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Reaction of 2-alkoxy-4,5-diphenyl-1,3-oxazin-6-one with different alcohols and elucidation of the products

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Background and Aims: Diarylheterocycle scaffold and other central ring pharmacophore templates have been extensively studied as cyclooxygenase (COX) inhibitors. In pursuit of our research on design and synthesis of COX inhibitors, we focused on the synthesis of diarylheterocycles with central six-membered lactone 1,3-oxazin-6-one and 2,3-dihydro-6H-1,3-oxazin-6-one which is expected to inhibit the COX enzyme. Results: Sasaki and co-workers in J. Org. Chem. 1971, 36, 2451 claimed the synthesis of 2,2-dialkoxy-4,5-diphenyl-2,3-dihydro-6H-1,3-oxazin-6-one . In present work, reaction of 2-alkoxy-4,5-diphenyl-1,3-oxazin-6-one with methanol was studied and the product of the reaction was determined. X-Ray and other spectroscopic data showed their suggested structure is not correct. (Z)-Alkyl 3-(alkoxycarbonylamino)-2,3-diphenylacrylate was the real structure. Furthermore, the mechanistic formation of compound is discussed and a series of (Z)-Alkyl 3-(alkoxycarbonylamino)-2,3-diphenylacrylate were synthesized and characterized.. Conclusions: The present study reveals the novel carbamate-ester structure that was wrongly assigned in the past. Furthermore, a mechanistic formation and cleavage of 1,3-oxazin-6-one ring was discussed. The result of our finding was published in J. Heterocycl. Chem. 2012, 49, 358.

Keywords: Diarylheterocycle, Cyclooxygenase, 1,3-oxazin-6-one, X-ray