A Convenient Synthesis of Aryl-Substituted *N*-Carbamoyl/*N*-Thiocarbamoyl Narcotine and Related Compounds

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The reaction of nornarcotine and 5-bromonornarcotine, synthesized from noscapine, with suitable aromatic isocyanates or isothiocyanates provides a general method for the synthesis of aryl-substituted *N*-carbamoyl or *N*-thiocarbamoylnarcotine and related compounds. Similarly, **15a** has been prepared *via* the reduction of the lactone ring moiety of noscapine. Also, an improved procedure, which utilizes narcotine *N*-oxide · HCl for generation of nornarcotine, is described.

Introduction. – Alkaloids and their analogs are important targets in chemical synthesis mainly because a large number of these compounds possess pronounced biological and pharmacological activities [1]. The basic isoquinoline-skeletal structure of various aporphine alkaloids, namely, (±)-thaliporphine, (±)-*N*-methylaurotetanine, and (±)-isoboldine have been found to be of significant biological and biogenetic interest [2]. Noscapine, for example, a phthalide-isoquinoline alkaloid derived from opium, known for its antitussive action [3][4] has recently been described as a prospective antineoplastic agent [5]. *Ye et al.* reported that noscapine has potent antitumor activity against solid lymphoid tumors induced in mice and, hence, exhibits outstanding therapeutic potential. In our earlier communication, we focussed on structural modulations of papaverine, a naturally occurring isoquinoline-based alkaloid isolated from *Papaver somniferum* [6], and reported the synthesis of urea/thiourea derivatives of papaverine, which were found to be more efficacious in terms of specificity and action in their antispasmodic effect. On similar lines of thought, we have also synthesized *N*-carbamoyl/*N*-thiocarbamoyl analogs of noscapine and other related compounds, which might prove as well to be more efficacious and less cytotoxic. Hence, new synthetic methodologies leading to novel antitumor agents are highly desired. In a recent publication from our laboratory [7], we have discussed the structure and the fragmentation patterns of narcotine and *N*-carbamoyl/*N*-thiocarbamoyl analogs of narcotine-related compounds. In the present paper, our interest circumscribes the synthetic procedures of *N*-demethylation and preparation of *N*-carbamoyl/*N*-thiocarbamoyl analogs of narcotine. It is the purpose of this communication to show how the target compound nornarcotine (**3a**) and other similar *N*-demethylated narcotine derivatives can be prepared in a few straightforward steps starting from noscapine (**1a**) and their further derivatization with aryl isocyanates and aryl isothiocyanates yielded the desired title compunds (*Scheme 1*).