DISCOVERY AND DEVELOPMENT OF LAQUINIMOD

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With roquinimex as lead compound a selection of 3-quinolinecarboxamide derivatives were synthesized and evaluated for treatment of the autoimmune disease multiple sclerosis. Structure-activity relationships were established in animal studies and from these laquinimod was chosen as the candidate drug due to its good potency and advantaged toxicological profile compared to roquinimex. The medicinal chemistry route used phosgene and sodium hydride as reagents and the route suffered from tedious work up as well as unreliable quality. A safe and practical route starting from readily available 2-amino-6-chlorobenzoic acid is described. The route includes a novel and efficient reaction in which a methyl ester was converted to an amide in excellent yield and purity.