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ALLYLIC AMIDATION. AN INVESTIGATION OF NITROSOCARBONYLMETHANE FOR DIRECT ALLYLIC FUNCTIONALIZATION OF OLEFINS

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Summary: Nitrosocarbonylmethane reacts with a variety of olefins <u>via</u> an ene pathway, yielding N-substituted hydroxamic acid products in a preparatively useful reaction. With unsymmetrical olefins, observed regiochemical preferences can be rationalized by a mechanism involving electrophilic addition of nitrogen to the olefin.

Recently, we reported the first examples of intramolecular ene reactions of acylnitroso compounds, and observed that these processes afforded remarkably high yields of product under unusually mild thermal conditions.[1] Several questions emerge from this work, among them the extent to which entropic assistance by intramolecularity affects the rates and regiospecificity of intramolecular cases. In order to probe such questions, as well as to establish the synthetic utility of a possible bimolecular process, we have examined the reaction of nitrosocarbonylmethane with several representative olefins.

The results, as shown in Table 1,reveal an interesting inherent regiospecificity for such ene processes, and illustrate some interesting reactivity constraints on the bimolecular ene process.

All ene reactions were carried out as shown in equation (1). Thus, nitrosocarbonylmethane was generated by thermal fragmentation of its Diels-Alder adduct with 9,10-dimethylanthracene (DMA).[2,3] Three methods were employed. Inexpensive olefins with appropriate boiling points (cyclohexene, 1-octene) were taken as solvent (Method A). Reactions were carried out in benzene for the other entries, using 1.1 to 1.2 eq. of olefin, either in refluxing benzene (Method B), with olefin concentration 0.2 M, or in sealed tubes (80° oil bath) with an olefin concentration of 1.0 M (Method C). Products were isolated by chromatography over Florisil, and characterized by NMR and IR spectroscopy.[4] The results are tabulated in Table 1 below.

In the case of the simpler olefins such as cyclohexene, 1-octene, and 2-methyl-1-phenylpropene, where only one possible ene reaction exists, preparatively useful yields of N-alkylhydroxamic acids are obtained. As expected, 1-octene yields a mixture of <u>cis</u> and <u>trans</u> products in a <u>ca.</u> 1:1 ratio. However, 1-phenylcyclohexene and 1-<u>p</u>-methoxyphenylcyclohexene also give excellent

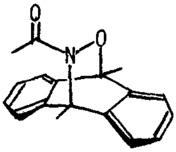
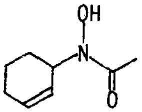
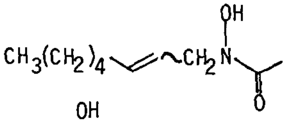
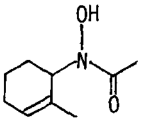
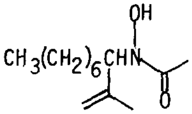
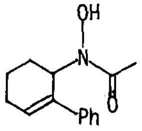
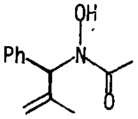
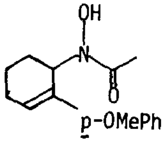
(1) Olefin +  $\xrightarrow{\Delta}$ DMA + Ene Product

TABLE I

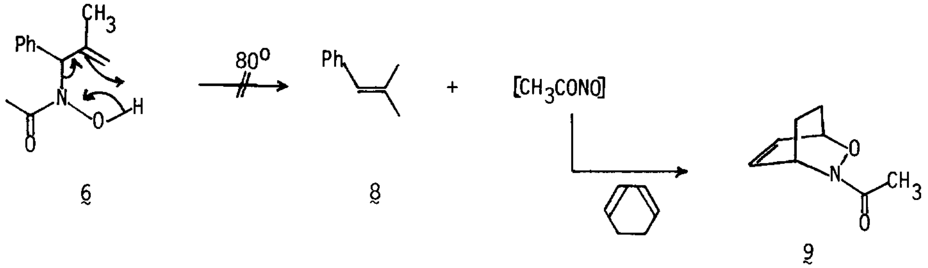
Olefin	Method		Product	(Yield)
cyclohexene	A	1		(85)
1-octene	A	2	 $CH_3(CH_2)_4CH=CHCH_2N(OH)COCH_3$	(83)
1-methycyclohexene	C	3		(92)
2-methyl-2-decene	C	4	 $CH_3(CH_2)_6CHN(OH)COCH_3$	(83)
1-phenylcyclohexene	C	5		(95)
2-methyl-1-phenylpropene	C	6		(88)
1-p-methoxyphenylcyclohexene	B	7		(89)
1,1-diphenyl-1-propene	C		NONE	(0)

yields of a single product even though two ene possibilities exist. The observed regiospecificity is in agreement with expectation for two step process, or a concerted but nonsynchronous process, in which C-N bond formation to electron deficient nitrogen runs ahead of abstraction of allylic hydrogen by nitroso oxygen.[5] Parallel results are also obtained with less structural bias, as in the cases of 2-methyl-2-decene and 1-methylcyclohexene.[6]

An interesting result was obtained upon attempted ene reaction with 1,1-diphenyl-1-propene, where isolable quantities of ene product were not obtained. Furthermore, no formation of the expected ene product could be detected by NMR examination of the crude reaction product. Apparently, the loss of olefin conjugation with two phenyl groups is sufficiently unfavorable to preclude ene reaction in this case. Deconjugation of one phenyl substituent can be accomplished, however, as evidenced by the facile conversion of 2-methyl-1-phenylpropene to the expected ene product in 88% isolated yields.

Qualitatively, the bimolecular processes reported herein proceed at considerably slower rates than the intramolecular examples reported previously.[1] Thus, reaction times of 24 hr. or longer are typical for the bimolecular experiments, while intramolecular examples require only *ca*. 3-4 hr. for consumption of starting material.

That the observed regiospecificity results from kinetic, rather than thermodynamic, control was indicated by resubjection of ene product 6 to 80° thermolysis in the presence of 1.0 M 1,3-cyclohexadiene, an efficient trap for nitrosocarbonylmethane. After 120 hr., ene product 6 was recovered unchanged; Diels-Alder adduct 9 and olefin 8 were not detected.[7] Note equation (2) below.

(2) 

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References

1. G.E. Keck and R.R. Webb, Tetrahedron Lett., 1185 (1979).

2. G.E. Keck, Tetrahedron Lett., 4367 (1978).

3. a) G.W. Kirby and J.C. Sweeny, J.C.S. Chem. Comm., 704 (1973).

   b) For a recent review of the chemistry of acylnitroso compounds including their efficient [4+2] cycloadditions with conjugated dienes note G.W. Kirby, Chem. Soc. Rev., **6**, 1 (1977).

4. a) All yields reported are isolated yields of chromatographically homogeneous material.

   b) Satisfactory NMR and IR spectral data were obtained for all of the ene products reported. Many of these were further characterized by acetylation, and also by reductive cleavage of the acetates by our previously described procedure,[1] affording the corresponding amides

5. S. Inagaki, H. Fugimoto, and K. Fukui, J. Am. Chem. Soc., **98**, 4693 (1976).

6. We were unable to detect the isomeric exocyclic methylene compound from 1-methylcyclohexene. The possibility that the hydroxamic acid product is sufficiently acidic to catalyze isomerization of this material to the more stable observed product (**3**) seems unlikely since **3** did not isomerize methylenecyclohexene to methylcyclohexene under the reaction conditions.

7. The adduct **9** between nitrosocarbonylmethane and 1,3-cyclohexadiene is stable under the conditions of attempted retroene fragmentation of **6**.

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