Supplementary Material Available: Full NMR data for compounds 5–10 and 15–18 (1 page). Ordering information is given on any current masthead page.

Masakatsu Shibasaki,* Mikiko Sodeoka, Yuji Ogawa

Sagami Chemical Research Center, Nishi-Ohnuma Sagamihara, Kanagawa 229, Japan Received June 18, 1984

Regioselectivity in the Intermolecular Diels-Alder Reaction of Acyl Nitroso Compounds (C-Nitrosocarbonyl Compounds) and Nitrosoformates (O-Nitrosocarbonyl Compounds)

Summary: A study of the regioselectivity of the intermolecular Diels-Alder reaction of (nitrosocarbonyl)benzene and methyl nitrosoformate with representative electronrich and electron-deficient 2-substituted-1,3-cyclohexadienes is described.

Sir: The orientation of the intermolecular Diels-Alder addition of aryl nitroso compounds with dienes has been investigated in detail and a rationalization of the observed regioselectivity has been presented on the basis of consideration of the relative stabilization of the two possible dipolar transition states.^{2,3} The predicted and observed product in the cycloaddition of nitrosobenzene with isoprene is shown in eq 1. By contrast, a study of re-



gioselectivity of the addition of nitrosobenzene with β myrcene, a 2-alkyl-substituted-1,3-butadiene, revealed a marked dependence on reaction temperature and solvent.⁴ Similarily, the observed, though not predicted, product of the addition of α -chloronitrosocyclohexane with isoprene, eq 2, possesses the reversed orientation of addition.⁵ In



the absence of a better rationalization this reversal in regioselectivity has been attributed to steric factors despite the fact that such effects must be relatively removed from the reaction centers.

Herein, we detail a study of the orientation of the intermolecular^{2,6} Diels-Alder reaction of acyl nitroso com-

Table I. Diels-Alder Reaction of Nitrosocarbonyl Compounds with 2-Substituted 1,3-Cyclohexadienes

-		, . .		
substrate	conditions ^a	product(s)	% yield ^b	
1	A, CH ₂ Cl ₂ , 25 °C, 1 h	2/3	45/16	
	0 °C, 1 h		31/24	
	A, DMF, 25 °C, 3 h		23/5	
	0 °C, 3 h		30/13	
	B, CH ₂ Cl ₂ , 40 °C, 5 h		11/4	
	B, C_6H_6 , 60 °C, 5 h		43/12	
1	C, CH ₂ Cl ₂ , 25 °C, 1 h	4/5	$72^{'}(50/16)^{c}$	
6	A, CH ₂ Cl ₂ , 25 °C, 1 h	7/8	47/16	
	A, DMF, 25 °C, 3 h	,	47/16	
6	C, DMF, 25 °C, 3 h	9/10	30/11	

^aA: Benzoyl hydroxamic acid^{12a} (2.2 equiv) was added dropwise to a solution of diene and (n-Bu)₄NIO₄^{12b} (2.31 equiv). B: A solution of diene and the (nitrosocarbonyl)benzene-9,10-dimethylanthracene adduct^{3,6} (1.1 equiv) was warmed at the described temperature. C: Methyl *N*-hydroxycarbamate^{12c} (2.2 equiv) was added dropwise to a solution of the diene and (n-Bu)₄NIO₄^{12b} (2.31 equiv). ^bAll products exhibited the expected ¹H NMR, IR, and MS characteristics consistent with the assigned structure and gave satisfactory C, H, N analysis or HRMS information. All yields (ratios) are based on purified, separated material isolated by chromatography (SiO₂). ^c The inseparable, purified adducts 4/5 (72% combined yield) were deprotected; 1.2 equiv of (n-Bu)₄NF, THF, 25 °C, 30 min; and the isomeric alcohols were separated (50% and 16% yield, respectively) and fully characterized.

pounds, (nitrosocarbonyl)benzene and methyl nitrosoformate, with weakly electron-rich and electron-deficient 2-substituted-1,3-cyclohexadienes.^{2,6} The observed results, detailed in eq 3 and 4 and Table I, are consistent with the prediction that nitrosocarbonyl compounds behave as well-defined electron-deficient 2π components in a normal (HOMO_{diene} controlled)⁷ Diels–Alder reaction with electron-rich 2-substituted dienes and additionally illustrate that they may serve as useful 2π components in regioselective Diels–Alder reactions with electron-deficient 2substituted-1,3-cyclohexadienes. The latter results are consistent with either a normal (HOMO_{diene} controlled) or inverse electron demand (LUMO_{diene} controlled)⁷ Diels– Alder reaction.

Thermal cycloaddition of (nitrosocarbonyl)benzene and methyl nitrosoformate with the weakly electron-rich 2-[[(*tert*-butyldimethylsilyl)oxy]methyl]-1,3-cyclohexadiene (1) afforded predominately the para⁸ adducts 2 and 4. The



structure of 2, the major regioisomer of the addition of (nitrosocarbonyl)benzene with 2-[[(tert-butyldimethyl-silyl)oxy]methyl]-1,3-cyclohexadiene (1), was confirmed by X-ray analysis.⁹ The identification of 4, the major

 ^{(1) (}a) Searle Scholar recipient, 1981-85. National Institutes of Health research career development award recipient, 1983-1988 (CA 00898).
 (b) Undergraduate research participant.

<sup>Undergraduate research participant.
(2) For reviews including Diels-Alder reactions of electrophilic C</sup>nitroso compounds, see: Kirby, G. W. Chem. Soc. Rev. 1977, 6, 1. Weinreb, S. M.; Staib, R. R. Tetrahedron 1982, 38, 3087.
(3) (a) Kresze, G.; Firl, J. Fort. Chem. Forsch. 1969, 11, 245. (b)

 ^{(3) (}a) Kresze, G.; Firl, J. Fort. Chem. Forsch. 1969, 11, 245. (b)
 Wichterle, D.; Kolinsky, M. Chem. Listy 1953, 47, 1787. Kresze, G.;
 Kosbahn, W. Tetrahedron 1971, 27, 1931. Kresze, G.; Saitner, H.; Kosbahn, W. Ibid. 1971, 27, 1941. Taylor, E. C.; McDaniel, K.; Skotnicki, J.
 S. J. Org. Chem. 1984, 49, 2500.

<sup>Nosolin, W. Ibid. 1971, 27, 1941. Taylor, E. C.; McDaniel, K.; Skotnicki, J.
S. J. Org. Chem. 1984, 49, 2500.
(4) Sasaki, T.; Eguchi, S.; Ishii, T.; Yamada, H. J. Org. Chem. 1970, 35, 4273. The addition of electron-withdrawing groups to the aryl nitroso compound accelerate the rate of cycloaddition and appear to reverse the observed regioselectivity, see: Givens, R. S.; Choo, D. J.; Merchant, Stitt, R. P.; Matuszewski, B. Tetrahedron Lett. 1982, 23, 1327 and ref 3a.
(5) Labaziewicz, H.; Riddell, F. G. J. Chem. Soc., Perkin Trans 1 1979, 3000</sup>

 ⁽a) Labaziewicz, H., Riddell, F. G. J. Chem. Soc., Fermi Frank, N. J.; Playtis,
 A. J.; Skoag, F.; Schmitz, R. Y. J. Am. Chem. Soc. 1971, 93, 3056. Leonard,
 N. J.; Playtis, A. J. J. Chem. Soc., Chem. Commun. 1972, 133.

⁽⁶⁾ For recent intramolecular acyl nitroso Diels-Alder reactions, see: Keck, G. E.; Nickell, D. G. J. Am. Chem. Soc. 1980, 102, 3632. Keck, G. E.; Fleming, S. A. Tetrahedron Lett. 1978, 4763. Keck, G. E. Tetrahedron Lett. 1978, 4767.

⁽⁷⁾ Houk, K. N. J. Am. Chem. Soc. 1973, 95, 4092. Burnier, J. S.; Jorgensen, W. L. J. Org. Chem. 1983, 48, 3923.

⁽⁸⁾ Alternatively, the major para adducts may be described as the "proximal" adducts and minor, meta adducts may be described as "distal" adducts. "Proximal" and "distal" refer to the relative orientation (distance) of the dienophile center of highest priority (nitroso oxygen) with the diene center of highest priority (substituted center of the cyclohexadiene). We thank a referee for suggesting this nomenclature.

⁽⁹⁾ X-ray structure analysis was carried out on the free alcohol generated from 2 (1.2 equiv of $(n-Bu)_4$ NF, THF, 25 °C, 15 min, 74%) and was performed by Crystalytics Company, Lincoln, NE. Full details of the X-ray structure determination are provided in the supplementary material section.

adduct of the reaction of methyl nitrosoformate with 1, was drawn by analogy with the results obtained with (nitrosocarbonyl)benzene. The reaction solvent, reaction temperature, and source of the nitrosocarbonyl compound, while influencing the overall yield of the reaction, have little effect on the observed ratio of regioadducts, indicating little polar character in the transition state of the cycloaddition.

Parallel studies with an electron-deficient 2-substituted-1,3-cyclohexadiene, methyl 1,3-cyclohexadiene 2carboxylate (6), eq 4 and Table I, provided related findings.



The para⁸ adducts 7 and 9 were formed predominately and the ratio of products, 7:8 and 9:10, showed no marked dependence on the reaction conditions. The observed regioselectivity is consistent with either a normal (HOMO_{diene} controlled) or inverse electron demand (LUMO_{diene} controlled)⁷ Diels–Alder reaction and appears to contradict the predictions that can be drawn intuitively from similar studies with methyl 1,3-cyclohexadiene-1carboxylate.¹⁰ The structure of the minor adducts 3 and 8 were confirmed by the chemical correlation as detailed



(a) 1.2 equiv of (n-Bu)₄NF, THF, 25 °C, 15 min, 74%.
(b) MnO₂ (10 wt equiv), CH₂Cl₂, 25 °C, 1 h, 70%. (c)
1,3-Butadiene, mesitylene, 140 °C, 48 h, 70%. (d)
Pyridinium dichromate (2 equiv), DMF, 25 °C, 9 h;
CH₂N₂, ether, 0 °C, 51%. (e) 1,3-Butadiene, mesitylene, 140 °C, 48 h, 70%.

in eq 5 providing $11.^{11}$ An identical correlation of the major adducts 2 and 7 confirmed the remaining structure 7 and provided $12,^{11}$ eq 6. The assignment of the adducts 9/10 was made by analogy to 7/8.

The ease with which the acyl nitroso dienophiles may be generated and their ability to participate in intermolecular Diels-Alder reactions with predictable, regiose-

this and related work will be the subject of future work. (12) (a) Hauser, C. R.; Renfrow, W. B., Jr. "Organic Syntheses"; Wiley: New York, 1948; Collect. Vol. 2, p 67. (b) Available from Sigma Chemical Company. (c) Boyland, E.; Nery, R. Analyst 1964, 89, 520.

(6) 2
$$\frac{18\%}{a-d}$$
 $(0-N-COPh + 7)$

lective orientation suggest that their use should complement the use of aryl and α -chloro nitroso compounds. Application of such studies are in progress.

Acknowledgment. This work was assisted financially by the Searle Scholars Program. We thank Professor G. E. Keck for helpful suggestions and comments.

Registry No. 1, 92011-93-3; 2, 92011-94-4; 3, 92011-95-5; 4, 92011-96-6; 5, 92011-97-7; 6, 40002-24-2; 7, 92011-98-8; 8, 92011-99-9; 9, 92012-00-5; 10, 92012-01-6; 11, 92012-06-1; 12, 92012-05-0; PhC(O)NO, 58696-10-9; ONC(O)OMe, 92012-02-7; *N*-benzoyl 3-aza-6-(hydroxymethyl)-2-oxabicyclo[2.2.2]oct-5-ene, 92012-03-8; *N*-benzoyl 3-aza-2-oxabicyclo[2.2.2]oct-5-ene-6-carboxaldehyde, 92012-04-9.

Supplementary Material Available: Complete experimental and spectral details; full details of the X-ray structure determination of the free alcohol generated from 2 (22 pages). Ordering information is given on any current masthead page.

Dale L. Boger,^{*1a} Mona Patel^{1b}

Department of Medicinal Chemistry The University of Kansas Lawrence, Kansas 66045 Received June 15, 1984

Furfural Dimethylhydrazone: A Versatile Diene for Arene Cycloaromatization

Summary: Dienophiles such as maleic anhydride react with furfural dimethylhydrazone (CHCl₃) at room temperature to give essentially quantitative yields of the corresponding trisubstituted benzenes; in contrast, reaction with 1,4-naphthoquinone results in retention of the furan oxygen in the initial 1:1 cycloadduct and, after acid hydrolysis, a good yield of 1-formyl-4-hydroxy-9,10-anthraquinone.

Sir: 1,4-Cycloadditions to furans with alkenic and alkynic dienophiles have resulted in a variety of 7-oxabicyclo-[2.2.1]heptanes, -heptenes, and benzene derivatives.¹ These reactions, together with those of thiophenes^{2a} and N-aminopyrrole^{2b} derivatives, have found applications in the synthesis of substituted benzenes and for the annulation of benzene rings. 2-Vinylfurans and alkenic dienophiles, however, result in benzo[b]furan derivatives.³

We have found that furfural dimethylhydrazone⁴ (1, R = H) also behaves as a reactive diene, 1,4-addition occuring to the furanoid system rather than to the azadiene⁵ moiety

(4) Todd, D. J. Am. Chem. Soc. 1949, 71, 1353.

⁽¹⁰⁾ Baldwin, J. E.; Bailey, P. D.; Gallacher, G.; Singleton, K. A.; Wallace, P. M. J. Chem. Soc., Chem. Commun. 1983, 1049. For related studies, see: Belleau, B.; Au-Young, Y.-K. J. Am. Chem. Soc. 1963, 85, 64 and ref 3a.

⁽¹¹⁾ The tentative stereochemical assignment of 12, and by analogy 11, is based on the non-correlation of material derived from 12 with a structure of known relative configuration. Chemical correlation would have proven the cis- $(1\beta,4\beta,9\beta,10\beta)$ - Δ^6 -octalin stereochemistry. Details of this and related work will be the subject of future work.

⁽¹⁾ For recent reviews, see: Dean, F. M. Adv. Heterocycl. Chem. 1981, 30, 168; 1982, 31, 237. Wong, H. N. C.; Ng, T.-K.; Wong, T.-Y. Heterocycles 1984, 22, 875. Wong, H. N. C.; Ng, T.-K.; Wong, T.-Y.; Xing, Y. D. Heterocycles 1983. 20. 1815.

<sup>D. Heterocycles 1983, 20, 1815.
(2) (a) Helder, R.; Wynberg, H. Tetrahedron Lett. 1972, 605. However, see: Reinhoudt, D. N.; Volger, H. C.; Kouwenhover, C. G.; Wynberg, H.; Helder, R. Tetrahedron Lett. 1972, 5269. (b) Schultz, A. G.; Shen, M. Tetrahedron Lett. 1979, 2969 and references therein. Schultz, A. G.; Shen, M.; Ravichandran, R. Tetrahedron Lett. 1981, 22, 1767. Schultz, A. G.; Shen, M. Tetrahedron Lett. 1981, 22, 3347.</sup>

G. Tetrahedron Lett. 1981, 22, 3347.
 (3) Noland, W. E.; Lee, C. K.; Bae, S. K.; Chung, B. Y.; Hahn, C. S.;
 Kim, K. J. J. Org. Chem. 1983, 48, 2488. Davidson, W. J.; Elix, J. A. Aust.
 J. Chem. 1970, 23, 2119; 1973, 26, 1059.