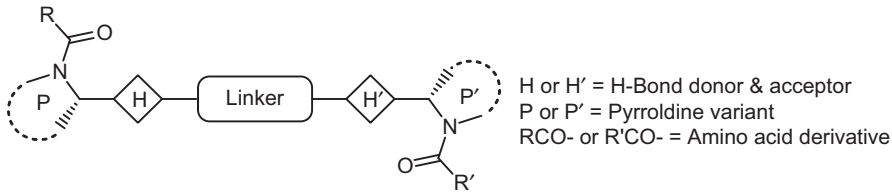

Figure 1.6 Topology of key pharmacophores needed to effect potent and pan-genotypic NS5A inhibition.

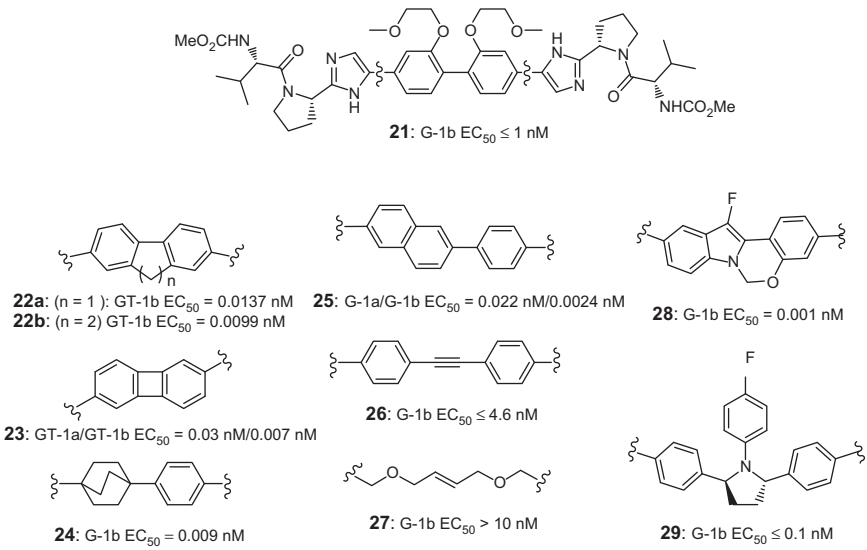

Figure 1.7 Bis-imidazole core analogs.

a methyl carbamate of an alkyl- or an arylglycine or *N*,*N*-dialkyl derivatives of an arylglycine for the amino acid fragment, and have primarily focused on modifications to the central core and the pyrrolidine regions.

The survey of central core elements has largely been directed towards uncovering alternate scaffolds that maintain the topological disposition of the key peripheral pharmacophoric moieties of **1** (Figure 1.7). Conceptually, the least disruptive strategy involves utilizing the biphenyl core and examining the effect of substitution at every position of the biphenyl moiety, including the installation of bridging elements, as exemplified by compounds **21**–**23**.[31–33] In a case where the bridging element is a single bond, as in **23**, the point of attachment of one of the imidazole moieties is changed to a *meta* position, presumably to reestablish a more linear disposition of the peripheral entities.[34]

Replacement of one of the phenyl groups with a bicylooctane group, as in compound **24** and central scaffold elongations (see **25**, **26** and **29** in Figure 1.7) resulted in compounds claimed to exhibit sub-nanomolar inhibitory potencies