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Synthesis and structure elucidation of dihydro-metabolites of the synthetic cathinones pentedrone and methylone

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Abstract

Background: Synthetic cathinones are new psychoactive substances widely abused due to their psychostimulant effects. Among them, pentedrone and methylone are part of the most consumed in the USA and Europe [1]. The metabolism of synthetic cathinones is well described in literature. Methylone can undergo, for instance, *N*-demethylation, *O*-demethylation, *N*-oxidation, and *β*-keto reduction to afford the metabolites nor-methylone, dihydroxymethcathinone (DHMC), *N*-hydroxymethylone and dihydromethylone, respectively [2]. For pentedrone, metabolites resulting from *N*-demethylation and *β*-keto reduction have been described resulting in the formation of nor-pentedrone and dihydropentedrone [3]. Although synthetic cathinones are widely studied, information about the biological effects of their metabolites is scarce. Moreover, to perform studies with metabolites, their synthesis is required. **Objective:** The aims of this work were the synthesis of the dihydro metabolites of pentedrone and methylone by reduction of the parent compounds with sodium borohydride and structure elucidation by spectroscopic methods [4]. **Methods:** Sodium borohydride (3 e.q.) was added to a solution of pentedrone or methylone in ethanol. The reaction was stirred in an ice bath for 15 min and then at room temperature for 2 h. The solvent was evaporated, the residue diluted with water and pH was adjusted to 12–14. An extraction was performed with ethyl acetate and the combined organic layers were dried with anhydrous sodium sulphate, filtered, and evaporated to afford the reduced metabolites. The structure elucidation was performed by IR, GC-MS, ^{1}H and ^{13}C-NMR. **Results and Conclusions:** Dihydropentedrone and dihydromethylone were successfully synthetized with good yields (64-96%) being their structure elucidated by spectroscopic methods. In future work, the synthesis of other metabolites of pentedrone and methylone will be attempted for further toxicology studies.

Keywords: metabolites; metabolism, organic synthesis; structure elucidation; synthetic cathinones

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