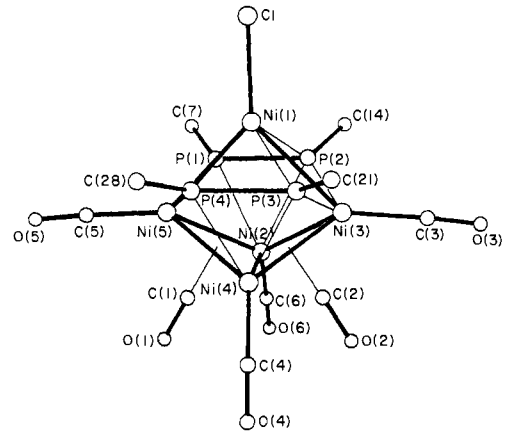

Figure 1. Computer-generated diagram of **1** showing numbering scheme. The $SiMe_3$ groups are not shown for clarity. Some important bond distances (Å) and angles (deg): P(1)-P(2) = 2.085 (4), P(3)-P(4) = 2.098 (4), Ni(2)-Ni(4) = 2.528 (2); Ni(3)-Ni(2), -Ni(4) = 2.556 (2), 2.560 (2); Ni(5)-Ni(2), -Ni(4) = 2.583 (2), 2.559 (2); Ni(1)-Ni(3), -Ni(5) = 2.706 (2), 2.682 (2); C(1)-Ni(5), -Ni(2), -Ni(4) = 1.955 (13), 2.088 (9), 2.050 (12); similarly for C(2); Ni-C distances for terminal carbonyls average 1.795 (3); Ni-Cl = 2.229 (7); Ni(2)-Ni(5)-Ni(4) = 58.9 (1); P(2)-Ni(1)-P(3) = 100.7 (1); P(2)-Ni(1)-P(4) = 125.4 (1); Ni(1)-P(3)-Ni(3) = 72.3 (1); Ni(3)-P(3)-Ni(4) = 68.3 (1); P(3)-Ni(4)-P(4) = 52.4 (1).

P-Ni(2), and P-Ni(3) distances are almost 0.2 Å longer, averaging ca. 2.37 Å. The P(1)-P(2) and P(3)-P(4) distances are 2.085 (4) and 2.098 (4) Å. These lengths are quite close to the average distances for a P-P double bond, 2.02-2.06 Å, and very much shorter than the 2.2-2.5 Å average for a P-P single bond. The P···P distances between each of the diphosphene moieties are long, P(2)-P(3) = 3.672 and P(1)-P(4) = 3.680 Å precluding any P-P bonding between diphosphene units.

We believe the structure of **1** is unique for several reasons: (i) it is the first example of a metal cluster that involves essentially unsupported heavier main-group element double bonds as an integral part of the framework;[9] (ii) the diphosphene ligands are also interesting since they are in the cis configuration, and with one exception[9] all published structural data have dealt with trans diphosphenes only; (iii) so far as we are aware there are no other transition-metal clusters involving nine-atom frameworks in a geometry resembling **1**.

Several other aspects of the structure of **1** are also worthy of comment. Each of the diphosphene ligands behaves as a σ-donor toward Ni(3) and Ni(5), which results in fairly short Ni-P distances. The Ni-P distances involving Ni(1), Ni(2), and Ni(4) are among the longest reported.[8,10] These bond lengths suggest that the diphosphenes are behaving as very weak π-bonding ligands toward these three nickel atoms. Another feature of interest of **1** is that it has an odd number of electrons. Ni(1) is in the formal oxidation state of 1+ while the other nickel atoms are neutral.

The synthetic route to **1** again demonstrates the powerful effect of steric factors on the product obtained. Dahl and Lower have reported that a very similar reaction between PCl_2Ph and $[Ni_6(CO)_{12}]^{2-}$ gave the species $Ni_8(CO)_8(\mu_4\text{-}PPh)_6$ involving a cubic arrangement of nickel atoms with each face capped by a μ_4-phenylphosphido group.[11] Substituting the phenyl group with $CH(SiMe_3)_2$ results in a drastic change in the nature of the product. Studies using a variety of bulky substituents at the phosphorus atom are now under way in this laboratory.

Acknowledgment. We are grateful to the Research Corporation and NSF (CHE-8116355) for financial support.

Registry No. 1, 88703-05-3; $Na_2[Ni_6(CO)_{12}]$, 88669-39-0; $P[CH(SiMe_3)_2]Cl_2$, 76505-20-9.

Supplementary Material Available: Listing of atom coordinates, temperature factors, and bond distances and angles and structure factor tables for **1** (39 pages). Ordering information is given on any current masthead page.

(8) McAuliffe, C. A. "Phosphine, Arsine and Stibine Complexes of the Transition Elements"; Elsevier: Amsterdam, 1973; p 129-144.

(9) Vahrenkamp, H.; Wolters, D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 154. This paper describes the structure and preparation of the compound $[[Fe(CO)_3]_2(P\text{-}t\text{-}Bu)_2]$, which has two Fe and two P atoms in a tetrahedral array. The complex has the cis diphosphene moiety *t*-BuP=P-*t*-Bu bonded to $(CO)_3Fe\text{-}Fe(CO)_3$ with mutually perpindicular PP and FeFe axes. In this sense the PP double bond is "supported" by iron carbonyl although the PP distance is 2.059 (3) Å, consistent with a PP double bond formulation.

(10) Hope, H.; Olmstead, M. M.; Power, P. P.; Viggiano, M. *Inorg. Chem.*, in press. The complex $[Ni(CN)_2[P(CH_2OH)Ph_2]_3]$ has an Ni-P bond length of 2.400 (3) Å.

(11) Lower, L. D.; Dahl, L. F. *J. Am. Chem. Soc.* **1976**, *98*, 5046-5047.

Intramolecular Alkoxypalladation/Carbonylation of Alkenes

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Furan and pyran rings occur frequently in current synthesis targets such as the ionophore antibiotics,[1] and new synthesis methods are increasingly important. Hydroxyalkenes of appropriate length can be activated by Pd(II) toward addition of the hydroxy group to the double bond. The product would be an alkylpalladium(II) complex which might be usefully cleaved by CO or other agents.[2] In this paper, we consider the selectivity parameters in general aliphatic cases, including a short stereoselective synthesis of a glandular secretion from the civet cat, compound **1a**.[7,8]

Our simplest test case is compound **1a** from the civet cat. Initial studies were carried out with the racemic alcohol **2**.[9] The Pd(II)-catalyzed cyclizations are operationally simple. A mixture

(1) For example, the ionophore antibiotics: ApSimon, J. "The Total Synthesis of Natural Products"; Wiley-Interscience: New York, 1976; Vol. 4, p 263.

(2) The intermolecular addition of nucleophiles to alkenepalladium(II) complexes is very general,[3] but catalytic addition/CO trapping is usually not efficient. (a) For general examples of 1-alkenes in catalytic alkoxycarbonylation (50-60% yields) and studies with disubstituted alkenes (low yields), see: James, D. E.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 1810. (b) For examples of stoichiometric addition of secondary amines to 1-alkenes followed by CO insertion and full characterization of the intermediate acylpalladium(II) complex, see: Hegedus, L. S.; Siirala-Hansen, K. *Ibid.* **1974**, *97*, 1184. (c) For examples of stoichiometric addition of carbon nucleophiles followed by CO trapping ("carboacylation"), see: Hegedus, L. S.; Darlington, W. H. *Ibid.* **1980**, *102*, 4980. The intramolecular version is also well-known,[4-6] but trapping with CO is successful only in special cases.[5,6]

(3) For a general discussion, see: (a) Collman, J. P.; Hegedus, L. S., "Principles and Applications of Organotransition Metal Chemistry"; University Science Books: Mill Valley, CA, 1980; pp 585-590. (b) Davies, S. G. "Organotransition Metal Chemistry: Applications to Organic Synthesis"; Pergamon Press: Oxford, 1982; pp 157-162. (c) Tsuji, J. "Organic Synthesis with Palladium Compounds"; Springer-Verlag: Berlin, 1980; pp 5-35. Many examples with oxygen nucleophiles are known. For discussion and leading references, see: Trost, B. M. *Tetrahedron* **1977**, *33*, 2615-2649.

(4) Hegedus, L. S.; McKearing, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 2444 and references therein.

(5) For an example involving amines, amides, and carboxylate, with CO trapping, see: Hegedus, L. S.; Allen, G. F.; Olsen, D. J. *J. Am. Chem Soc.* **1980**, *102*, 3583.

(6) (a) Semmelhack, M. F.; Zask, A. *J. Am. Chem. Soc.* **1983**, *105*, 2034. (b) Semmelhack, M. F.; Bozell, J. J.; Sato, T.; Wulff, W.; Spiess, E.; Zask, A. *Ibid.* **1982**, *104*, 5850.

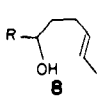
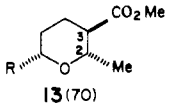
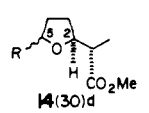
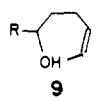
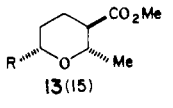
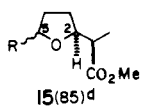
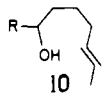
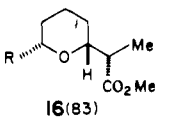
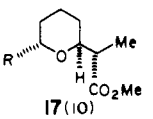
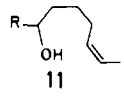
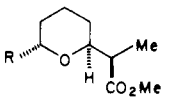
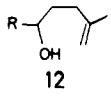
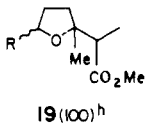
(7) For isolation, structure determination, and the first synthesis, see: Mauer, B.; Grieder, A.; Thommen, W. *Helv. Chim. Acta* **1979**, *62*, 44.

(8) For previous syntheses of the racemic product, see: (a) Kim, Y.; Mundy, B. P. *J. Org. Chem.* **1982**, *47*, 3556. (b) Ley, S. V.; Lygo, B.; Molines, H.; Morton, J. K. *J. Chem. Soc., Chem. Commun.* **1982**, 1251. For a synthesis of the natural optical isomer, see: (c) Seebach, D.; Pohmakotr, M. *Helv. Chim. Acta* **1979**, *62*, 843. **Note Added in Proof**: A synthesis of racemic **1a** was reported after this manuscript was submitted: Bates, H. A.; Deng, P.-N. *J. Org. Chem.* **1983**, *48*, 4479.

(9) For typical procedures, structure elucidation, and complete characterization data, see the supplementary material.

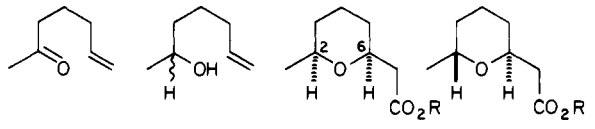
0002-7863/84/1506-1496$01.50/0

Table I. Cyclizations of Hydroxyalkenes with Pd(II) and CO

entry	reactant alcohol[a]	yield, %[b]	product(s) (% of total)[c]
1	 **8**	84%	 **13**(70)  **14**(30)[d]
2	 **9**	65%	 **13**(15)  **15**(85)[d]
3	 **10**	88%[e,f]	 **16**(83)  **17**(10)
4	 **11**	84%	 **18**(97)[g]
5	 **12**	87%	 **19**(100)[h]

[a] R = isobutyl. [b] The yield is based on the weight of a distilled sample, all carbonylated isomers together. [c] The ratios are based on GLPC peak area ratios, assuming equal molar response in the flame ionization detector. [d] An inseparable mixture of two diastereoisomers was obtained (see text). [e] Starting material (10) was recovered (6%). [f] A component amounting to 4% of the total peak area remains unidentified. [g] Two isomers of the main product were detected, in trace amounts. [h] The product was a 1:1 mixture of diastereoisomers, inseparable by TLC and GLPC.

of **2**, cupric chloride (3.0 mol equiv), and palladium chloride (0.1 mol equiv) in methyl alcohol under ca. 1.1 atm of CO was stirred at 25 °C for 17 h. After removal of the methyl alcohol, the residue was triturated with pentane to give the crude organic products. Short-path distillation provided a colorless liquid (74% yield) consisting of two components in the ratio of ca. 20:1.[9] The major component was isolated by column chromatography (50% yield) and identified as **4b**.[9] The minor isomer was also obtained pure



3 **2** (racemic) **7** (2S) **1** (2S,6S) **a**: R = H **b**: R = Me **5**: R = Me **6**: R = H **4** (racemic) **a**: R = H **b**: R = Me

(5% yield) and was identified as the trans isomer, **5**.[9] Both esters were hydrolyzed and the spectral data on the acids (**4a**, **6**) were correlated with published data.[7,8] Reduction of **3** with a yeast preparation[10] produced optically pure alcohol **7**.[9] Cyclization as before gave the cis ester as the optically pure isomer **1b**, essentially identical, including optical rotation,[9] with the ester derived from natural civet cat acid.

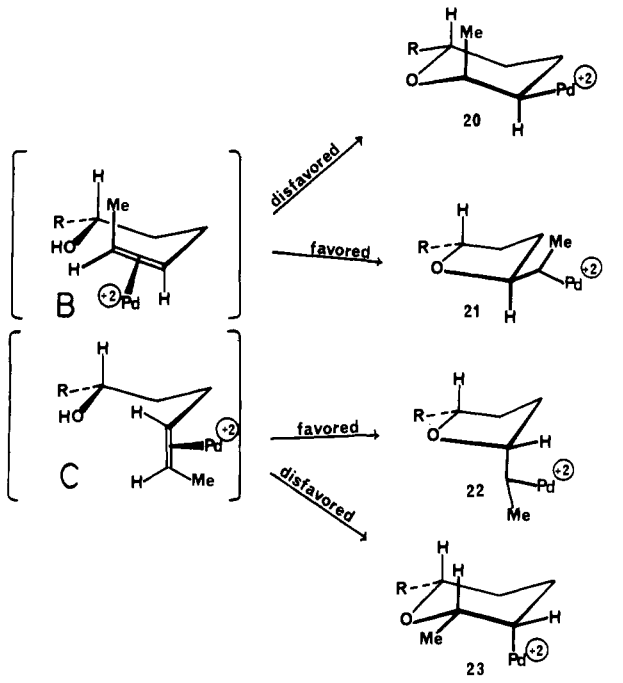
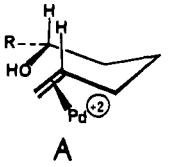


Figure 1. Cyclization conformations.

Table I presents the results obtained with five other hydroxyalkenes,[9] **8**–**12** which are chosen to test for ring-size preferences (5 vs. 6, 6 vs. 7) and the effect of the alkene geometry on the selectivity. In the formation of 5- vs. 6-membered rings (entries 1 and 2), the alkene geometry plays a dominant role. The *E* alkene, **8**, leads to predominantly the 6-membered ring (**13**), as a single diastereoisomer.[11] The furan is formed as a mixture of two diastereoisomers, which we assign as epimeric at C-5 (in **14**).[11] The *Z* alkene produces mainly furan **15**, again as an inseparable mixture of diastereoisomers,[11] accompanied by pyran **13**. No trace of 7-membered ring products appear from **10** and **11** (entries **3** and **4**), and a single diastereoisomer is strongly preferred in each case (**16** and **18**).[11] Consistent with the preference for nucleophile addition at the more substituted end of the Pd-activated alkenes in intermolecular cases,[2a] the 1,1-disubstituted alkene **12** gives furan products exclusively, in high yield (entry 5). A 1:1 mixture of diastereoisomers is obtained, not unexpected using pictures similar to those in Figure 1.

The formation of **16** and **18** follow in a simple way from a reactant conformation such as A, using a chain cyclohexane



template.[12] Similar pictures from **8** and **9** give some understanding of the ring-size preferences. For example, from **9**, two reactant conformations might be written (B, C). From each of them, ring closure to give a pyran forces at least one substituent (Me or Pd) axial (**20**, **23**) while the 2,5-disubstituted furan (**21**, **22**) has minimum nonbonded interactions.

Acknowledgment. We acknowledge financial support from the National Institutes of Health through a research grant to M.F.S. (GM-31352) and a Graduate Traineeship to C.B. We are also grateful for important contributions to structure analysis by NMR from Mary Baum at Princeton and the service of the Yale Re-

(10) Asymmetric reduction of ketones and aldehydes using fermenting yeast is well-known. For a discussion and examples, see: (a) MacLeod, R.; Prosser, H.; Fikentscher, L.; Lanyi, J.; Mosher, H. *Biochemistry* **1964**, *3*, 838. (b) Le Orian, C.; Greene, A. E. *J. Am. Chem. Soc.* **1982**, *104*, 5473–5483. For dialkyl ketones, low chemical yields and fair optical yield have been reported.

(11) This information has been obtained; details are given in supplementary material.

(12) This same type of selectivity has been observed in the cyclizations of phosphate onto alkenes promoted by iodine. See: Bartlett, P. A.; Jernstedt, K. K. *J. Am. Chem. Soc.* **1977**, *99*, 4829.

gional NMR Facility. In addition, we wish to thank the Johnson-Matthey Corp. for a generous gift of palladium chloride.

Supplementary Material Available: Representative experimental procedures, characterization data, and full spectral and analytical data for compounds **8-19** (8 pages). Ordering information on any current masthead page.

Synthesis and Rearrangement of Methanesulfonate Esters of *N*-Hydroxyacetanilides. A Model for a Penultimate Carcinogen

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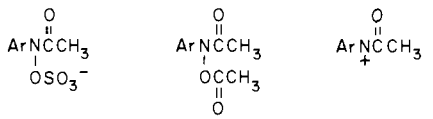
Received November 23, 1983

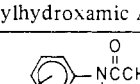
Extensive studies[2] indicate that the extreme carcinogenicity of certain arylamines is due to metabolic conversions that result in the formation of sulfate[2] or acetate[3] esters of hydroxamic acids, such as **1** and **2**, respectively, which then ionize to form the



1 **2** **3**

acylarylnitrenium ion **3** as the ultimate electrophilic carcinogen.[2,4] Unfortunately, relatively little evidence exists for the heterolytic cleavage of the sulfonate esters of *N*-arylhydroxamic acids, primarily because previous attempts to prepare this class of compounds have led mostly to materials with rearranged structures.[5,6] We now wish to report on the synthesis, isolation, and characterization of a series of methanesulfonate esters of monosubstituted *N*-arylhydroxamic acids. We have demonstrated, through a classical Hammett $\sigma^+\rho$ study that cleavage of the N-O bond of these esters occurs in a heterolytic manner with $\rho = -9.24$.

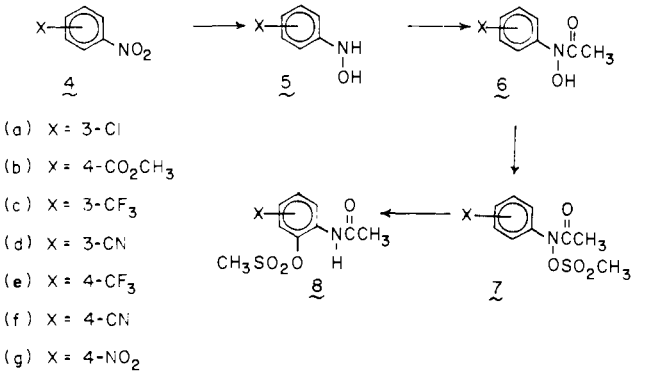
Table I. Kinetics of Rearrangement of Monosubstituted *N*-Arylhydroxamic Acid *O*-Methanesulfonates in Chloroform-d_1



X	$k_{25\,°C}$, s^{-1} [a]	k_{rel}	σ^+
7a, X = 3-Cl	1.31×10^{-4}	2690	0.399
7b, X = 4-CO_2CH_3	3.33×10^{-5}	684	0.489
7c, X = 3-CF_3	1.84×10^{-5}	378	0.520
7d, X = 3-CN	1.95×10^{-6}	40	0.562
7e, X = 4-CF_3	1.41×10^{-6}	29	0.612
7f, X = 4-CN	4.05×10^{-7}	8	0.659
7g, X = 4-NO_2	4.87×10^{-8}	1	0.790

[a] Rates extrapolated from higher temperatures. Kinetics were measured at 40-110 °C.

In a general procedure, the appropriate substituted nitrobenzene derivatives, **4**, were reduced to the corresponding *N*-arylhydroxylamines, **5**, with zinc dust, ammonium chloride, and aqueous ethanol.[7,8] Treatment of **5** with acetyl chloride in ether with an aqueous sodium bicarbonate second phase at 0 °C gave **6a-f**.[8-10] For the preparation of **6g**,[8] it was necessary to use a



two-step procedure, which involved bisacetylation of **5g** followed by removal of the *O*-acetyl group through transesterification with methanol in 41% overall yield. The hydroxamic acids **6a-g** were converted into the corresponding sulfonates, **7a-g**,[8] by reaction with methanesulfonyl chloride and triethylamine in methylene chloride below 0 °C (**7a-d**) or below 25 °C (**7e-g**).

The thermal rearrangements of **7a-g** were measured in chloroform-d_1 and were followed by ^1H NMR by monitoring the disappearance of the mesylate methyl group of **7** and the appearance of a new mesylate methyl group for the *internal return product*.[11] Table I lists the rates of rearrangement that were observed. All rate studies were followed for at least three half-lives and showed excellent pseudo-first-order kinetics. Application of the Hammett equation showed that the rate data correlated excellently with σ^+ and gave $\rho = -9.24$ ($r = 0.984$). This exceptionally large ρ leaves little doubt that the N-O bonds of sulfonate esters of *N*-arylhydroxamic acids undergo facile heterolytic cleavage, even in relatively nonpolar solvent environments such as chloroform. In all cases the product was that of internal return to the ortho position of the aryl moiety of the acetanilide.[12]

(1) Deceased September 2, 1983.

(2) Kriek, E.; Westra, J. G. In "Chemical Carcinogens and DNA"; Grover, P. L., Ed.; CRC Press: Boca Raton, FL, 1979; Vol. 2, pp 1-28. Miller, J. A.; Miller, E. C. *Prog. Exp. Tumor Res.* **1969**, *11*, 273. Scribner, J. D.; Miller, J. A.; Miller, E. C. *Cancer Res.* **1970**, *30*, 15. Miller, J. A. *Ibid.* **1970**, *30*, 559. Suss, R.; Kinzel, U.; Scribner, J. D. "Cancer Experiments and Concepts"; Springer-Verlag: New York, 1973; pp 22-42. Cramer, W. J.; Miller, J. A.; Miller, E. C. *J. Biol. Chem.* **1960**, *235*, 885. Weisburger, J. H.; Weisburger, E. K. *Pharmacol. Rev.* **1973**, *25*, 1. See also: Miller, E. C. *Cancer Res.* **1978**, *38*, 1479. Scribner, J. D. *J. Org. Chem.* **1976**, *41*, 3820. Miller, E. C.; Miller, J. A. *Cancer* **1981**, *77*, 2327. Ford, G. P.; Scribner, J. D. *J. Am. Chem. Soc.* **1981**, *103*, 4281. DeBaun, J. R.; Rowley, J. Y.; Miller, E. C.; Miller, J. A. *Proc. Soc. Exp. Biol. Med.* **1968**, *129*, 268. Weisburger, J. H.; Yamamoto, R. S.; Williams, G. M.; Grantham, P. H.; Matsushima, T.; Weisburger, E. K. *Cancer Res.* **1972**, *32*, 491.

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