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Synthesis of some new tricyclic 4(3H)-quinazolinone derivatives

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Background and Aims: 4(3H)-Quinazolinone ring backbone have been incorporated in several important heterocyclic compounds. Some of those have been prepared for their antibacterial, antifungal, and anticancer properties. Quinazolinone based natural products demanding more structurally complex precursors have been constructed indirectly via oxidation of dehydroquinazolinone and aza-witting condensation. Most of these procedures have significant drawbacks such as long reaction times, harsh reaction condition, difficult workup, and use of environmentally toxic reagents or media. In contrast to the hitherto described methods, herein, in a simple and direct method, the preparation of the tricyclic quinazolinone target compounds was reported.
Methods: A number of quinazolinone derivatives were prepared by the condensation of 5-bromo- or 5-nitro-substituted anthranilic acids with chloro-acyl chlorides. Anthranilic acid derivatives were treated with either 3-chloro-propionyl chloride or 4-chloro-butyryl chloride to yield the corresponding N-acyl-anthranilic acids. The resultants were reacted with acetic anhydride to afford the benzoxazinone intermediates, which upon condensation with elected amines in either DMF (Dimethylformamid) or ethanol gave the corresponding tricyclic 4(3H)-quinazolinone derivatives.
Results: Melting points were determined in open capillaries using electrothermal 9200 melting point apparatus and are uncorrected. IR (KBr discs) was recorded with a WQF -510 FT-IR spectrophotometer. 1H-NMR spectra were recorded on Bruker 400 MHz spectrometers using TMS (tetramethylsilane) as an internal standard and either DMSO-d6 or CDCl3 as solvents. Mass spectra were recorded on Shimadzu Mass spectrometer.
Conclusions: Application of chloro acyl chloride instead of acyl chloride in quinazolinone synthetic procedures resulted in a second ring closure. This second ring closure was achieved when an intramolecular nucleophilic attack to the end methylen chloride group was possible. Formation of highly stable five- or six-membered ring may be counted as a good reason for this ring closure. Generally, reaction in DMF resulted in more clean reactions with higher yields compared with that of ethanol.

Keywords: Anthranilic acid; Benzoxazinone; Tricyclic quinazolinone