

SPONTANEOUS [2+2] MACROCYCLIZATION THROUGH DYNAMIC COVALENT AMINAL BONDS

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Aminals are characterized by the connectivity of two amino groups to the same carbon atom, being the nitrogenated equivalent of acetals. Unlike acetals, aminals have been slightly underexplored in dynamic covalent chemistry due to their inherent instability.^[1] In addition, stable aminals from primary amines are rare since they exist in solution in equilibrium with other species, Figure 1a. We have recently described the formation of stable and dynamic aminals^[2] that represents, to the best of our knowledge, the first example from primary amines and carbonyl compounds. Furthermore, inspired by the preparation of macrocycles through a templated reaction^[3], we have reported the preparation of stable [2+2] macrocycles by aminal bonds formation between aromatic dialdehydes and bis(1,3)-diamines based in 3,3'-diaminopivalic compounds,^[4] Figure 1b.

Macrocycles have been characterized by NMR and MS, showing that, despite the large number of possibilities within the corresponding dynamic equilibrium, a single [2+2] macrocycle is mainly formed, without requiring the presence of any template. These macrocycles keep a dynamic behaviour and a surprising water stability, opening the door to be applied in new stimuli-responsive materials for biomedical applications.

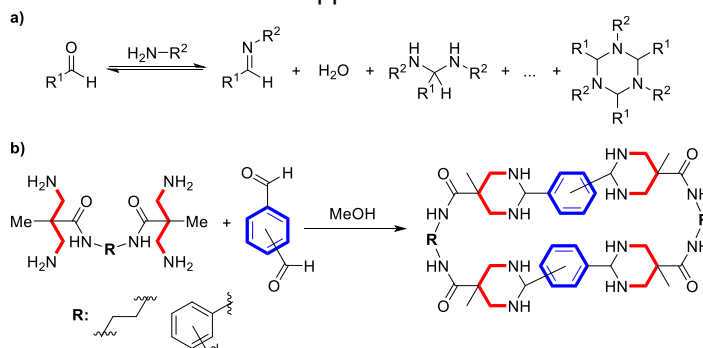


Figure 1: a) Equilibrium of species after reaction of primary amines and carbonyl compounds. b) Formation of [2+2] macrocycles by aminal bonds.

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