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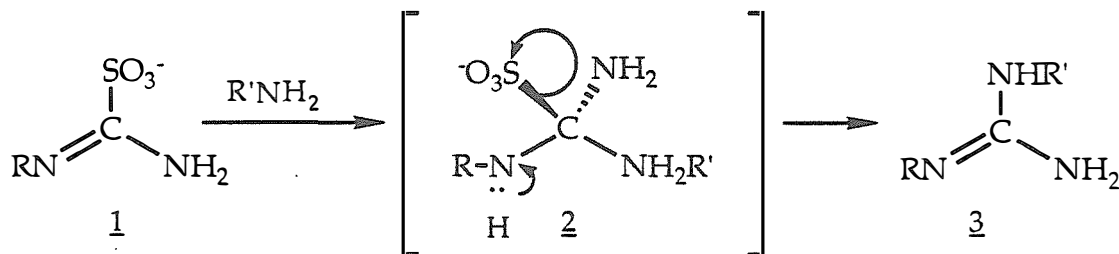
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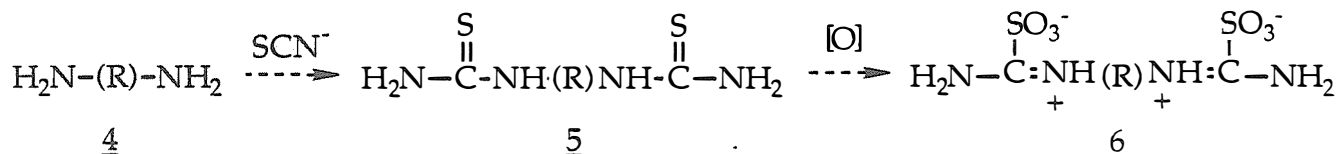
SYNTHESIS OF ALIPHATIC BIS(THIOUREAS)

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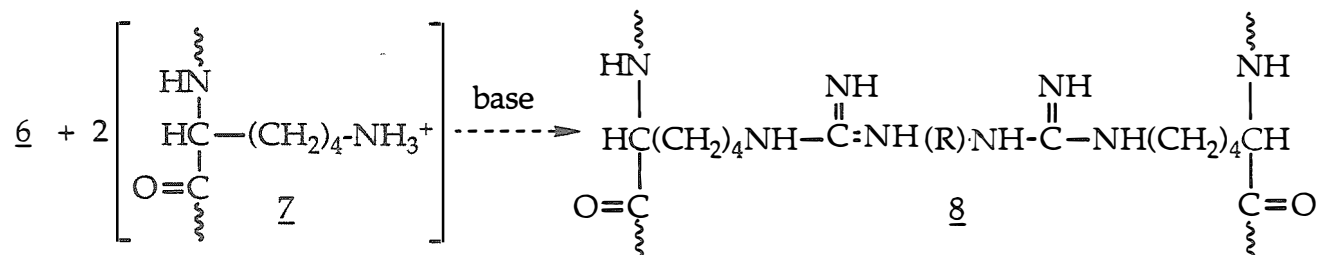
Oxidation of monofunctional thioureas to the corresponding thiourea-S,S,S-trioxides has been previously studied. Both Miller and Bischoff have shown that guanidino acids can be readily synthesized from thiourea oxides (1) and nucleophilic amino acids. The resulting reaction is hypothesized to take place via a tetrahedral intermediate (2), which then collapses to form the guanidino acid (3) and SO_3^{2-} .



The successful oxidation of the monofunctional thioureas to the corresponding thiourea-S,S,S-trioxides suggests that the oxidation of N,N'-bis(thioureas) (5) to the corresponding bis(thiourea) oxides (6) should also be feasible.



Consequently, these homobifunctional molecules may then be vulnerable to nucleophilic attack at two sites, resulting in a molecular "bridge" spanning the two nucleophiles. If the two attacking nucleophiles are side chains of amino acid residues--such as lysine or cysteine--within a protein (7), the protein(s) would then be cross-linked (8).



To this end we have attempted the synthesis of bifunctional thioureas by several methods.