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FL6, FL10, FL12 and FL13 displayed much lower, or even non-significant inhibition, indicating that the deletion of the methoxy in position 8 (FL6) or the introduction of a methyl ester (FL10), monomethylamide (FL13), dimethylamide (FL12) are detrimental to eIF4F-dependent translation inhibition. The primary amide FL14 retained a good activity, indicating a preference for a strong H-bond donor in this area of the pharmacophore. Acylation (FL19, FL20, FL 21) or inversion of configuration of the hydroxy in position 2 abolished the inhibitory activity. Introduction of a fluorine in position 3" also exerted a deleterious effect (compare FL31 with FL3 and FL18 with FL14). The hydroxy in position 2 could be replaced by a formylamino (FL23), an acetylamino (FL28) or a dimethylaminoacetylamino moiety with the unnatural configuration. This substituent effect was able to compensate for the deleterious introduction of a fluorine in position 3" (FL33, FL36). The replacement of the bromine in position 4' by a chlorine prevented the effect on translation.

Chemical formula of flavaglines used in this study