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CARBON-NITROGEN BOND FORMATION *VIA* ACYL-NITROSO COMPOUNDS INTRAMOLECULAR ENE PROCESSES

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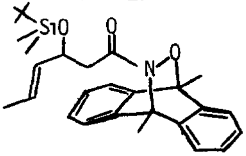
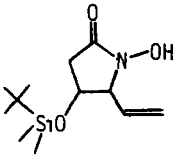
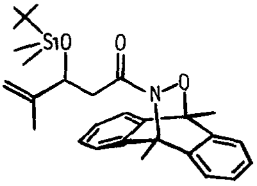
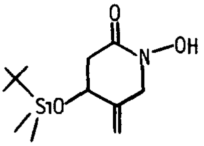
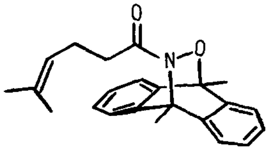
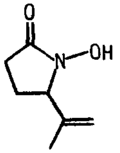
Acyl-nitroso compounds, having the general formula RCONO, are exceptionally reactive species which have never been directly observed or isolated due to their extreme reactivity.[1] The high reactivity of these compounds makes them attractive intermediates for a number of synthetic operations Because of our interest in C-N bond forming reactions of acyl-nitroso compounds for possible applications to alkaloid total synthesis,[2] we have been led to investigate intramolecular ene reactions of acyl-nitroso compounds Little is known about the ene reactivity of such compounds [1]

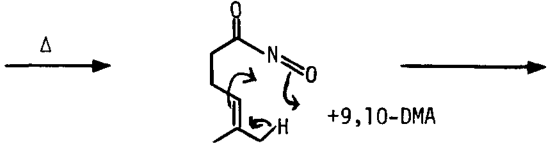
The Diels-Alder adduct between nitrosocarbonylmethane and 9,10-dimethylanthracene, prepared as previously described,[1,2] is readily converted to its lithium enolate upon treatment with 1 2 eq of lithium diisopropylamide in THF-HMPA at -78° C. The enolate was found to condense readily with α,β unsaturated aldehydes to afford exclusively products of 1,2 addition in moderate yields. Similarly, the enolate smoothly alkylated with 1-bromo-3-methyl-2-butene to afford ene substrate **3** in good yield. The adducts prepared by condensation with methacrolein and crotonaldehyde were readily converted, essentially quantitatively, to their corresponding *tert*-butyl dimethylsilyl ethers. Substrates prepared for study are summarized in Table I.[3]

TABLE I. ENE REACTION SUBSTRATES AND PRODUCTS

	Substrate	Yield^(a),b^		Ene Product	Yield^a^
1		65%	**4**		100%
2		50%	**5**		100%
3		74%	**6**		100%

(a) All yields reported are isolated yields, (b) for those substrates prepared *via* condensation-silyation, the reported yield is an overall yield for the two steps

Using substrates 1-3 in Table I, the intramolecular ene process was effected simply by heating benzene solutions at reflux for 3-5 hr, with tlc monitoring of reactant consumption. Thus, retro-Diels-Alder fragmentation serves to liberate the highly reactive acyl-nitroso moiety, which then undergoes the intramolecular ene reaction with facility.

3


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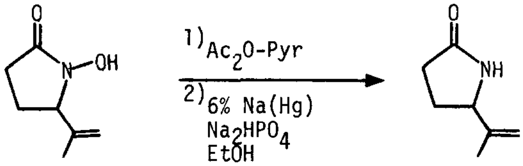
Isolation of products was accomplished by chromatography over Florisil, affording the ene products shown in Table I in the indicated yields. Dimethylanthracene is very easily separated from the rather polar cyclic hydroxamic acids and is thus easily recycled. Inspection of Table I reveals that the intramolecular ene reactions of both types I (1 and 3) and II (2) are facile processes.^{4}

The cyclic hydroxamic acids obtained by this process are O-acetylated in quantitative yield by exposure to acetic anhydride-pyridine at 23^0 for 10 min. Reductive cleavage^5 of the N-O bond in the acetates then affords the corresponding lactams in high yields. Using this procedure, for example, 6 was converted to lactam 7 in 98% isolated yield.

6


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The mild conditions of the processes described above make them particularly attractive for employment in natural products synthesis. Further studies to delineate the scope and generality of the above reactions, as well as extension to natural products total synthesis, are in progress in our laboratories and will be reported in due course.

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