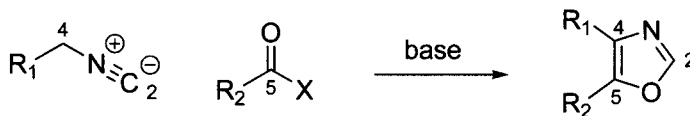
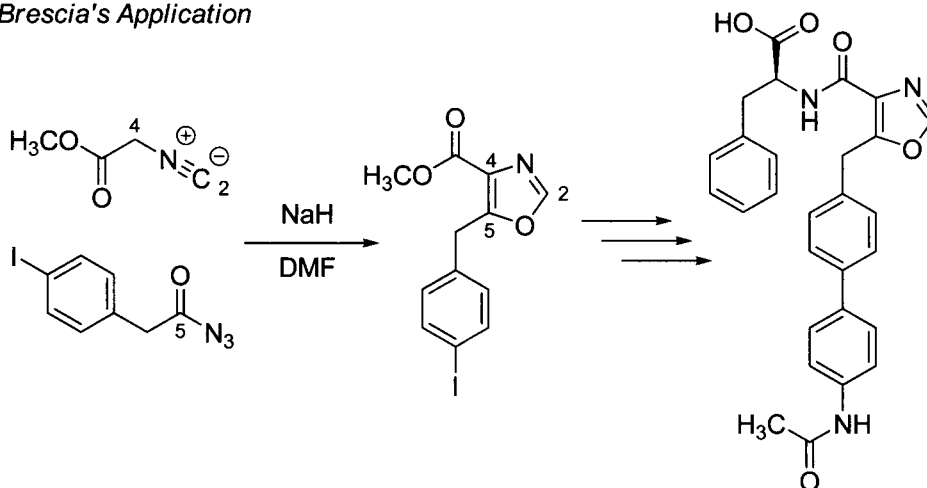


*The Schöllkopf Reaction**Brescia's Application**van Leusen oxazole synthesis*

*p*-Tolylsulfonylmethyl isocyanide (TosMIC) is an active methylene compound that reacts with aldehydes under basic conditions to yield 5-substituted oxazoles.<sup>30</sup> The reaction is quite similar in appearance to the Schöllkopf reaction. Here, the C5 substituent is introduced through the aldehyde, and the C4 substituent arises from the TosMIC reagent (C2 must necessarily remain unsubstituted). Aromatic and heteroaromatic aldehydes are tolerated in this synthesis. The isocyanide can be substituted with an alkyl, aryl, allyl, or benzyl group to prepare 4,5-disubstituted oxazoles.<sup>31</sup> The key intermediate in the synthesis of VX-497, a hepatitis C drug candidate, incorporates the van Leusen synthesis in 96% yield.<sup>32</sup>

*The van Leusen Oxazole Synthesis*