Carbamates I: Structural and conformational study of eight Methoxyphenyl-*N*-pyridinylcarbamates

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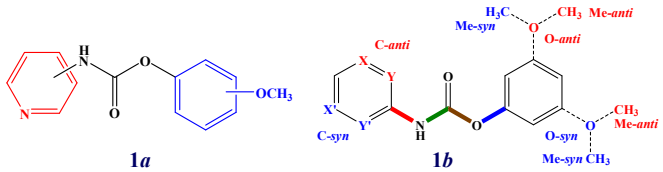
Introduction

Crystal and molecular structures of phenyl carbamates are relatively unexplored. Only 33 basic phenylcarbamates are present on the Cambridge Structure Database with no phenyl-*N*-pyridinylcarbamates (Scheme 1a). Our field is structural systematics and isomer grids by bridging solid state crystallography and *in silico* molecular modeling with conformational analysis as a central tool.[1-3] A 3×3 isomer grid of nine Methoxyphenyl-*N*-pyridinylcarbamates ($C_{13}H_{12}N_2O_3$) as **CxxOMe** (x = *para-*/*meta-*/*ortho-*) was synthesized and studied to determine their crystal structures and correlate structural relationships from both *ab initio* calculations and the solid-state using conformational analysis. Eight of nine crystal structures were determined using single crystal X-ray diffraction. All isomers form N-H···N hydrogen bonds as the primary interaction, with one isomer (**CmmOMe**, **Fig. 1**) forming a relatively unusual disordered hydrogen bonded trimer *via* N-H···N interactions, while the **CoxOMe** isomers (**Figs. 2**, **3** and **5**) form N-H···N hydrogen bonded dimers.



Scheme 1*a* Schematic diagram of the **CxxOMe** isomers (above left). **Scheme 1*b***. **CxxOMe** conformational preferences as **C-*anti*/C-*syn***, **O-*anti*/O-*syn*** and **Me-*anti*/Me-*syn*** (above right).

Experimental methods

The isomers were synthesised using condensation reactions of 4-/3-/2-aminopyridines with commercially available methoxyphenyl chloroformates or the Curtius rearrangement. All isomers were characterised by ^{1}H-NMR, ^{13}C-NMR and IR. Single crystal X-ray data (Mo) were collected on an Oxford Diffraction Gemini S-Ultra diffractometer at 294(1) K: with θ range from 2-26° (100% data to 25°).

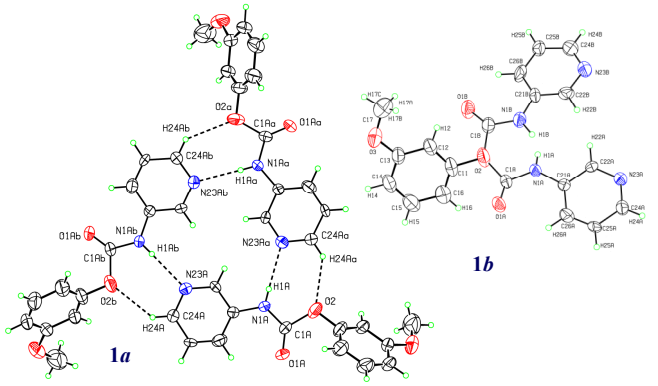


Fig. 1: (*a*) The **CmmOMe** trimer (only A is shown; *a* = 2-y,1+x-y,z; *b* = 1-x+y,2-x,z), (*b*) the **CmmOMe** disorder showing the A part (**O-*syn*** conformation, 50% occupancy) and B part (**O-*anti*** conformation, 50% occupancy)

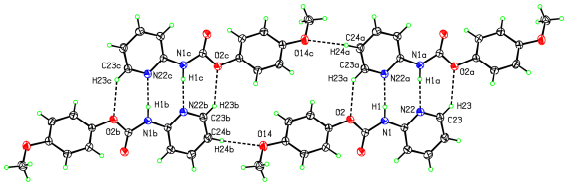


Fig. 2: Hydrogen bonding in **CopOMe** (*a* = 1-x,1-y,1-z; *b* = x,-1+y,z; *c* = 1-x,-y,1-z)

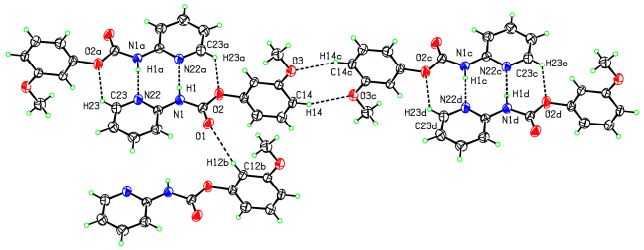


Fig. 3: Hydrogen bonding in **ComOMe** (*a* = 2-x,-y,1-z; *b* = -1+x,y,z; *c* = 2-x,1-y,-z; d = x,1+y,-1+z)

Table 1. Selected crystallographic data and relevant structural features for **CxxOMe**

Name	*SG*	*Z*/*Z*'	Volume/ Å^3	*R* factor	C_6/C_5N/°	N…N/Å	Packing
CppOMe	$P2_1/n$	4/1	1218.60(5)	0.0416	56.93(4)	2.9182(15)	1-D chains
CpmOMe	$P2_1/c$	4/1	1208.45(4)	0.0460	73.89(5)	2.9360(15)	1-D chains
CpoOMe	$P2_1/c$	4/1	1144.29(7)	0.0480	86.15(6)	2.998(2)	1-D chains
CmpOMe	$P2_12_12_1$	4/1	1201.86(4)	0.0278	61.01(6)	2.9130(19)	1-D chains
CmmOMe	*R*3*c*	18/1	5511.2(2)	0.0311	50.60(43) 61.70(38)	2.970(6) 2.965(7)	Trimer
CopOMe	$P2_1/c$	4/1	1166.44(16)	0.0433	53.28(3)	2.9886(16)	Dimer
ComOMe	*P*$\bar{1}$	2/1	603.40(10)	0.0584	82.94(7)	2.983(3)	Dimer
CooOMe	*P*$\bar{1}$	2/1	577.02(13)	0.0314	89.05(4)	3.0297(17)	Dimer

In silico methods

The **CxxOMe** isomer optimisation and conformational analysis providing PES diagrams was performed using *ab initio* calculations (B3LYP/6-311++G**) on isolated (*gas-phase*) molecules using the Gaussian03/09 software package. Corresponding solid state structure dihedral angles are plotted in the *gas phase* PES diagrams relative to the dihedral angles of the optimised structures.

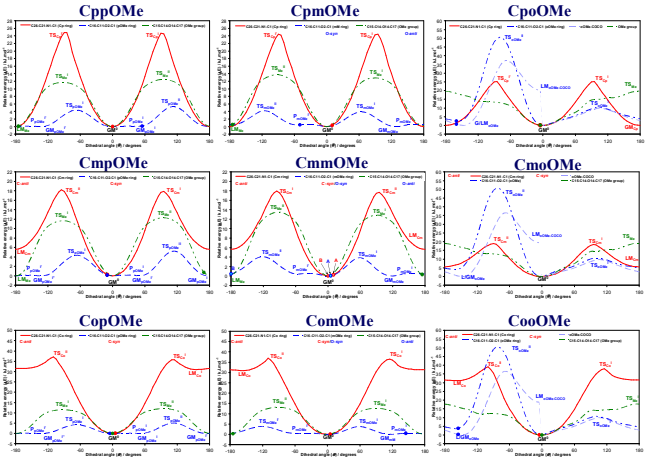


Fig. 4 The nine PES conformational analysis diagrams for the **CxxOMe** (*gas-phase*)

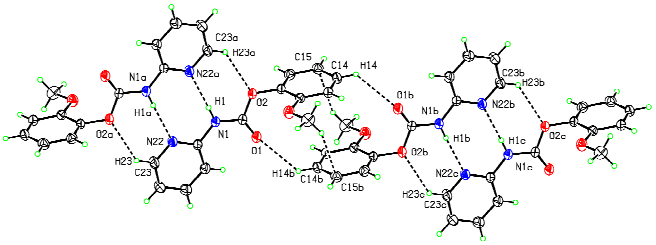


Fig. 5: Hydrogen bonding in **CooOMe** (*a* = 1-x,1-y,1-z; *b* = 1-x,2-y,-z; *c* = x,1+y,-1+z)

Results and Conclusion

This structural systematic study provides eight molecular and crystal structures of methoxyphenyl-*N*-pyridinylcarbamates. The principal interaction in all **CxxOMe** crystal structures is N-H···N hydrogen bonding giving 1-D chains (**CpxOMe** and **CmpOMe**), trimer (**CmmOMe, Fig. 1**) and dimers (**CoxOMe**, **Figs. 2, 3, 4**). In most isomers, additional C-H···O interaction are crucial for aggregation. The most remarkable structure is **CmmOMe** (*R3c, Z*=18), a relatively rare example of a hydrogen bonded trimer. It is disordered about the **O**-ring torsion angle: 50% **O-*anti*** and 50% in the **O-*syn*** conformation. All three **CoxOMe** isomers form dimers as $R^2_2(8)$ rings *via* N-H···N interactions, similar to **Mxx**/**Fxx**[1,3] with aiding C-H···O interactions. The methoxy group engages into important secondary hydrogen bonding. The conformational analyses shows a high flexibility of the methoxyphenyl ring with a limitation in the *ortho* isomers. The solid state and the modelled conformations are mismatched in 3 of the 8 molecules where the CH_3O- groups and *meta*-methoxyphenyl rings (**mOMe**) (solid state structures) adopt *meta*-stable or unstable conformations as compared to the optimised models. The solid state CH_3O- group adopts both conformations plausible due to the small energy difference. **Note:** The **CmoOMe** crystal structure forms hydrogen bonded trimers exhibiting two distinct types of trimer conformation (*Crystal Growth & Design*, 2013, *in press*).

References:

1. P. Mocilac, M. Tallon, A.J. Lough and **J.F. Gallagher**, *CrystEngComm*, 2010, **12**, 3080-3090.
2. P. Mocilac, A.J. Lough and **J.F. Gallagher**, *CrystEngComm*, 2011, **13**, 1899-1909.
3. P. Mocilac and **J.F. Gallagher**, *Acta Crystallogr. Sect. B-Struct. Sci.*, 2012, **B68**, 189-203.

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