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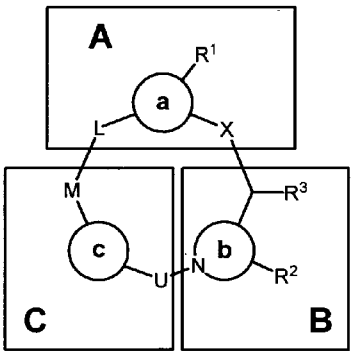
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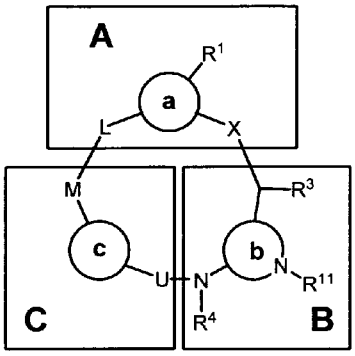
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(54) Title: CONFORMATIONALLY CONSTRAINED, FULLY SYNTHETIC MACROCYCLIC COMPOUNDS



Ia



Ib

(57) Abstract: Conformationally restricted, spatially defined 12-30 membered macrocyclic ring systems of formulae Ia and Ib are constituted by three distinct molecular parts: Template A, conformation Modulator B and Bridge C. These macrocycles Ia and Ib are readily manufactured by parallel synthesis or combinatorial chemistry in solution or on solid phase. They are designed to interact with a variety of specific biological target classes, examples being the agonistic or antagonistic activity on G-protein coupled receptors (GPCRs), ion channels and signal transduction pathways. In particular, these macrocycles act as antagonists of the motilin receptor, the FP receptor and the purinergic receptors $P2Y_1$, as modulators of the serotonin receptor of subtype $5\text{-}HT_{2B}$, as blockers of the voltage-gated potassium channel $K_v1.3$ and as inhibitors of the β-catenin-dependent "canonical" Wnt pathway. Thus they are showing great potential as medicaments for a variety of diseases.

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