Journal of Fluorine Chemistry 192 (2016) 86–97

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Titration characteristics of fluorous 1,2,3-triazol-4-ylmethyl ethers, bis(1,2,3-triazol-4-ylmethyl) ethers and bis(1,2,3-triazol-4-ylmethyl) amines

Dominic V. Francis, Jason B. Harper, Roger W. Read*

School of Chemistry, The University of New South Wales, UNSW, Sydney, NSW, 2052, Australia

ARTICLE INFO

Article history:
Received 27 July 2016
Received in revised form 17 October 2016
Accepted 18 October 2016
Available online 26 October 2016

Keywords:
Fluorous surfactants
Functional ligands
Heterocycles
Organofluorine
Ion binding

ABSTRACT

The titration of a series of fluorous bis(1,2,3-triazol-4-ylmethyl) molecules with camphorsulfonic acid has been examined by ^{1}H NMR spectroscopy to investigate any conformational changes that might occur on protonation; it is envisaged that this information will assist in predicting their potential as ligands. Structure activity relationships based on the equilibrium constants of protonation and changes in chemical shift of the H5 triazolyl signals provide consistent information that support weak but evident cooperativity between the triazolyl rings in bis-triazolylmethyl ethers. This is overridden by replacement of the ether oxygen with a secondary amino group, but similar principles apply in subsequent protonation. An attempt is made to interpret the cooperative behavior.

1. Introduction

The processes of protonation, alkylation and metal complexation of 1,2,3-triazoles have attracted considerable interest for some time, and led to several reviews in recent years [1–3]. In particular, some research groups have compared experimental observations and theoretical predictions to interpret the basicity of 1,2,3-triazoles [4], while others have applied theory to understand their protonation and tautomerism [5]. Still others have recognised the non-regiospecificity of alkylation in alkaline, neutral and acidic media, and have attempted to optimise the yields of N(1)- and N(2)-alkylation [1,6] with electrophilic reagents.

1-Alkyl-1,2,3-triazoles can similarly serve as bases and nitrogen donor ligands through their N2 and N3 heteroatoms [2,3,7], although the conjugative influence of the pi electrons associated with N1 generally makes the N3 heteroatom the stronger donor. 1-Alkyl-4-(alkoxymethyl)-1,2,3-triazoles [8–16], 1-alkyl-4-[(alkylamino)methyl]-1,2,3-triazoles [17] and 1-alkyl-4-[(dialkylamino)methyl]-1,2,3-triazoles [17–23] are all known sub-classes of the 1-alkyl-1,2,3-triazoles, but none have been studied in any detail for their basicity nor their ligand properties. Their structures suggest that they should be further biased towards ligation by the N3 heteroatom because of the potential of the pendant 4-(heteroatomic)methyl substituent to contribute towards chelate ligand behaviour.

A very few bis(1-alkyl-1,2,3-triazolyl-4-methyl) ethers [11,14] and no corresponding amines have been reported. They would be expected to behave like their mono-heterocyclic counterparts, but they present additional and alternative chelate ligand possibilities, including ML and M_2L motifs (Fig. 1a). Conversely, there is potential in mono- and bis-1,2,3-triazol-4-ylmethylheteroatom systems for equally interesting, *albeit* weak, anion binding because of the presence of C5–H donor atoms (Fig. 1b). This is especially so where the heteroatom is a secondary amine (X = NH) group [3].

Equivalent 1-polyfluoroalkyl structures have not been studied for ligand properties previously, but the electronegativity of fluorine is well known to negatively influence the electron density around neighbouring substituents (important in biological applications [24]) while offering minimal halogen bonding opportunities [25,26]. Some modulation of the ligand properties of these derivatives would therefore be expected with little interference from competitive halogen bonding.

Recent access to fluorous bis(triazol-4-ylmethyl) ethers and amines [14,27] prompted a systematic study of the ligand properties of the molecules.

Investigations [28–33] into the effects of protonation and metal coordination of other nitrogen-containing macrocycles have established that there is consistently a red shift in the UV absorptions of these macrocycles on either protonation or metal

* Corresponding author at: School of Chemistry, University of New South Wales, UNSW, Sydney, NSW, 2052, Australia.
E-mail address: r.read@unsw.edu.au (R.W. Read).

http://dx.doi.org/10.1016/j.jfluchem.2016.10.012
0022-1139/

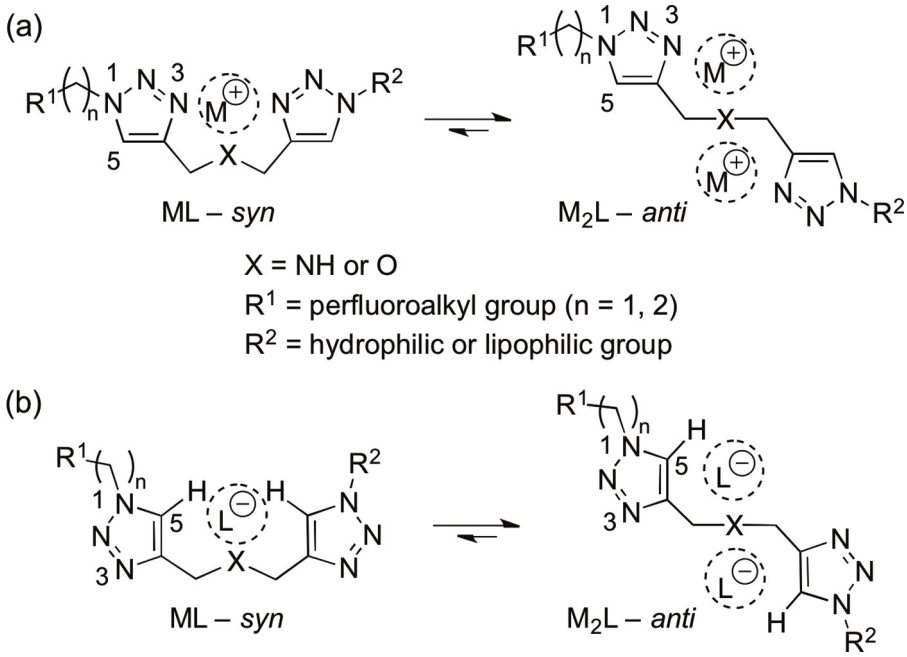


Fig. 1. Generic structures of the target bistriazole compounds showing the potential binding pockets (dashed circles) for (a) cations (M^+) and (b) anions (L^-).

coordination to the nitrogen atom. NMR experiments have similarly revealed shifts in conformational equilibria in non-fluorous bis-tetrahydroisoquinolines in response to changes in the pH of media through tracking of NMR chemical shift values and proton-proton spin coupling constants [34,35].

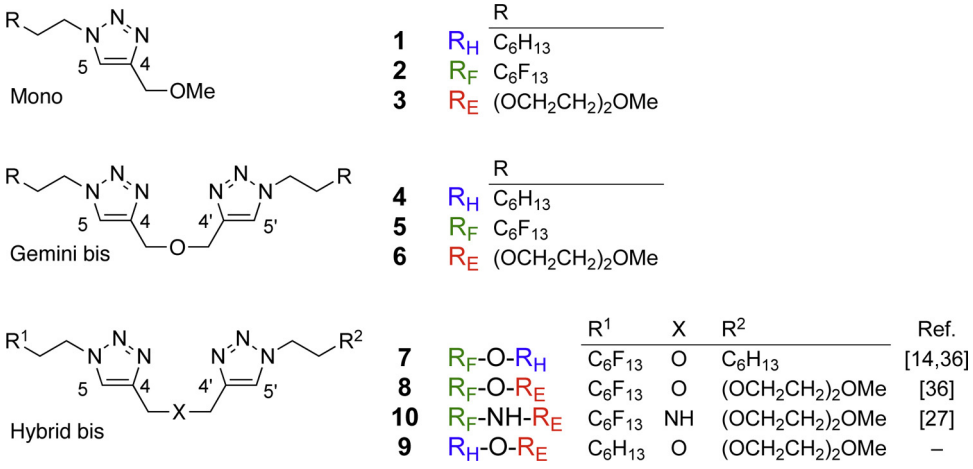
This paper sets out to elucidate the potential of bistriazolylmethyl ether and amine derivatives for ligand functionality through acid titration experiments and compares the roles of moderate length 1-alkyl (1-*n*-octyl) and 1-polyfluoroalkyl (1-perfluorohexylethyl), and 1-(methoxydiethyleneoxyethyl) triazole substituents in these molecules. In order to establish baseline data, acid titration experiments were performed on new mono-1,2,3-triazol-4-ylmethyl methyl ethers **1–3** and gemini bistriazolylmethyl ethers **4–6**, as well as known hybrid bis-triazolylmethyl ethers **7** and **8** [14,36], new hybrid ether **9**, and a single hybrid bistriazolylmethyl amine **10** [27] (Fig. 2).

2. Results and discussion

2.1. Preliminary studies

The majority of triazoles **1**–**10** were new and prepared through methods analogous to those reported previously [14,27,36–39] involving copper catalysed azide-alkyne dipolar cycloaddition. Titration experiments involved the sequential addition of camphorsulfonic acid (CSA) to a solution of the desired triazole in deuteriochloroform; the acid was chosen due to its high strength in water (pK_a 1.2) and ease of measurement given that it is solid. After each addition, a ^{1}H NMR spectrum was recorded and it was noted that there were distinctive changes in the chemical shift of signals, particularly those due to H5 and H5'.

An initial question that needed to be considered was the stoichiometry of the protonation event. Through analysis of the



		R
1	R_H	C_6H_{13}
2	R_F	C_6F_{13}
3	R_E	$(OCH_2CH_2)_2OMe$

		R
4	R_H	C_6H_{13}
5	R_F	C_6F_{13}
6	R_E	$(OCH_2CH_2)_2OMe$

		R^1	X	R^2	Ref.
7	R_F-O-R_H	C_6F_{13}	O	C_6H_{13}	[14,36]
8	R_F-O-R_E	C_6F_{13}	O	$(OCH_2CH_2)_2OMe$	[36]
10	R_F-NH-R_E	C_6F_{13}	NH	$(OCH_2CH_2)_2OMe$	[27]
9	R_H-O-R_E	C_6H_{13}	O	$(OCH_2CH_2)_2OMe$	–

Fig. 2. Monotriazolyl ether **1-3**, gemini bistriazolyl ether **4-6**, hybrid bistriazolyl ether **7-9**, and hybrid bistriazolyl amine **10.**