NEW DIRECTIONS IN HETEROCYCLIC SYNTHESIS USING METALATED AMIDES

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The methodological exploration and synthetic application of ortho lithiated benzamides (M = Li) has been the central theme in our laboratories during the past few years (Accts. Chem. Research 1982, 15, 306). Recent results concerning the utility of these species for the regio-specific construction of polysubstituted aromatics will be described. Transmetalation \( (M = Li \rightarrow MgBr) \) allows the introduction of allyl (2a) and aliphatic aldehyde (2b) units and thereby access to phthalides and isocoumarins. Introduction of a \( ^{1}NH_{2} \) synthon into 1a leads to previously inaccessible anthranilamides (2c). Masking of more reactive metalation aromatic (3) and o-toluidine methyl (4) sites by silicon opens new avenues to diversely functionalized aromatics and, therefrom, phthalides with "peri" methyl groups (5) and contiguous substitution patterns (6). Directed ortho metalation of O-aryl carbamates has been achieved leading to species 7 which provide new routes to o-substituted phenols and, by a 1,3 O to C carbamoyl shift, to salicylamides.

The scope and limitation of these methodologies will be delineated, their utility for the synthesis of heterocycles will be highlighted, and up to date progress on their application to the construction of several classes of natural products will be presented.