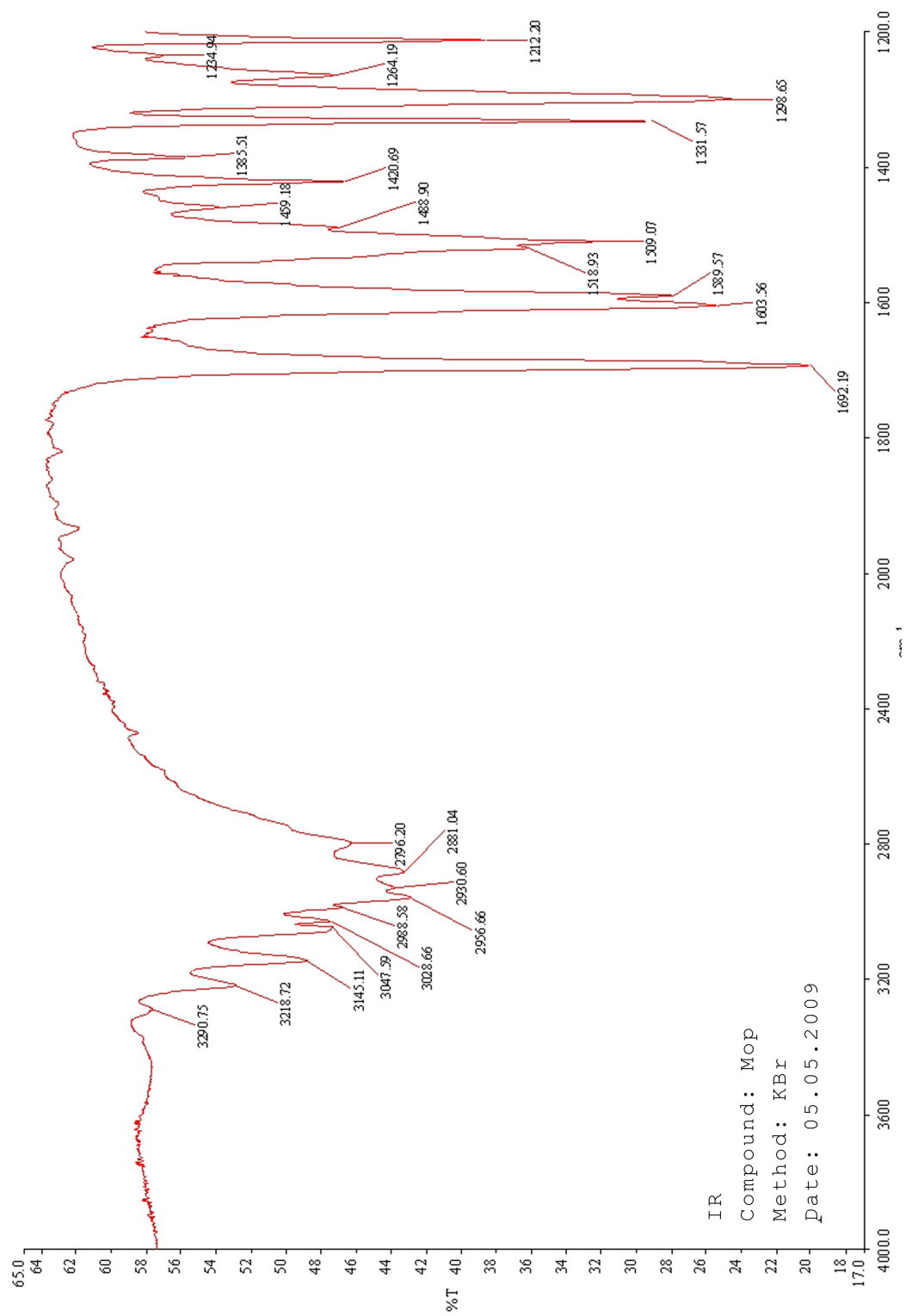


IR
Compound: Mpp
Method: KBr
Date: 01.05.2009

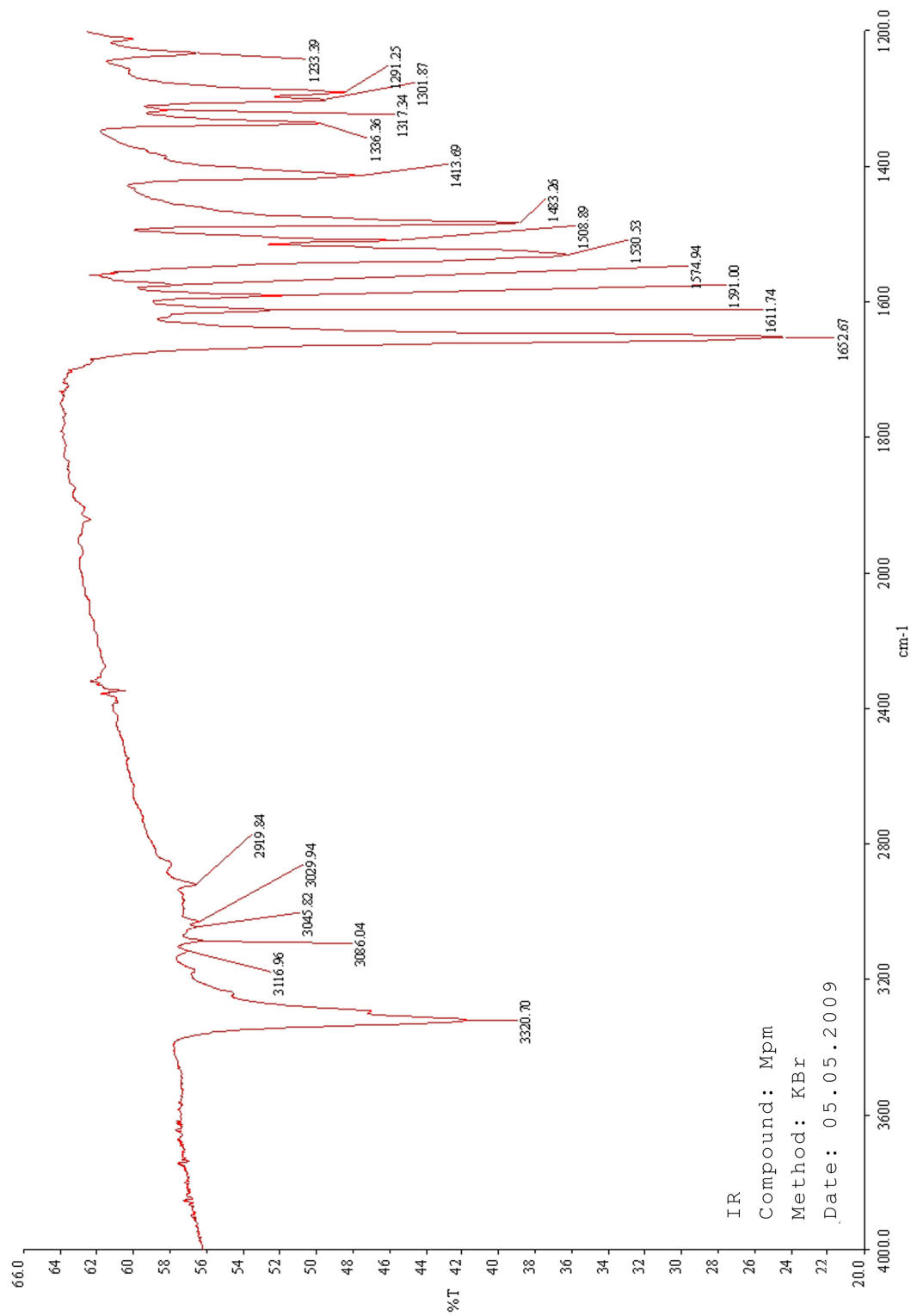
3.2. Mmp



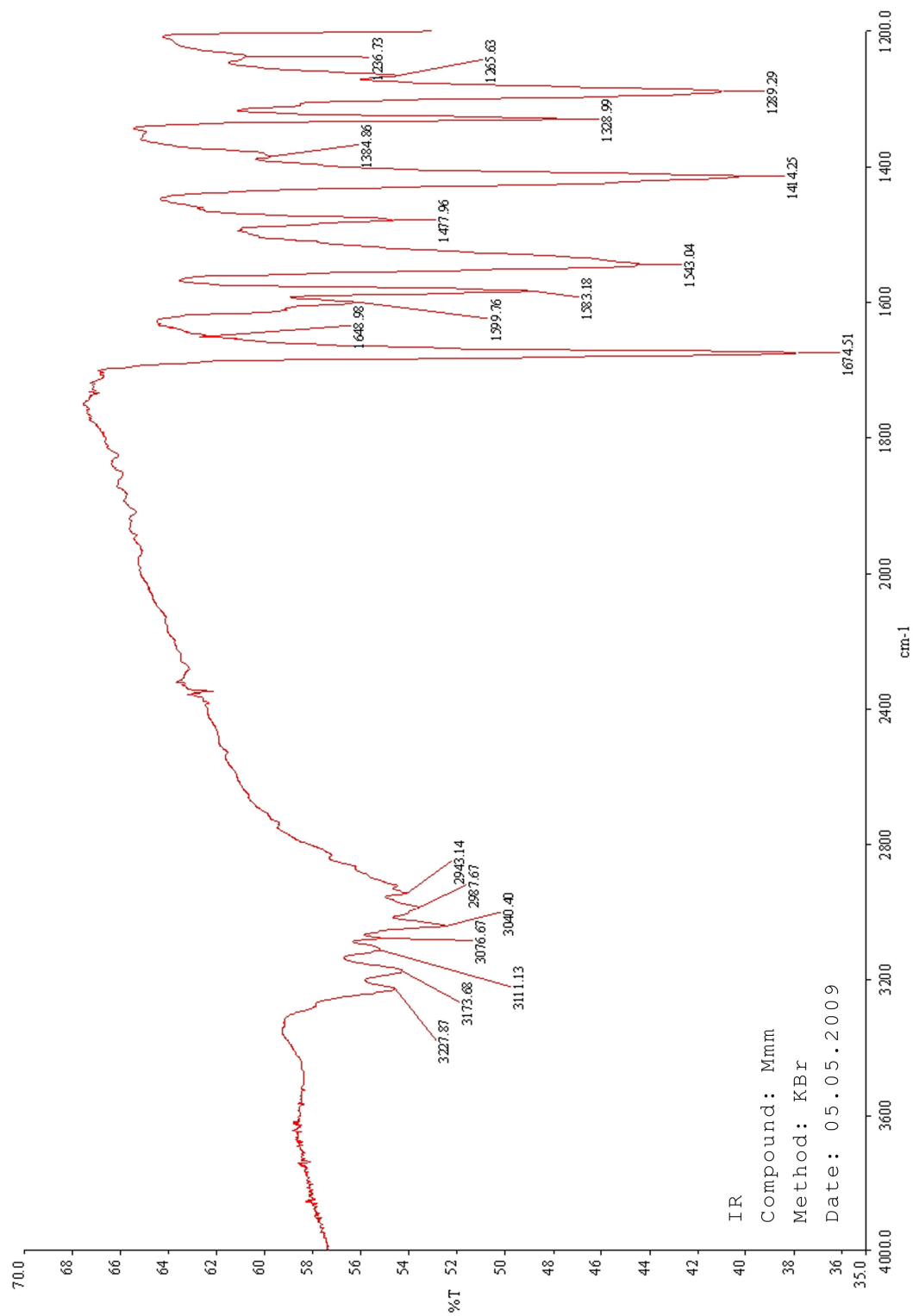
3.3. Mop



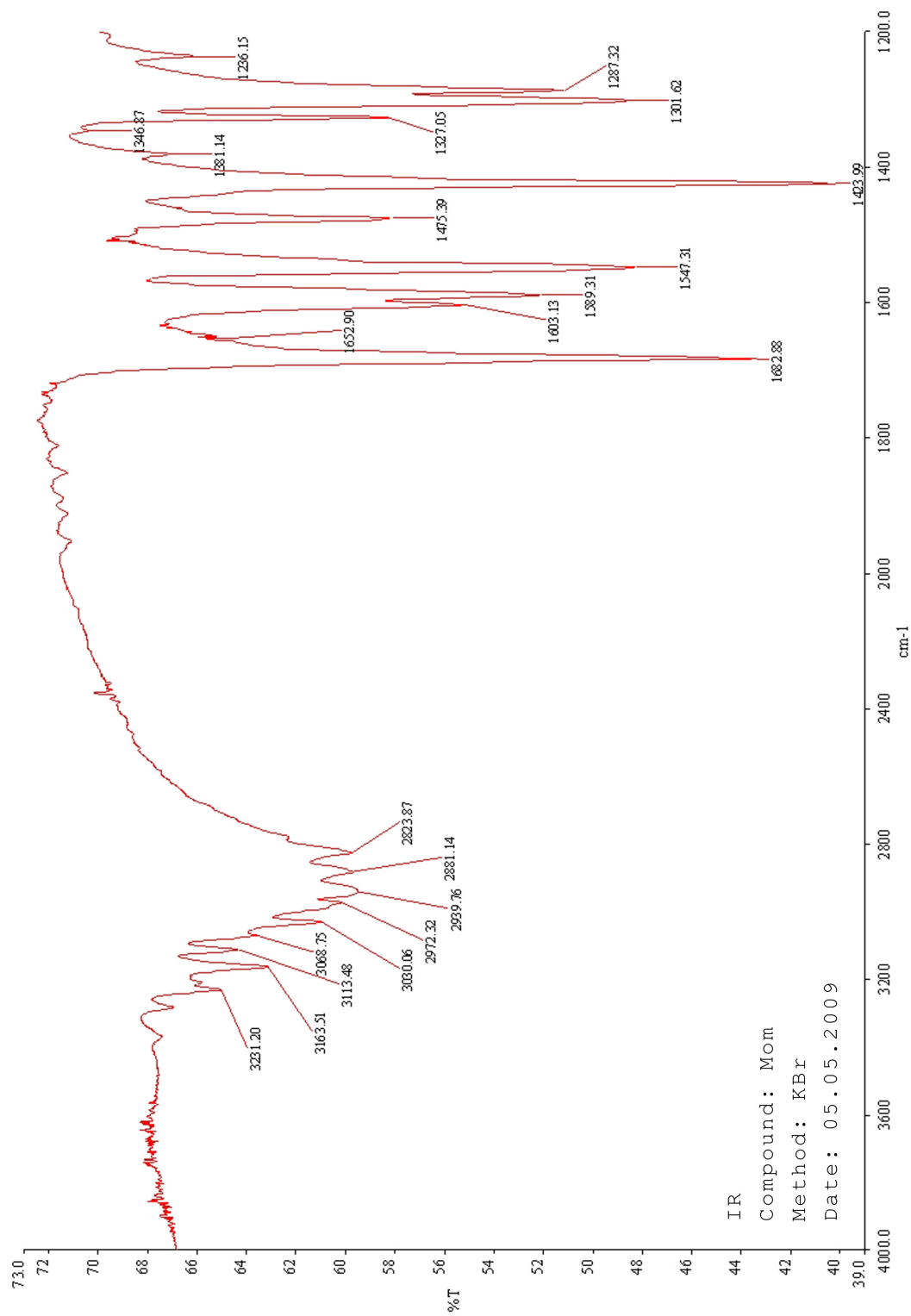
3.4. Mpm



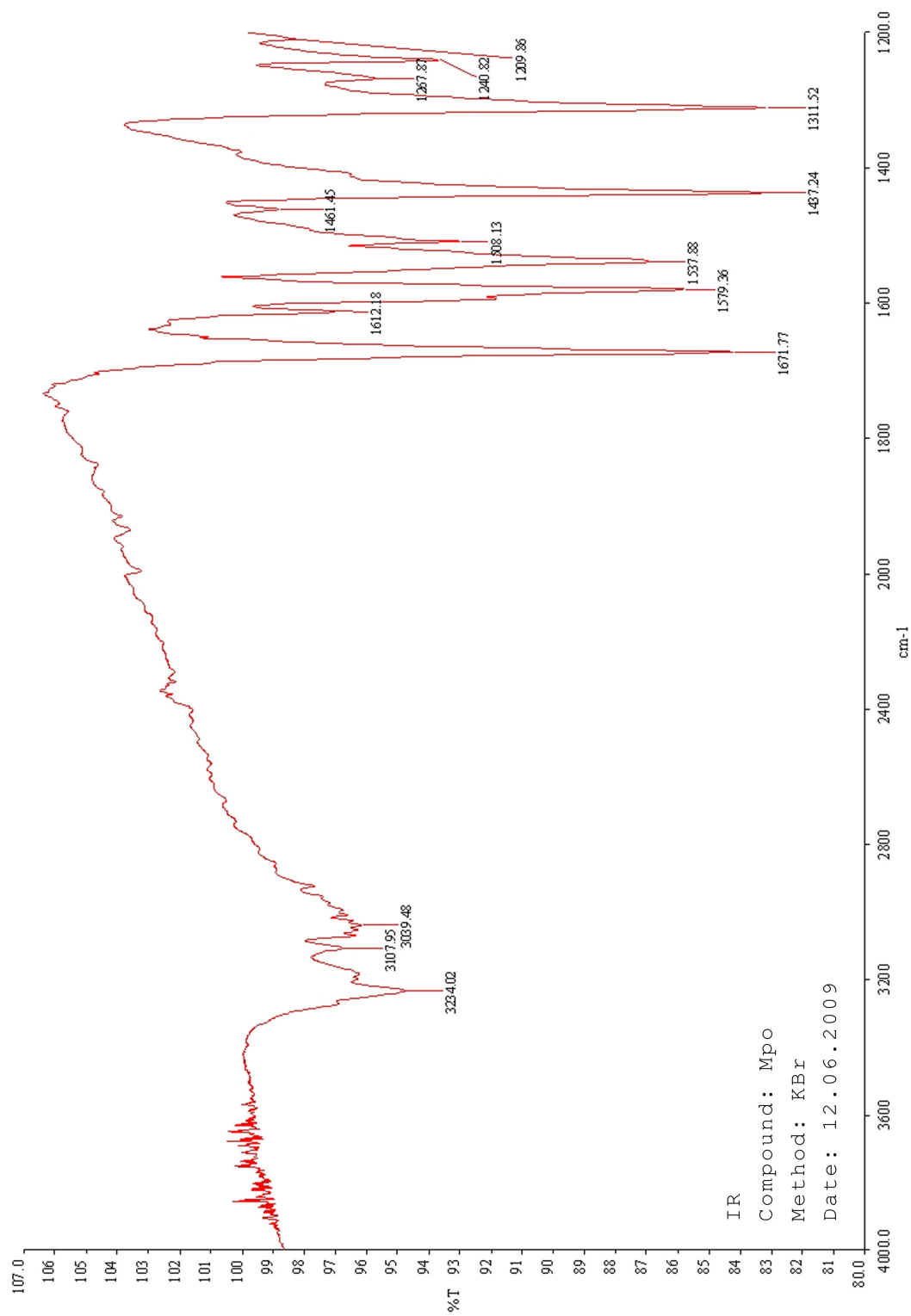
3.5. Mmm



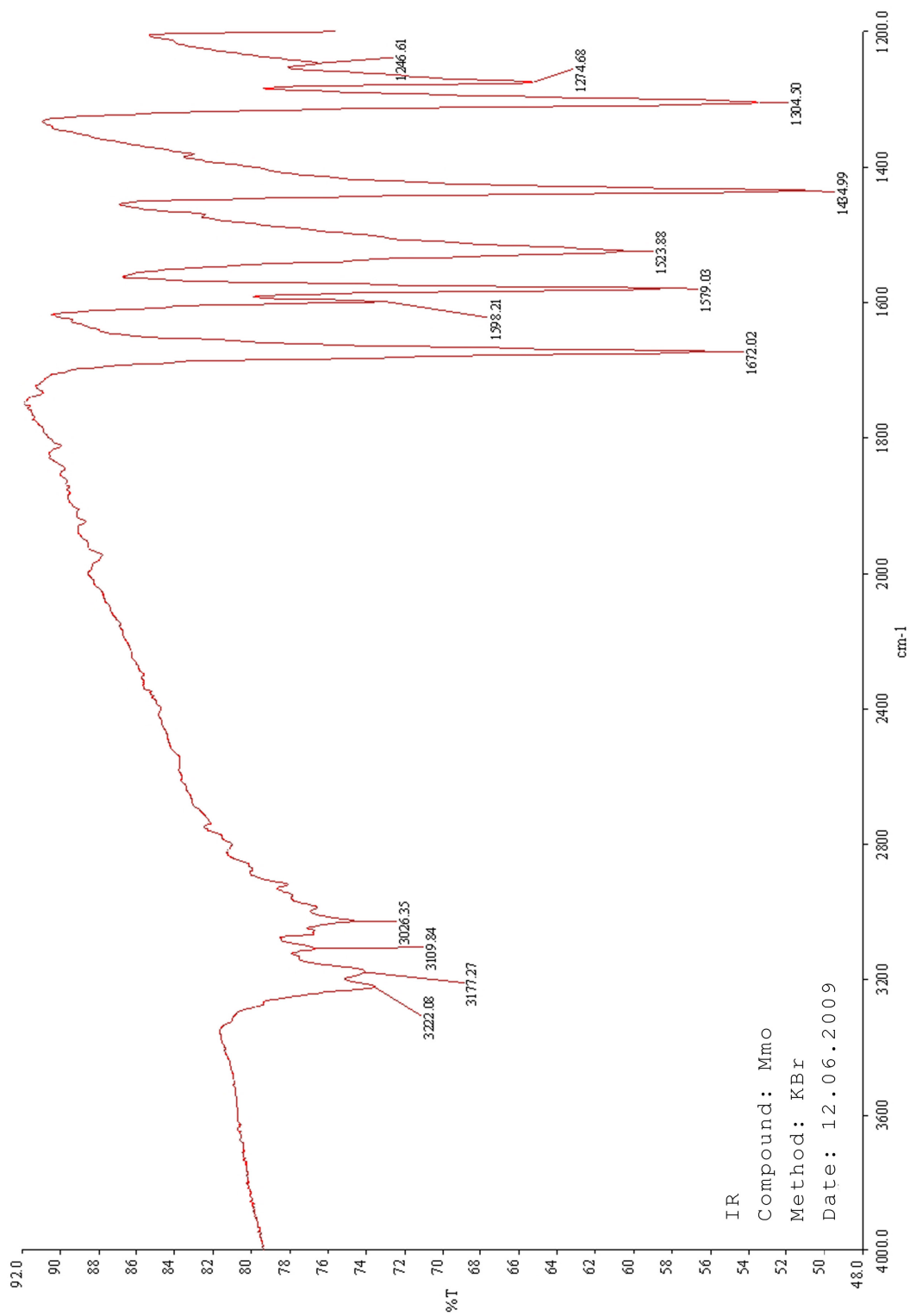
3.6. Mom



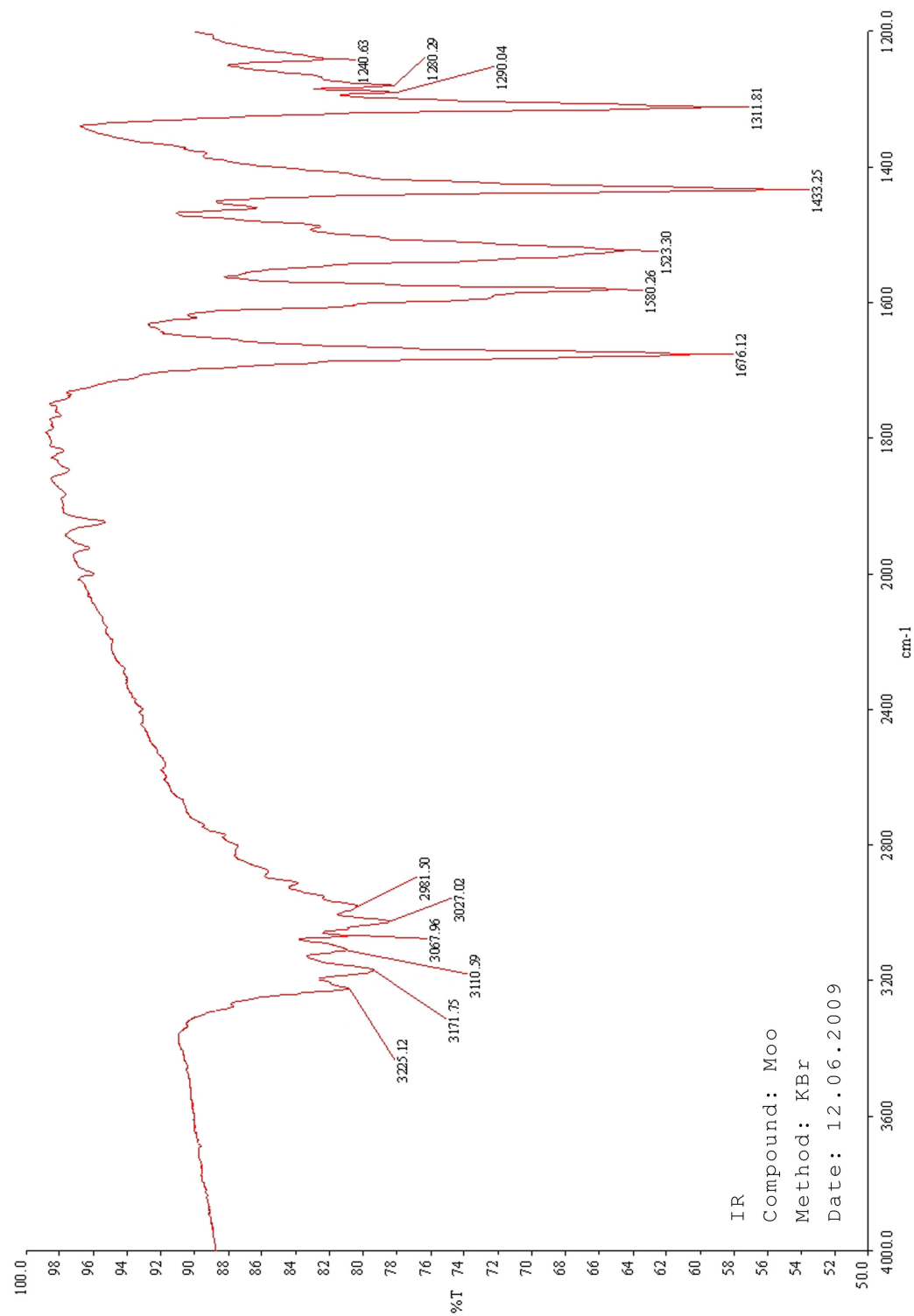
3.7. Mpo



3.8. Mmo



3.9. Moo



4. Molecular and crystal structure data for Mxx derivatives.

The essential feature for eight of the **Mxx** crystal structures (**x** = *para*-/*meta*-/*ortho*) is that they aggregate in the solid-state *via* N-H...N_{pyridine} hydrogen bonds, but in different space groups. The O=C carbonyl group only participates in weak intra- and intermolecular C-H...O contacts in the majority of structures. Only for the **Mpm** structure is the N-H...O=C interactions the primary hydrogen bonding feature. However, in the **Mxo** series cyclic centrosymmetric $R^2_2(8)$ rings of N-H...N intermolecular interactions are the main hydrogen bonding feature.

4.1. Mxp series

4.1.1. Mpp molecular and crystal structure

Apart from rotational disorder in the CH₃ group, the molecular structure is as expected for benzamides. The crystal structure in space group $P2_1/n$ (No. 14) is similar to the reported **Fpp** [Donnelly *et al.*, 2008] structure in terms of the N-H...N_{pyridine} bonding (N...N is 3.105(3) Å) and is isostructural with the series of five molecules in Table 5 (McMahon *et al.*, 2008). It is not isomorphous with **Fpp** but for a *b*, *c* cell swop (Unit cell parameters for **Fpp** = *a* = 5.65, *b* = 11.39, *c* = 15.43 Å, β = 95.60°; transformed unit cell parameters for **Mpp** = *a* = 5.70, *b* = 16.89, *c* = 11.34 Å, β = 107.88°). The N-H...N_{pyridine} hydrogen bonding dominates the primary interactions in the **Fxp** structures where the pyridine N atom is *para*-substituted. **Mpp** differs from these **Fxp** compounds by having a CH₃ group and not the substituted F atoms as in **Fpp**, **Fmp**, **Fop**, (III) and the parent benzamide in Table 5 of McMahon *et al.*, 2008. The N-H...N interactions in **Mpp** form a one-dimensional chain along the *c*-axis direction as $C(6)$ chains (and parallel to the [-101] plane) and augmented by weak C-H...O and C-H... π (arene) interactions involving the C26-H26 atoms. The C₆/C₅N interplanar angle is 46.03(9)°.

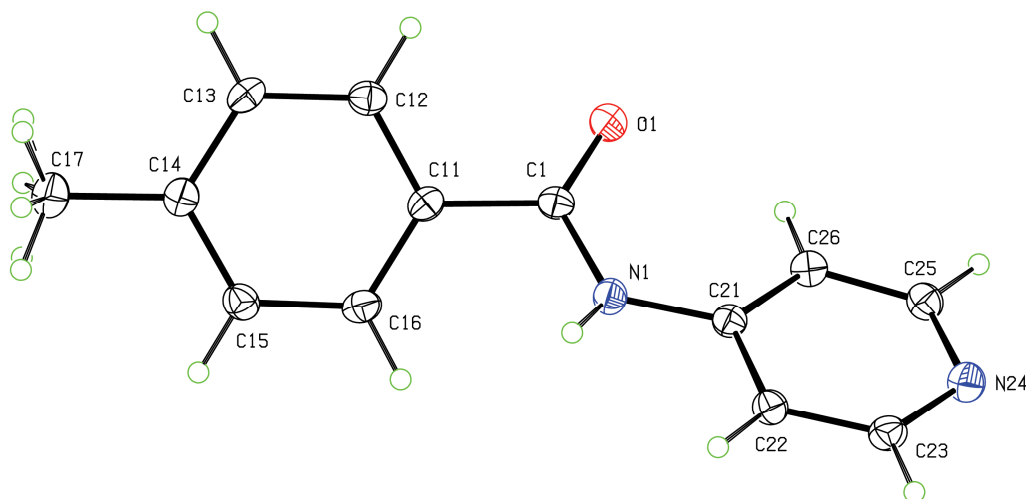


Figure 2. An ORTEP diagram of Mpp with displacement ellipsoids drawn at the 30% probability level.

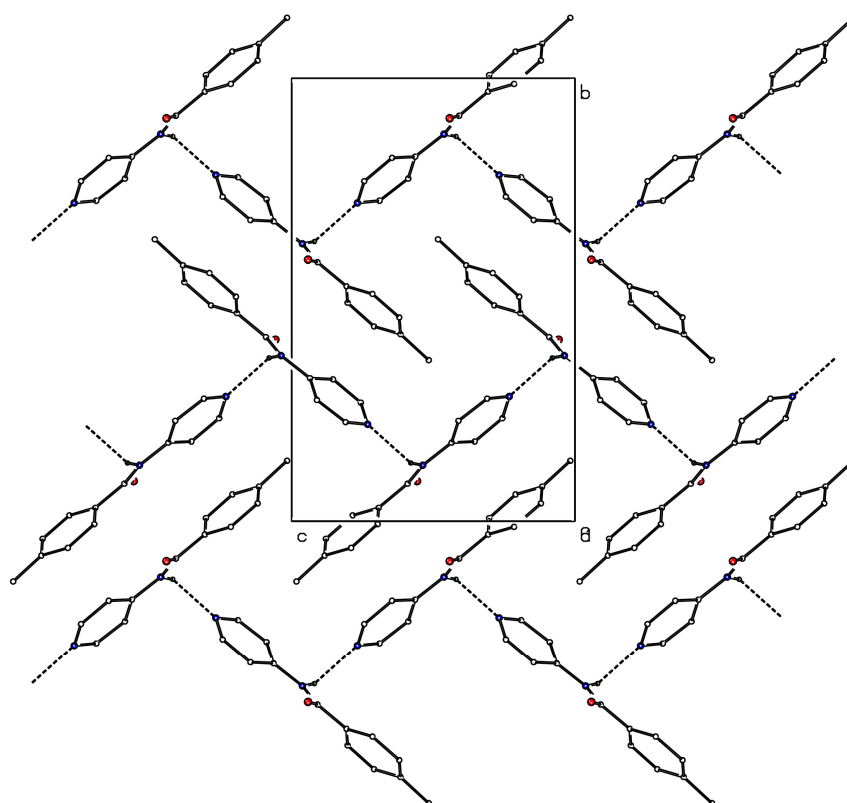


Figure 3. The primary N-H...N hydrogen bonding along the *c*-axis direction in **Mmp** and isostructural with the related fluoro derivative **Fpp**.

4.1.2. Mmp molecular and crystal structure

The **Mmp** structure crystallizes in P^{-1} (No. 2) with $Z'=2$ and with differences between the O1-C1-C11 angles of $[121.2(2)^\circ, 119.7(2)^\circ]$ and C1-N1-C21 $[127.6(2)^\circ, 125.5(2)^\circ]$ for molecules A and B, respectively. Torsion angle differences of *ca.* 8° are evident by different A, B molecular data values for C1-N1-C21-C22 of $12.9(4)^\circ, 20.2(4)^\circ$, respectively. Aggregation is driven by N-H...N_{pyridine} hydrogen bonding. This involves alternating $_{A/B}N...N_{B/A}$ distances of 3.058(3), 3.059(3) Å, but with N-H...N angles of $142(3)^\circ$ (for A→B), $172(3)^\circ$ (for B→A). This highlights the strain and distortions in incorporating two molecules within the asymmetric unit and with the molecular packing as the A→B molecules link by *C*(6) chains and *vice versa*. The two N-H...N hydrogen bonds combine and aggregate as a one-dimensional column and parallel to the (110) plane. These 1-D columns interlock with symmetry related columns along the *c*-axis direction forming 2-D sheets *via* C-H...O interactions (involving C17A). The 3-D crystal structure assembles between parallel sheets with weak interactions *via* C-H...O (involving C23A) and short C-H... π (arene) interactions involving C25A...[C11B,...,C26B], with a H25A...Cg distance of 2.65 Å, where Cg is the aromatic ring centroid. Unlike the **Mpp** structure, the C_6/C_5N interplanar angles are essentially co-planar at $4.84(15)^\circ, 5.47(12)^\circ$ for molecules A and B, respectively.

4.1.3. Mop molecular and crystal structure

Mop crystallises in *Pc* (No. 7) with $Z'=2$ and with molecular disorder in one of the molecules. The solution of the **Mop** structure failed in space group $P2_1/c$ (No. 14) despite the systematic absences indicating that this was a favourable choice. However, attempts to solve and refine in both *Pc* (No. 7) and $P2_1$ (No. 4) proved successful. The *Pc* structure provides the better solution and refinement to an *R*-factor of 0.076, a WGHT card of 0.14 and residual electron density for the top 26 peaks of $+0.57 \text{ e.}\text{\AA}^{-3}$ to $+0.26 \text{ e.}\text{\AA}^{-3}$ and indicating possible molecular disorder at molecule A. Refinement of these residual peaks as sensible chemical sites as a minor conformation of molecule A labelled as C drops the *R*-factor from 0.076 to 0.057 and a final *R*-factor of 0.056, WGHT of 0.09 and a range of residual electron density from $+0.18 \text{ e.}\text{\AA}^{-3}$ to $-0.20 \text{ e.}\text{\AA}^{-3}$. The minor component C has 10.1(6) % site occupancy and occupies the same molecular volume element as the major molecule A sites. Of the nine **Mxx** isomers the volume of the **Mop** is the largest and this is almost certainly due to the disordered A/C component.

Molecules A and B are identical and with practically no differences in molecular geometric data. The only difference between the two molecules is the disorder (A/C) at the molecule A location. The N-H...N_{pyridine} interactions

(intermolecular N...N distances of 2.952(5) Å, 2.950 Å) dominates the hydrogen bonding with additional C-H...O contacts. The N...N interactions aggregate as A/C→A/C and B→B molecules in *C*(6) zigzag chains and parallel to the (-102) plane. The C₆/C₅N planes are almost orthogonal and due to the steric hindrance from the *ortho*-methyl groups and are at angles of 81.79(15)° and 81.58(14)°. Differences between the major orientation (A) and molecule (B) are for C1-N1-C21-C22 which are respectively, -155.2(4)° and -27.4(6)°.

4.2. Mxm series

4.2.1. Mpm molecular and crystal structure

Mpm crystallizes with 4 molecules in P1 (No.1). The data were merged prior to refinement and the resulting Flack parameter is meaningless. The crystallization of four molecules in P1 is **unusual** but all four molecules differ in their molecular conformations and can be distinguished as two distinct sets with molecules A, B and C, D, whereby the C₆/C₅N interplanar ring angles are oriented at angles of *ca.* 65° for molecules A, B at [65.13(11)°, 64.04(10)°] (with differences > 3σ(I)) and close to co-planarity at 0° in C, D at [1.5(2)°, 1.9(2)°]. The bond lengths and angles are normal and are all similar and <3σ level for the related geometric data. However, there are subtle differences in the torsion angles and intermolecular hydrogen bonds. For example with respect to distances across the molecules [intramolecular distances], the N23...C17 molecular distances vary and differ from 10.134(6) Å (in A), 10.118(6) (in B), 9.985(6) Å (in C) to 9.940(6) Å (in D) a difference of 0.2 Å! Clearly the four molecules are different.

The molecules aggregate as A...A..., B...B... etc. 1-D chains *via* four separate and distinct N-H...O=C interactions and along the *b*-axis (010) direction with N...O distances of 3.029(6), 3.016(5), 3.085(6) and 3.085(5) Å for molecules A to D, respectively. Apart from weak C-H...π(arene) contacts – these are the primary interaction in the crystal structure. Two weak CH₃...N_{pyridine} interactions with H...N 2.60 Å and angles of 159°/156° are also present involving C to D and D to C linking the independent C, D chains in two-dimensions. This molecule **Mpm** is unusual in that it is the only **Mxx** molecule which crystallizes with N-H...O=C as the primary interaction and not N-H...N_{pyridine} as the primary hydrogen bonding motif and given its unusual Z'=4 in P1 should at some stage be the subject of a thorough variable temperature study.

The crystallization of four molecules in the asymmetric/unit cell is interesting in the absence of disorder and with clear and subtle distinctions between the four molecules (there are NO matrix correlation coefficients above 0.5). A solution can be obtained in space group P⁻1 (No. 2), but one of the molecules is disordered and the *R*-factor remains stubbornly high and at *R* = 0.2.

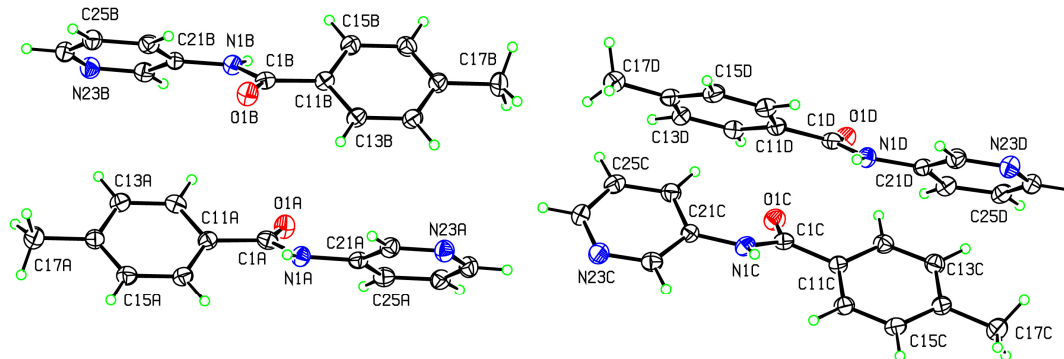
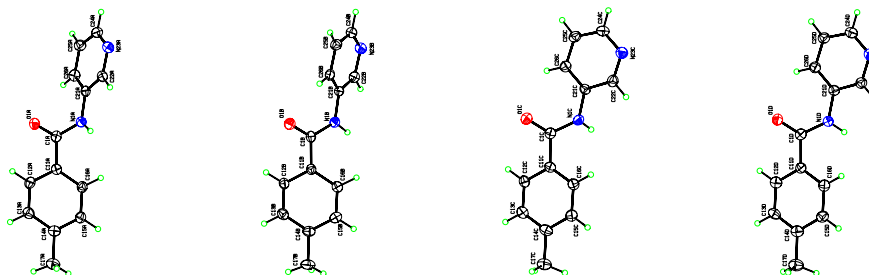


Figure 4. The four molecules (A) to (D) in the asymmetric unit of **Mpm** and similar views of (A) to (D) below.



4.2.2. Mmm molecular and crystal structure

The **Mmm** structure crystallizes in P-1 (No. 2) with $Z'=2$ with the two molecules differing by 10° in their corresponding dihedral angles. For example the C_6/C_5N interplanar angles are $55.57(10)^\circ$ and $65.70(10)^\circ$ in molecules A and B while the O1-C1-C11-C16 angles are $156.8(3)^\circ$ and $146.1(3)^\circ$, for A and B, respectively. It is a *non-merohedral* twinned crystal and however, there is no discernible disorder in the molecular components. There is also a significant difference between the C17...N23 A/B distances.

Molecules aggregate *via* $_{A/B}N-H...N_{B/A}$ hydrogen bonding as $C(5)$ chains along the b -axis or (010) direction [at distances of 2.998 (4) Å and 3.006(4) Å]. Two C-H... π (arene) interactions are present involving C22A and C22B. Of the carbonyl O atoms, only O1B is involved in a weak $CH_3...O=C$ interaction while O1A is not involved in any intermolecular interactions.

4.2.3. Mom molecular and crystal structure

The **Mom** structure crystallizes in $Pca2_1$ with $Z'=1$. The primary interaction is the N-H...N_{pyridine} intermolecular interaction forming 1-D $C(5)$ chains along the a -axis direction with a N...N distance of 2.946(2) Å and two C-H...O interactions complete the interactions – one intra-, one intermolecular. There is also a weak C-H... π (arene) interaction. The C_6/C_5N rings are mutually oriented at $71.20(5)^\circ$. This is one of the most regular of the **Mxx** structures without disorder, twinning or potential pseudosymmetry problems.

4.3. Mxo series

The primary hydrogen bonding in all three **Mxo** derivatives is centrosymmetric, symmetrical $_{(amide)}N-H...N_{(pyridine)}$ with graph set $R^2_2(8)$ that is remarkably similar for all three **Mxo** structures. In tandem with this hydrogen bonded cyclic ring system there are intra- and intermolecular C-H...O=C contacts present. The principal difference between all three structures is the presence of an intra-dimer C-H... π (arene) interaction which is shortest in **Moo**. The three structures **Mpo**, **Mmo**, **Moo** are **isostructural** but they are **not isomorphous**.

4.3.1. Mpo molecular and crystal structure

The cyclic hydrogen bonded dimer forms about inversion centres with an N...N distance of 3.1081(15) Å. The dimers are further linked into a 1-D *zig-zag* chain *via* C-H...O interactions about inversion centres and parallel to the (11-2) plane. Chains stack and are linked *via* weak contacts. The shortest C-H... π (arene) contacts have C...Cg distances of 3.5556(14) and 3.7056(14) Å with C-H...Cg angles of 123° , 134° : this is too long to be a meaningful interaction. The room temperature study of **Mpo** (XIFNIK) has been reported and archived as data depository material. **Mpo** is similar to this structure and only differs in interaction data due to the difference in the experimental data collection temperature. The interplanar angle between the C_6 and C_5N rings is $45.34(4)^\circ$ in **Mpo**.

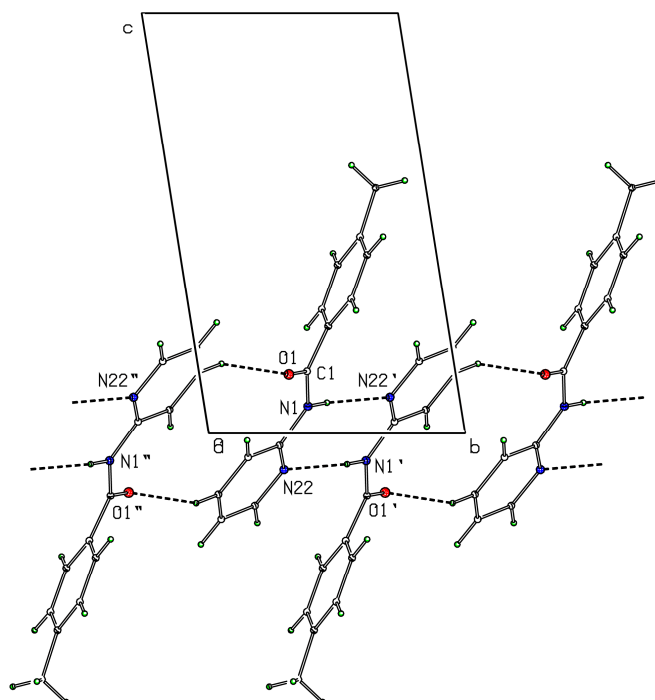


Figure 5. The primary hydrogen bonding in Mpo with the cyclic N-H...N dimers forming zig-zag chains along the b-axis direction.

4.3.2. Mmo molecular and crystal structure

The cyclic hydrogen bonded dimer forms about inversion centres with an N...N distance of 3.106(3) Å. Dimers are arranged and linked *via* weak C-H...O and C-H... π (arene) contacts. The interplanar angle between the C₆ and C₅N rings is 70.55(7)°. The major difference between **Mpo** and **Mmo** is the angle of the intradimer C-H... π (arene) contact.

4.3.3. Moo molecular and crystal structure

The cyclic hydrogen bonded dimer forms about inversion centres with an N...N distance of 3.076(2) Å. In tandem is the formation of a C-H... π (arene) interaction, as C23-H23...[C11,...,C16] about inversion centres, such that all six C23...C₁₁₋₁₆ interaction distances are in the range 3.472(2) to 3.836(3) Å (and with six H23...C₁₁₋₁₆ from 2.71 to 2.92 Å); this highlights the symmetrical nature of this interaction. The short interaction C-H... π (arene) details are H23...Cg1 = 2.46 Å, C23...Cg1 = 3.3875(18) Å and C23-H23...Cg1 = 167°. Dimers are further linked arranged *via* weak C-H...O and C-H... π (arene) contacts. There are **very few** examples available in the literature that contain shorter C-H... π (arene) geometric data apart from analogous interactions in ionic structures, whereby much of the interaction is charge-based or assisted.

For overall comparisons, the interplanar angle between the C₆ and C₅N rings is 84.79(5)° showing an increasing trend towards aromatic rings that are perpendicular along the **Mxo** series.

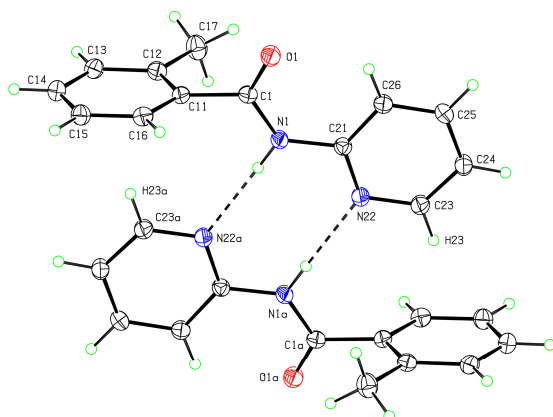


Figure 6. An ORTEP diagram of the hydrogen bonded dimer in **Moo** (graph-set $R^2_2(8)$) with displacement ellipsoids drawn at the 30% probability level: atom H23 represents the H atom involved in the short C23-H23... π (arene) interaction.

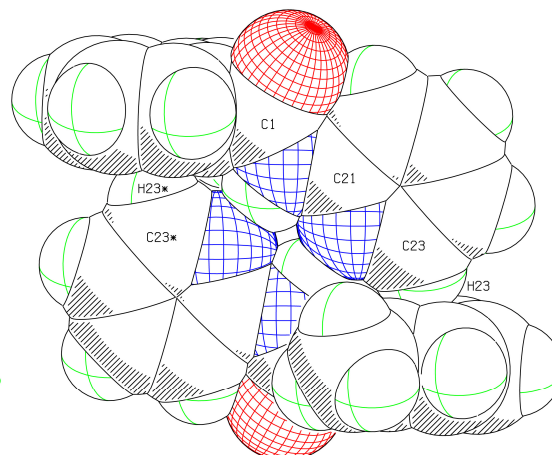


Figure 7. A view of the **Moo** 'dimeric' unit showing the N-H...N and C-H... π (arene) intermolecular interactions with atoms are depicted as their van der Waals spheres: atoms with suffix a are related by inversion symmetry.

4.3.4. A CSD search for interactions related to **Moo**.

A 'restricted' search was performed on normalised aromatic C-H... π (arene) interactions (C-H = 1.083 Å) with the following limits of H...Cg between 2 and 2.5 Å, C...Cg between 3 and 3.4 Å and C-H...Cg between 160 and 180° (Cg is the aromatic ring centroid for CSD calculations). For the version 2.30 + 4 updates a total of 41 'hits' were obtained (of which 38 contain a metal): a total of 51 'hits' are obtained when 'normal' bond lengths of C-H = 0.95 Å are used. The majority of these 'hits' are organometallic/metal-organic and are intramolecular in nature and principally due to the orientation of the aromatic ring towards another aromatic ring within the same molecule and typically separated by 5-7 bonds. The search was conducted with the purpose of finding short, symmetrical C-H... π (arene) interactions.

In **Moo** with the C23-H23 bond length normalised to 1.083 Å (a factor of 1.14 longer than the SHELXL97 standard bond length of 0.95 Å), the short interaction details are H23...Cg1 = 2.33 Å with C23-H23...Cg1 = 166°. The range of H23...[C11,...,C16] distances all span from 2.61 to 2.80 Å.

The CSD codes for structures with short intermolecular C₆-H... π (C₆) interactions include ICEXUJ (a Zr complex) and LEXJOO (Au derivative): whereas in LETYUE the solvent is disordered with large displacement ellipsoids. In ICEXUJ, the geometric data are 2.32 Å, 3.373 Å, 163° between the C₆ rings of indenyl groups, whereas, in LEXJOO or triphenylphosphine-(3H-5-phenyl-1,2,3-triazol-4-yl)-gold(I) the geometric data are even shorter with data of 2.26 Å, 3.303 Å, 161° and this interaction forms in tandem with the 'tight' N-H...N interaction between the triazole moieties. The **Moo** data are comparable to the geometric data to these structures.

Examples with intramolecular interactions include both QEZRAO (2.25 Å, 3.32 Å, 171°) and TEGJOF (2.23 Å, 3.31 Å, 178°), which with WIXHIV (2.20 Å, 3.26 Å, 168°) are where the H atom direction is constrained by the ligand geometry and steric bulk. In VAGFIS10 the interaction is constrained by the geometrical demands within the molecule.

4.4. Overall trends in **Mxx** (Unit cell volumes)

The trend in unit cell volumes is that in each of the **Mxp**, **Mxm**, **Mxo** series has increasing the unit cell volume increasing from *para*- to *meta*- to *ortho*-, but when analysing as **Mpx**, **Mmx**, **Mox** has the *meta* structure series with the largest unit cell volume.

4.5. Table 1. Experimental details for the **Mxx** compounds:

For all structures: C₁₃H₁₂N₂O, M_r = 212.25. Experiments were carried out at 150 K with Mo K α radiation on a Nonius kappaCCD diffractometer, apart from **Mpo** on a Bruker ApexII. H atoms were treated by a mixture of independent and constrained refinement. In **Mop**, **Mpm** and **Mom**, the data were merged prior to final refinement and the Flack parameter is meaningless.

Crystal data	Mpp	Mmp	Mop	Mpm	Mmm
Crystal system, space group	Monoclinic, P2 ₁ /n (No.14)	Triclinic, P $\bar{1}$ (No.2)	Monoclinic, Pc (No.7)	Triclinic, P1 (No.1)	Triclinic, P $\bar{1}$ (No.2)
<i>a</i> , <i>b</i> , <i>c</i> (Å)	5.6975 (4), 16.8860 (13), 11.0191 (5)	8.1453 (6), 9.1925 (8), 14.5347 (15)	6.1091 (4), 25.558 (2), 7.7455 (2)	5.2023 (2), 7.7661 (4), 26.5219 (12)	9.4025 (4), 9.8640 (5), 12.4783 (7)
α , β , γ (°)	90, 101.594 (4), 90	87.088 (5), 88.102 (6), 76.456 (6)	90, 111.700 (2), 90	89.078 (3), 89.687 (3), 90.024 (2)	86.077 (2), 85.800 (3), 69.390 (3)
Volume (Å ³)	1038.49 (12)	1056.41 (16)	1123.65 (12)	1071.37 (8)	1079.21 (9)
<i>Z</i>	4	4	4	4	4
μ (mm ⁻¹)	0.09	0.09	0.08	0.09	0.09
Crystal size (mm)	0.26 × 0.20 × 0.15	0.20 × 0.06 × 0.06	0.50 × 0.15 × 0.13	0.40 × 0.25 × 0.14	0.20 × 0.20 × 0.12
Data collection					
Absorption correction	Multi-scan (SORTAV; Blessing, 1995)	Multi-scan (SORTAV; Blessing, 1995)	Multi-scan (SORTAV; Blessing, 1995)	Multi-scan (SORTAV; Blessing, 1995)	Multi-scan (SORTAV; Blessing, 1995)
<i>T</i> _{min} , <i>T</i> _{max}	0.978, 0.987	0.983, 0.995	0.837, 0.993	0.790, 0.987	0.635, 0.999
No. of measured, independent and observed reflections	7570, 2367, 1262 { <i>I</i> > 2 σ (<i>I</i>)}	12766, 4782, 2593 { <i>I</i> > 2 σ (<i>I</i>)}	8309, 2545, 1491 { <i>I</i> > 2 σ (<i>I</i>)}	14972, 4770, 3453 { <i>I</i> > 2 σ (<i>I</i>)}	4867, 4867, 2397 { <i>I</i> > 2 σ (<i>I</i>)}
<i>R</i> _{int}	0.072	0.095	0.068	0.106	0.000
Refinement					
R[<i>F</i> ² > 2 σ (<i>F</i> ²)], wR(<i>F</i> ²), <i>S</i>	0.066, 0.202, 1.00	0.066, 0.183, 1.01	0.056, 0.161, 1.02	0.059, 0.154, 1.05	0.076, 0.254, 1.01
No. of reflections	2367	4782	2545	4770	4867
No. of parameters	150	299	341	597	300
No. of restraints	0	0	6	3	0
<i>Dp</i> _{max} , <i>Dp</i> _{min} (e Å ⁻³)	0.35, -0.29	0.27, -0.23	0.18, -0.20	0.23, -0.25	0.40, -0.34

Crystal data	Mom	Mpo	Mmo	Moo
Crystal system, space group	Orthorhombic, Pca2 ₁ (No.29)	Triclinic, P ⁻ 1 (No.2)	Monoclinic, P2 ₁ /c (No.14)	Triclinic, P ⁻ 1 (No.2)
<i>a</i> , <i>b</i> , <i>c</i> (Å)	11.5170 (2), 10.4800 (3), 9.1960 (3)	5.9079 (3), 7.7140 (4), 12.2606 (8)	5.1480 (3), 13.9239 (14), 15.0042 (13)	7.2376 (4), 8.5035 (6), 9.0024 (5)
<i>α</i> , <i>β</i> , <i>γ</i> (°)	90, 90, 90	97.406 (2), 94.029 (2), 107.463 (2)	90, 98.000 (5), 90	92.327 (3), 97.349 (3), 95.259 (3)
Volume (Å ³)	1109.94 (5)	525.04 (5)	1065.04 (15)	546.42 (6)
<i>Z</i>	4	2	4	2
<i>μ</i> (mm ⁻¹)	0.08	0.09	0.09	0.08
Crystal size (mm)	0.40 × 0.36 × 0.32	0.35 × 0.20 × 0.16	0.36 × 0.16 × 0.12	0.32 × 0.30 × 0.30
Data collection				
Absorption correction	Multi-scan (SORTAV; Blessing, 1995)	Multi-scan (SADABS; Bruker, 2008)	Multi-scan (SORTAV; Blessing, 1995)	Multi-scan (SORTAV; Blessing, 1995)
<i>T</i> _{min} , <i>T</i> _{max}	0.829, 0.975	0.648, 0.756	0.790, 0.993	0.880, 0.987
No. of measured, independent and observed reflections	8920, 2500, 2086 { <i>I</i> > 2σ(<i>I</i>)}	6050, 2365, 1978 { <i>I</i> > 2σ(<i>I</i>)}	6938, 2433, 1322 { <i>I</i> > 2σ(<i>I</i>)}	5136, 2467, 1785 { <i>I</i> > 2σ(<i>I</i>)}
<i>R</i> _{int}	0.044	0.024	0.073	0.037
Refinement				
R[<i>F</i> ² > 2σ(<i>F</i> ²)], wR(<i>F</i> ²), <i>S</i>	0.041, 0.096, 1.11	0.039, 0.109, 1.05	0.065, 0.195, 1.02	0.063, 0.184, 1.08
No. of reflections	2500	2365	2433	2467
No. of parameters	151	150	150	150
No. of restraints	1	0	0	0
<i>Dp</i> _{max} , <i>Dp</i> _{min} (e Å ⁻³)	0.17, -0.17	0.32, -0.19	0.35, -0.30	0.43, -0.29

Computer programs: KappaCCD Server Software (Nonius, 1997), Bruker software (Bruker, 2008), DENZO-SMN (Otwinowski and Minor, 1997), SAINT (Bruker, 2008), SHELXS97 (Sheldrick, 2008), SHELXL97 (Sheldrick, 2008) and SORTX (McArdle, 1995), PLATON (Spek, 2003), SHELXL97 and PREP8 (Ferguson, 1998).

4.6. Table 2 - Primary hydrogen-bond and contact parameter data

<i>D</i> —H... <i>A</i>	<i>D</i> —H (Å)	H... <i>A</i> (Å)	<i>D</i> ... <i>A</i> (Å)	<i>D</i> —H... <i>A</i> (°)
Mpp [Z'=1]				
N1—H1...N24 ⁱ	0.83 (3)	2.42 (3)	3.105 (3)	141 (2)
C26—H26...O1	0.95	2.30	2.862 (3)	118
C26—H26...Cg1 ⁱⁱ	0.95	2.81	3.490 (3)	129
Mmp [Z'=2]				
N1A—H1A...N24B ⁱⁱⁱ	0.91 (2)	2.29 (3)	3.058 (3)	142 (2)
N1B—H1B...N24A ⁱⁱ	0.95 (3)	2.12 (3)	3.059 (3)	172 (3)
C12B—H12B...N24A ⁱⁱ	0.95	2.54	3.387 (3)	148
C17A—H17B...O1A ^{iv}	0.98	2.58	3.496 (3)	155
C22A—H22A...O1A	0.95	2.27	2.859 (3)	119
C22B—H22B...O1B	0.95	2.26	2.817 (3)	117
C23A—H23A...O1B ^v	0.95	2.38	3.202 (3)	144
C25A—H25A...Cg1 ^{vi}	0.95	2.65	3.593 (3)	170
Mop [Z'=2]				
N1A—H1A...N24A ^{vii}	0.97 (5)	1.99 (5)	2.952 (5)	174 (4)
N1B—H1B...N24B ^{viii}	0.96 (4)	2.00 (4)	2.950 (5)	171 (4)
N1C—H1C...N24C ^{vii}	0.86	2.24	3.10 (5)	176
C15A—H15A...O1A ^{ix}	0.93	2.48	3.344 (5)	154
C15B—H15B...O1B ^{ix}	0.93	2.49	3.351 (5)	154
C15C—H15C...O1C ^{ix}	0.93	2.48	3.32 (3)	151
Mpm [Z'=4] – only example with N-H...O=C interactions				
N1A—H1A...O1A ^{iv}	0.74 (6)	2.35 (6)	3.029 (6)	153 (6)
N1B—H1B...O1B ^x	0.87 (5)	2.19 (5)	3.016 (5)	160 (4)
N1C—H1C...O1C ^{iv}	0.71 (4)	2.39 (4)	3.085 (6)	167 (5)
N1D—H1D...O1D ^{iv}	0.86 (5)	2.26 (5)	3.085 (5)	162 (5)
C26A—H26A...O1A	0.95	2.43	2.868 (6)	108
C26B—H26B...O1B	0.95	2.41	2.860 (6)	109
C26C—H26C...O1C	0.95	2.36	2.866 (5)	113
C26D—H26D...O1D	0.95	2.38	2.864 (6)	111
Mmm [Z'=2]				
N1A—H1A...N23B ^{xi}	0.96 (4)	2.06 (4)	2.998 (4)	166 (3)
N1B—H1B...N23A ^{xii}	0.97 (3)	2.08 (3)	3.006 (4)	160 (2)
C22A—H22A...O1A	0.95	2.44	2.938 (4)	113
C22B—H22B...O1B	0.95	2.40	2.899 (4)	113
C22A—H22A...Cg1 ^{xiii}	0.95	2.78	3.563 (4)	141
C22B—H22B...Cg2 ^{xiv}	0.95	2.75	3.544 (4)	142

Mom [Z'=1]

N1—H1...N23 ^{xv}	0.93 (3)	2.01 (3)	2.946 (2)	175 (2)
C22—H22...O1	0.95	2.24	2.847 (2)	121
C24—H24...O1 ^{xvi}	0.95	2.55	3.283 (3)	134
C17—H17B...Cg1 ^{xvii}	0.98	2.76	3.542 (2)	138

Mpo [Z'=1] – the Mxo series with cyclic N-H...N interactions

N1—H1...N22 ^{xviii}	0.875 (18)	2.255 (18)	3.1081 (15)	164.6 (15)
C25—H25...O1 ^{xiii}	0.95	2.52	3.4165 (16)	157
C26—H26...O1	0.95	2.27	2.8707 (16)	121

Mmo [Z'=1]

N1—H1...N22 ^{xiv}	0.84 (3)	2.29 (3)	3.106 (3)	164 (3)
C15—H15...O1 ^{xix}	0.95	2.50	3.352 (3)	149.2
C26—H26...O1	0.95	2.37	2.869 (3)	112
C23—H23...Cg1 ^{xiv}	0.95	2.84	3.749 (3)	161

Moo [Z'=1]

N1—H1...N22 ^{xx}	0.90 (2)	2.18 (2)	3.076 (2)	177.6 (16)
C16—H16...O1 ^{xiv}	0.95	2.46	3.405 (2)	175
C25—H25...O1 ^{xxi}	0.95	2.51	3.237 (2)	134
C26—H26...O1	0.95	2.23	2.846 (2)	121
C23—H23...Cg1 ^{xx}	0.95	2.46	3.3875 (18)	167

Symmetry code(s): (i) $x+1/2, -y+1/2, z+1/2$; (ii) $-x+1, -y, -z+1$; (iii) $-x, -y+1, -z+1$; (iv) $x-1, y, z$; (v) $x+1, y-1, z$; (vi) $x, y-1, z$; (vii) $x+1, -y+1, z+1/2$; (viii) $x+1, -y, z+1/2$; (ix) $x+1, y, z+1$; (x) $x+1, y, z$; (xi) $-x+1, -y, -z$; (xii) $-x, -y+1, -z$; (xiii) $-x, -y, -z$; (xiv) $-x+1, -y+1, -z+1$; (xv) $x+1/2, -y+1, z$; (xvi) $-x, -y+1, z+1/2$; (xvii) $-x+1/2, y, z+1/2$; (xviii) $-x-1, -y+1, -z$; (xix) $-x+1, y+1/2, -z+3/2$; (xx) $-x+1, -y+1, -z$; (xxi) $-x+2, -y+1, -z+1$.

Table 3. Selected crystallographic data

Mxx	Space group	Z'	R-factors	Interaction (Å)	Packing
Mpp	$P2_1/n$	1	0.066, 0.202	3.105(3)	1-D chains
Mmp	P^{-1}	2	0.066, 0.183	3.058(3), 3.059(3)	2-D sheets
Mop	Pc	2	0.056, 0.161	2.952(5), 2.950(5)	1-D chains
Mpm	$P1$	4	0.059, 0.154	3.016(5)-3.085(6)	1-D chains
Mmm	P^{-1}	2	0.076, 0.254	2.998(4), 3.006(4)	1-D chains
Mom	$Pca2_1$	1	0.041, 0.096	2.946(2)	1-D chains
Mpo	P^{-1}	1	0.039, 0.109	3.1081(15)	Dimers
Mmo	$P2_1/c$	1	0.065, 0.195	3.106(3)	Dimers
Moo	P^{-1}	1	0.063, 0.184	3.076(3)	Dimers

5. *Ab initio* calculation results

5.1. Energy results

5.1.1. Table 4. Optimisations in *gas phase*

	E_{SCF}	δE_{SCF}	E_0	δE_0	E	δE	G	δG
Mpp	-683.2735	-22.31	-686.1659	-8.78	-686.1521	-8.22	-686.2085	-11.35
Mmp	-683.2729	-20.70	-686.1660	-9.14	-686.1523	-8.63	-686.2085	-11.34
Mop	-683.2694	-11.48	-686.1641	-4.11	-686.1506	-4.18	-686.2056	-3.89
Mpm	-683.2691	-10.85	-686.1643	-4.71	-686.1505	-4.10	-686.2070	-7.46
Mmm	-683.2685	-9.29	-686.1644	-5.03	-686.1507	-4.46	-686.2070	-7.45
Mom	-683.2650	0.00	-686.1625	0.00	-686.1490	0.00	-686.2042	0.00
Mpo	-683.2825	-45.89	-686.1743	-30.85	-686.1606	-30.42	-686.2170	-33.60
Mmo	-683.2818	-44.16	-686.1744	-31.06	-686.1607	-30.69	-686.2169	-33.38
Moo	-683.2781	-34.32	-686.1722	-25.40	-686.1587	-25.66	-686.2136	-24.74

5.1.2. Table 5 Optimisations in CH_2Cl_2

	E_{SCF}	δE_{SCF}	E_0	δE_0	E	δE	G	δG
Mpp	-683.3020	-27.34	-686.1911	-11.60	-686.1776	-11.55	-686.2326	-11.96
Mmp	-683.3009	-24.62	-686.1913	-12.25	-686.1777	-11.97	-686.2331	-13.26
Mop	-683.2970	-14.34	-686.1890	-6.28	-686.1756	-6.28	-686.2305	-6.46
Mpm	-683.2964	-12.88	-686.1887	-5.38	-686.1752	-5.27	-686.2303	-5.81
Mmm	-683.2955	-10.29	-686.1889	-5.96	-686.1753	-5.60	-686.2309	-7.40
Mom	-683.2915	0.00	-686.1869	0.00	-686.1732	0.00	-686.2281	0.00
Mpo	-683.3084	-44.15	-686.1975	-28.46	-686.1840	-28.34	-686.2393	-29.52
Mmo	-683.3074	-41.73	-686.1976	-28.75	-686.1841	-28.57	-686.2393	-29.61
Moo	-683.3033	-30.75	-686.1952	-22.52	-686.1818	-22.51	-686.2368	-23.03

5.1.3. Table 6. Optimisations in H_2O

	E_{SCF}	δE_{SCF}	E_0	δE_0	E	δE	G	δG
Mpp	-683.2956	-26.62	-686.1834	-12.18	-686.1698	-11.96	-686.2257	-12.64
Mmp	-683.2948	-24.53	-686.1831	-11.36	-686.1696	-11.49	-686.2248	-10.24
Mop	-683.2909	-14.16	-686.1813	-6.63	-686.1677	-6.63	-686.2235	-6.82
Mpm	-683.2901	-12.18	-686.1810	-5.84	-686.1673	-5.52	-686.2235	-6.94
Mmm	-683.2894	-10.35	-686.1807	-5.06	-686.1671	-5.06	-686.2224	-4.12
Mom	-683.2855	0.00	-686.1788	0.00	-686.1652	0.00	-686.2209	0.00
Mpo	-683.2991	-35.82	-686.1870	-21.67	-686.1734	-21.37	-686.2296	-22.87
Mmo	-683.2982	-33.39	-686.1867	-20.75	-686.1731	-20.62	-686.2291	-21.61
Moo	-683.2942	-22.99	-686.1846	-15.32	-686.1711	-15.45	-686.2265	-14.73

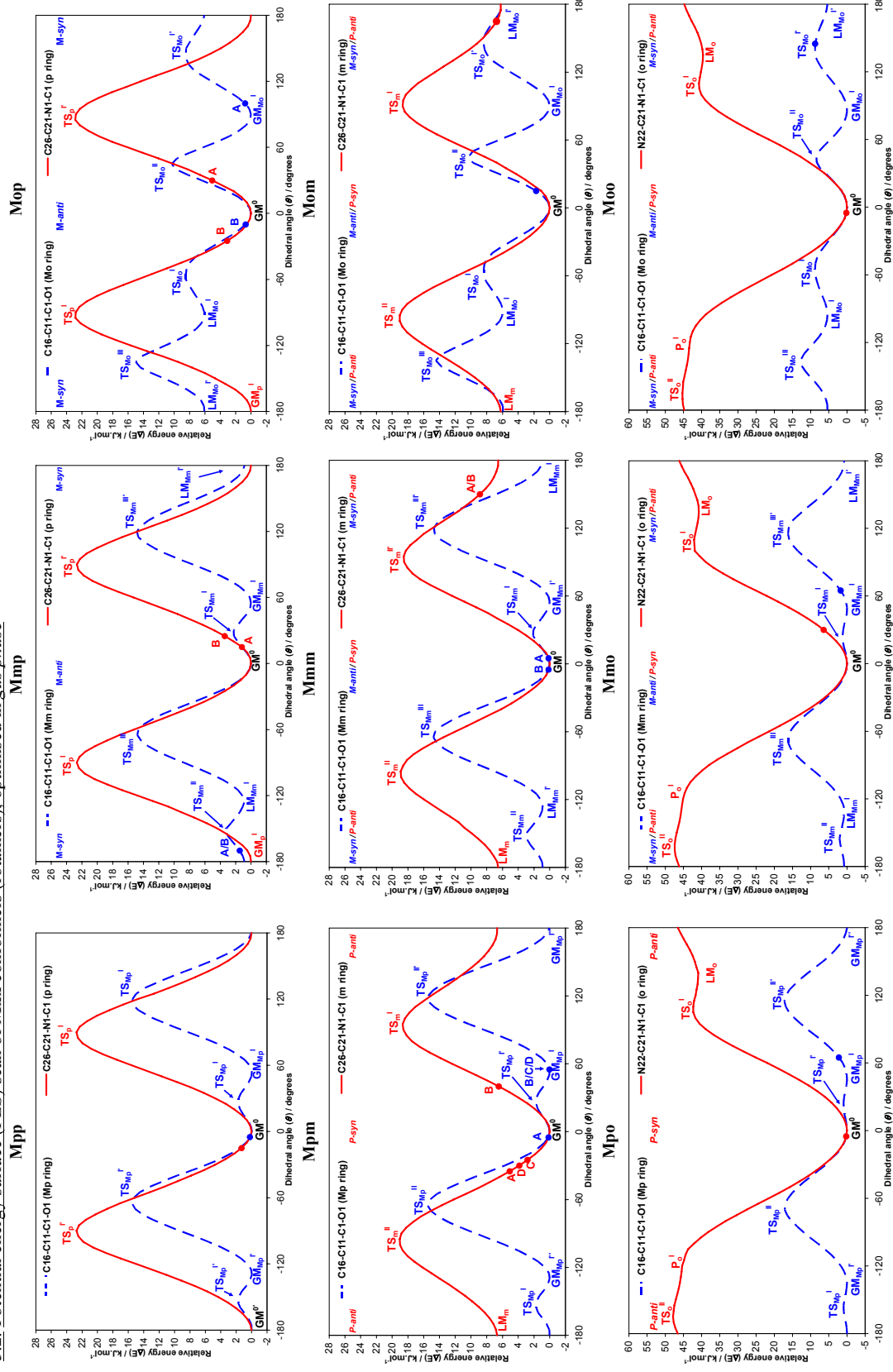
The tables present absolute values of electronic (E_{SCF}), zero point (E_0), energy (E) and Gibbs free energy (G) of **Mxx** molecules expressed in Hartrees (E_h). The relative energies (if **Mom** is taken as basis point) are shown in columns with suffix δ , and are expressed in kJ.mol^{-1} .

5.1.4. Table 7. Comparison of energies in different media

	<i>gas phase vs. CH₂CH₂</i>				<i>gas phase vs. H₂O</i>				<i>CH₂Cl₂ vs H₂O</i>				$\log K_{D/W}$
	ΔE_{SCF}	ΔE_0	ΔE	ΔG_{solv}	ΔE_{SCF}	ΔE_0	ΔE	ΔG_{solv}	ΔE_{SCF}	ΔE_0	ΔE	$\Delta \Delta G_{solv}$	
Mpp	-74.73	-66.25	-66.90	-63.36	-58.06	-46.12	-46.38	-45.15	-16.67	-20.13	-20.52	-18.21	3.19
Mmp	-73.62	-66.54	-66.91	-64.67	-57.59	-44.95	-45.51	-42.76	-16.03	-21.59	-21.41	-21.91	3.84
Mop	-72.55	-65.60	-65.68	-65.31	-56.43	-45.24	-45.11	-46.79	-16.12	-20.36	-20.57	-18.53	3.24
Mpm	-71.73	-64.10	-64.75	-61.09	-55.09	-43.85	-44.07	-43.33	-16.64	-20.25	-20.68	-17.76	3.11
Mmm	-70.70	-64.36	-64.71	-62.69	-54.82	-42.75	-43.25	-40.52	-15.88	-21.61	-21.46	-22.17	3.88
Mom	-69.70	-63.43	-63.58	-62.75	-53.75	-42.72	-42.65	-43.86	-15.94	-20.71	-20.93	-18.89	3.31
Mpo	-67.96	-61.04	-61.51	-58.67	-43.69	-33.54	-33.60	-33.12	-24.27	-27.50	-27.91	-25.55	4.48
Mmo	-67.26	-61.12	-61.46	-58.98	-42.98	-32.41	-32.58	-32.09	-24.28	-28.70	-28.88	-26.89	4.71
Moo	-66.13	-60.55	-60.42	-61.03	-42.42	-32.65	-32.44	-33.84	-23.70	-27.90	-27.99	-27.19	4.76

The table shows differences (Δ) of energies (E_{SCF} , E_0 , E and G) of **Mxx** compounds in different media expressed in kJ mol^{-1} . The ΔG_{solv} presents calculated energy of solvation, while $\Delta \Delta G_{solv}$ presents difference of energies of solvation in two different solvents (CH_2CH_2 and H_2O). The final variable, $\log K_{D/W}$ presents tentative (theoretical) values of partition coefficient of **Mxx** molecules between dichloromethane and water, calculated as $\log K_{D/W} = -\Delta \Delta G_{solv}/2.303RT$. This model has not been validated using exact experimental the values of $\log K_{D/W}$, therefore, it has exclusively relative (qualitative) not absolute (quantitative) significance, and the tentative values of $\log K_{D/W}$ should not be taken as final.

5.2. Potential energy surface (PES) scan of Mxx conformers (rotamers), optimised in gas phase



5.3. PES scan of **Mxx** conformers (rotamers), optimised in *gas phase* (full line), CH_2CH_2 (dashed line) and in H_2O (dotted line).

