Hydroformylation of Bisolefinic Amine Derivatives Catalyzed by Cobalt and Rhodium

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Three bisolefinic carbamates and five *N,N*-diallyl N-substituted amines have been subjected to hydroformylation conditions under catalysis by $HCo(CO)_4$, $Co(CO)_8$, and $(Ph_3P)_3Rh(H)CO$ in an attempt to prepare heterocyclic ketones. The products differ with amines and carbamates and with the catalyst. Carbamate **3** and $HCo(CO)_4$ gave 3-pyrrolidinone (**4**) in 45% yield. The cobalt-catalyzed reaction of **8** and rhodium-catalyzed reaction of **3** and of **8** afforded products arising from hydroformylation at the terminal olefinic carbon. These mixtures usually included 2-pyrrolidinone; cobalt-catalyzed hydroformylation of chlorinated allylamines **10–12** provided *N*-benzyl-2-pyrrolidinone (**14**) and *N,N*-dibutylbenzylamine (**16**). Direct synthesis of potential intermediates including **18** has permitted the delineation of mechanistic rationale.

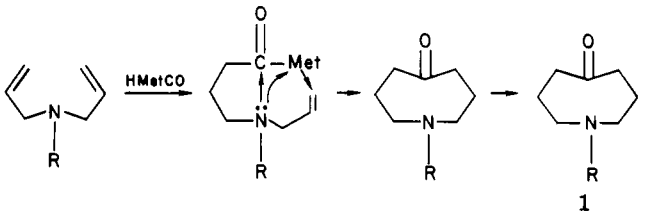
As part of a general program to develop new routes to medium-sized heterocycles for application to alkaloid synthesis,[1] we have examined the reactivity of several bisolefinic amines and carbamates toward cobalt and rhodium catalysts under hydroformylation conditions. This first report of tertiary nitrogen substrates establishes reactivity patterns in certain polyfunctional molecules with these catalysts.

The preparation of medium-sized heterocyclic rings remains a challenging synthetic transformation. Ring closure reactions of acyclic precursors to yield eight- through ten-membered nitrogen-containing rings have been limited to the Dieckmann reaction,[2] the acyloin reaction,[3] Friedel–Crafts acylations,[4] and a few other isolated examples.[5] We envisioned the general process outlined in Scheme I as a potential ring synthesis. In addition to the cobalt- and rhodium-mediated reactions reported here, analogous reactions using hydroboration,[5] and disodiotetracarbonylferrate,[6] have been examined.

Examples of hydroacylation reactions of α,ω-dienes which yield ketones are relatively rare. The preference for ketone formation is highly dependent on the relative geometry of the reactive groups within the substrate and the composition of the gas mixture used in the reaction.[8] The introduction of heteroatoms can alter the reaction course. Thus far only cyclopentanones and symmetrical acyclic ketones have been prepared by the hydroacylation process in reasonable yields.[8]

The hydroformylation systems most commonly used involve cobalt or rhodium catalysts. The most popular cobalt systems, usually using dicobalt octacarbonyl ($CO_2(CO)_8$) or hydridocobalt tetracarbonyl ($HCo(CO)_4$), have been studied in detail by Heck,[9] who has postulated the mechanism illustrated in Scheme II for ketone formation.

Scheme I



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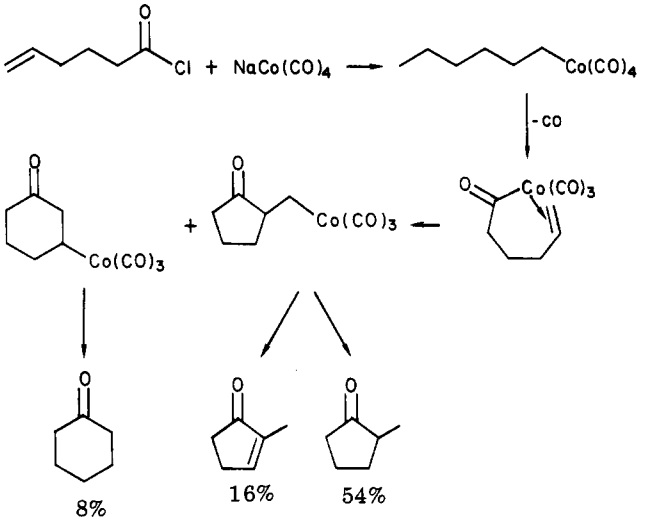
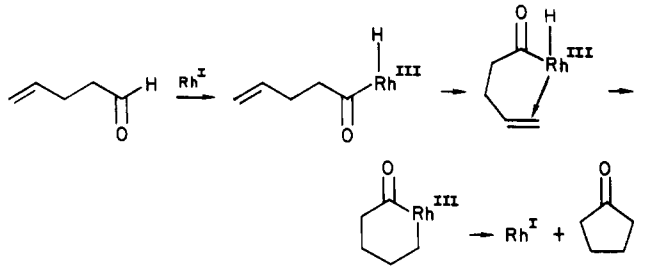
Scheme II



Scheme III



This scheme was based on product analysis and qualitative rate studies for the reaction of a series of olefinic acid chlorides ($CH_2{=}CH(CH_2)_nCOCl$) with $NaCo(CO)_4$ and on the reaction of 1,4-pentadiene with $HCo(CO)_4$ or with $Co_2(CO)_8$ and synthesis gas. Heck's observation that only a six-membered-ring ω-olefinic acylcobalt complex yielded a cyclic ketone suggests that there are severe geometrical

(1) For an alternative approach, see: Garst, M. E.; Bonfiglio, J. N.; Grudoski, D. A.; Marks, J. *J. Org. Chem.* **1980**, *45*, 2307.
(2) Leonard, N. J.; Sato, T. *J. Org. Chem.* **1969**, *34*, 1066 and previous papers in this series.
(3) Bloomfield, J. J.; Owsley, D. C.; Nelke, J. M. *Org. React.* **1976**, *23*, Chapter 2.
(4) Comer, W. T.; Catt, J. D.; Matier, W. L.; Combs, C. M.; Dykstra, S. J. *J. Heterocycl. Chem.* **1973**, *10*, 519.
(5) Garst, M. E.; Bonfiglio, J. N.; Marks, J., manuscript to be submitted to *J. Org. Chem.*
(6) Garst, M. E.; Marks, J., unpublished results.
(7) See ref 8a, p 116–118 for differences in these catalysts.
(8) For reviews, see: (a) Wender, I.; Pino, P. "Organic Synthesis via Metal Carbonyls"; Interscience: New York, 1968; Vol 1. (b) *Ibid.* 1977; Vol. 2. (c) Falbe, J., "Carbon Monoxide in Organic Synthesis"; Springer-Verlag: New York, 1970.
(9) Heck, R. *J. Am. Chem. Soc.*, **1963**, *85*, 3116; reviewed in *Adv. Organomet. Chem.* **1966**, *4*, 243.

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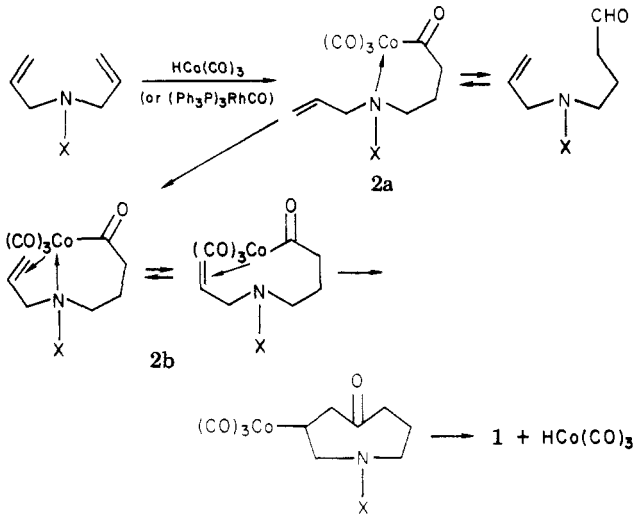
Scheme IV



constraints on cyclization by hydroacylation.

Introduction of nitrogen with a free NH into the olefin substrates serves to alter the reaction course drastically. The reaction process that ensues under hydroformylation conditions varies according to the nature of the substituent on nitrogen. For example, allylcarbamates undergo hydrogenolysis,[13] allylureas are susceptible to olefin reduction,[13] *N*-alkylallylamines afford *N*-alkyl-2-pyrrolidinones[14] and allylsulfonamides are unchanged[15] under the same reaction conditions. The pyrrolidinones may be formed via an acylcobalt species stabilized by nitrogen–cobalt or nitrogen–carbonyl interactions. After completion of our work, Stille[16] reported the rhodium-catalyzed hydroformylation of several olefinic amides, including *N*-allylacetamide, in which the transformation to amino aldehydes was observed. He demonstrated that rhodium-catalyzed isomerization of olefinic amides to enamides occurs to a significant extent.

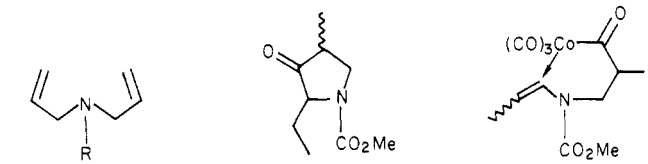
Rhodium-catalyzed hydroacylation represents a potentially useful process. Miller[10] and Laroch[11] have shown that 4-pentenals are cyclized to cyclopentanones by a number of rhodium catalysts. In the proposed mechanism (Scheme III) a six-membered-ring acyl metallocycle intermediate has been invoked. Suggs[12] has recently demonstrated the existence of a five-membered-ring acylrhodium metallocycle which was capable of undergoing intermolecular olefin addition to produce ketones. The Suggs complex contained nitrogen as an internal ligand. Taken together, this work[10,11,12] has thus shown that both nitrogen and olefins are capable of acting as intramolecular ligands with rhodium and that internally coordinated olefins can undergo insertion to yield cyclopentanones.

These observations suggested to us that hydroacylation of diallylamine derivatives might yield **1** directly (Scheme IV). The acyl metal species **2a**, a proposed intermediate in the hydroformylation of olefins, should afford **2b**, a π-complex potentially leading to **1**. That the formation of **2b** should be aided by the presence of a nitrogen atom in the substrate may be anticipated from two considerations. First, the nitrogen might lead, via metal coordination, to formation of the six-membered-ring intermediate **2a**. Once **2a** is established, the entropy loss expected for the formation of **2b** is far less than would be required for direct formation of complex **2b** in the absence of an internal ligand. Indeed, one may readily deduce from the Heck experiments[9] that there is an upper limit on the magnitude of the entropy loss which can accompany ring formation if the cyclization is to occur. A second effect of this nitrogen is to decrease the internal rotation of the allyl group in **2a**, relative to the carbocyclic analogue, due to the sp^2 character of the nitrogen. This hindered rotation further decreases the entropy loss accompanying cyclization. Variation of the substituent X and hence of the nitrogen lone pair availability enables one to influence the magnitude of both the above effects.[17]

With regard to the cobalt-catalyzed processes, it has been found that the outcome of the reaction is highly dependent on the nature of the cobalt carbonyl catalyst employed. Generation of the active cobalt species may be accomplished by any one of three methods as shown by Heck[9] and others:[18] i.e., in situ preparation of $HCo(CO)_4$ (the "active species") by hydrogenolysis of $Co_2(CO)_8$; the Co_2CO_8 may be used catalytically; (2) formation of $HCo(CO)_4$ by DMF induced disproportionation of $Co_2(CO)_8$ and subsequent acidification; (3) direct synthesis of the acylcobalt intermediate.[7] Experiments using these three approaches with cobalt have been completed by using as substrates *N*,*N*-diallyl carbamates, diallylamines, and related derivatives. This is the first report of the use of substrates containing tertiary nitrogens. The reactivity of these nitrogeneous compounds toward rhodium under hydroformylation conditions has also been examined. Although medium-sized rings have not been observed, reactivity patterns of these substrates toward cobalt and rhodium have been established and suggest the intermediacy of **2b**.

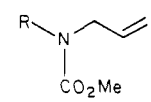
Results and Discussion

A. Cobalt. The report that 1,4-pentadiene undergoes carbonyl insertion with $HCo(CO)_4$ (1 equiv) to give 2-methylcyclopentanone in high yield[9] prompted our initial examination of the effect of this reagent on diallylcarbamate (**3**). Treatment of **3** with 1–3 equiv of $HCo(CO)_4$ in hexane under either N_2, CO, or H_2/CO atmosphere at ambient temperature resulted in 45–55% conversion to 2-ethyl-4-methyl-3-pyrrolidinone (**4**) accompanied by **3** and trace amounts of isomerized olefins, re-



3, R = CO_2Me
8, R = C_7H_7
9, R = C_6H_5

4 **5**

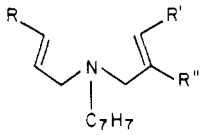


6, R = $CH_2CH_2CH{=}CH_2$
7, R = $CH_2CH{=}CHCH_3$

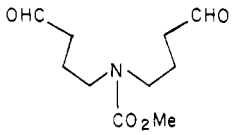
(10) Lochow, C. F.; Miller, R. G. *J. Am. Chem. Soc.* **1976**, *98*, 1281.
(11) Laroch, R. C.; Oertle, K.; Potter, G. F. *J. Am. Chem. Soc.* **1980**, *102*, 190.
(12) Suggs, J. W. *J. Am. Chem. Soc.* **1979**, *101*, 489.
(13) Falbe, J., unpublished work, cited in ref 8c, p 148.
(14) Falbe, J.; Korte, F. *Chem. Ber.* **1965**, *98*, 1928; *Tetrahedron Lett.* **1965**, 2677.
(15) Falbe, J.; Schulze-Steinen, H. J., unpublished work, cited in ref 8c, p 148.
(16) Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139, 2145.
(17) Shaw, B. *J. Am. Chem. Soc.* **1975**, *97*, 3856.
(18) (a) See ref 9. (b) Falbe, J. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 435. (c) Chalk, A. J.; Harrod, J. F. *Adv. Organomet. Chem.* **1968**, *6*, 119.

duction products, and aldehydes. Variations in either the amount of $HCo(CO)_4$, the gas composition, the reaction time, or the reaction temperature failed to increase the yield of **4**. The structure of **4** was determined by a combination of spectral and mechanistic considerations. The mass spectrum indicated the requisite "$H_2C{=}O$" addition (M^+ 173), but the NMR spectrum exhibited no aldehyde protons. The presence of 3-pyrrolidinone was indicated by the 1760 cm^{-1} stretch in the IR. The complex methyl region in the NMR spectrum and mechanistic considerations lead to the assignment of **4**. The formation of **4** may be rationalized as proceeding through intermediate **5** in which an olefin isomerization has occurred. We believe that olefin isomerization takes place after initial acylcobalt formation since we do not detect isomerized diene **19** by NMR. No other keto carbamates with the same molecular formula could be detected, all of which have been prepared in connection with related projects in our laboratory. The transformation of **3** into **4** is among the highest yielding reactions for the conversion of a bisolefin into a five-membered-ring ketone.[19]

We then attempted to determine the generality of this 3-pyrrolidinone preparation from other olefinic carbamates. The two *N*-allyl-*N*-butenylcarbamates **6** and **7** were treated with from 1–3 equiv of $HCo(CO)_4$. Compounds **6** and **7** yielded complex mixtures composed mainly of bishydroformylation products (bisaldehydes). These aldehyde mixtures formed in 40% yields were composed of all possible regioisomers characterized by NMR and GC/MS. The remaining material was starting diene (**6** or **7**) accompanied by small amounts of olefin reduction products. There was no indication of any keto carbamate formation (<5%). Thus we have been unable to extend this hydroacylation transformation (**3** to **4**) using $HCo(CO)_4$. We conclude from these experiments that the acylcobalt **2a** has very strict requirements for formation of the π-olefin complex necessary for the olefin isomerization and the second insertion. Addition of *N*,*N*-diallylalkylamines to a solution of $HCo(CO)_4$ with a pK_a value <1[20] results only in amine protonation and consequent catalyst inactivation.



10, R = Cl; R′ = R″ = H
11, R = R′ = Cl; R″ = H
12, R = R′ = H; R″ = Cl



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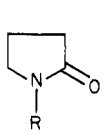
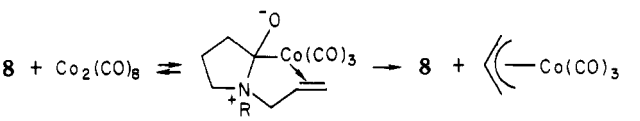


14, R = C_7H_7
15, R = C_6H_5

We next investigated the use of dicobalt octacarbonyl in benzene or toluene at elevated temperature under synthesis gas atmosphere (120 °C, CO/H_2 1:1, 1300–1400 psi). In contrast to hydridocobalt tetracarbonyl, dicobalt octacarbonyl is not inactivated by tertiary amines even though hydridocobalt tetracarbonyl is presumed to be the active species generated during the course of the reaction. In addition, complete conversion of olefinic substrates to products can be obtained with catalytic quantities of dicobalt octacarbonyl. Substrates **3** and **8**–**12** were tested. The reaction of $Co_2(CO)_8$ (0.2 equiv) with **3** gave a complex mixture, of which the major component we eventually identified as **13** by GC/MS comparisons (vide infra). No cyclic ketones (<1%) were observed. In contrast, **8** under the same conditions gave a 1:1 mixture of pyrrolidinone **14** and recovered **8** accompanied by little side product formation (<10%). Structure **14** was confirmed by comparison with an authentic sample prepared independently. Replacement of the N-substituent with a phenyl group did not significantly alter the reaction course. Thus **9** gave *N*-phenyl-2-pyrrolidone (**15**) as the major product. This transformation has some precedent in the conversion of *N*-alkylallylamines into *N*-alkyl-2-pyrrolidones under similar conditions.[14]

Scheme V



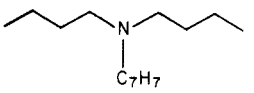
The exclusive formation of *N*-benzyl-2-pyrrolidinone rather than some of *N*-allyl-2-pyrrolidinone or *N*-propyl-2-pyrrolidinone suggests the possibility that the desired nitrogen–carbonyl interaction in the acylcobalt species is occurring (Scheme V). The putative, zwitterionic intermediate is then likely to eliminate a π-allylcobalt species. We have not detected either this suggested complex or nonvolatile products derived from it although the volatile reaction products have not been analyzed. Standard samples of the cyclic *N*-benzylamino ketones have permitted us to determine that no *N*-benzyl-5-azacyclooctanone and that less than 3% of any other cyclic ketone was formed.

To determine the effect of olefin substituents on the course of this reaction and to attempt to prepare functionalized 2-pyrrolidinones, we prepared amines **10**–**12**. Unexpectedly **10** and **11** gave nearly identical product mixtures comprised of two major products, each arising from hydroformylation at the terminal carbon. Preparative GC from each mixture afforded analytical samples of these products. One of them, *N*-benzyl-2-pyrrolidone (**14**) was contaminated by trace amounts of a substance lacking a new infrared carbonyl absorption. Thus the chlorine was reductively removed under the reaction conditions and hydroformylation occurred at the terminal carbon. Vinyl chlorides have been reported to undergo hydroformylation under similar conditions to afford β-chloro aldehydes.[21] Thus, if the hydroformylation is controlled by the olefinic chlorine moiety, compound **11** should afford products different from those of **8**. The formation **14** from both **8** and **11** implies that the *N*,*N*-dialkylmethylamino substituent is a more influential directing group than is chlorine.

Unexpectedly, the second major product from **11** was *N*,*N*-dibutylbenzylamine (**16**). Direct comparison of the spectra (IR, NMR, MS) of authentic **16** and the expected *N*,*N*-dipropylbenzylamine with the reaction product confirmed the assignment. Product **16** requires bishydroformylation at both terminal olefinic carbons followed by complete reduction. This result was rather unexpected but is not entirely unprecedented. The reduction of amino aldehydes and of amino alcohols to tertiary amines with $Rh_6(CO)_{16}/H_2O/CO$ has been reported by Laine.[22] We have not observed **16** from the reaction of **8**, and we have determined that *N*,*N*-dibenzyl(4-hydroxybutyl)amine (or the corresponding hydrochloride salt) is stable to these conditions. Furthermore, α-chlorostyrene and α-chlorostyrene–triethylamine do not provide propylbenzene or

(19) Klemchek, P. P. *Chem. Abstr.* **1962**, *56*, 1363.
(20) Several pK_A estimates have been made. The low solubility of $HCo(CO)_4$ (10^{-3}) precludes an accurate determination. A pK_a of 1 is a high estimate. See: Hieber, W., et al. *Z. Elektrochem.* **1953**, *57*, 235; *Angew. Chem.* **1961**, *73*, 364.
(21) For reports of hydroformylation of vinyl chlorides, see ref 8b, p 66, and ref 8c, p 56–75.
(22) Laine, R. M.; Thomas, D. W.; Cary, L. W. *J. Org. Chem.* **1979**, *44*, 4964.

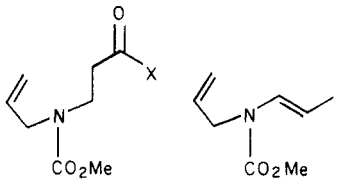
cumene as cobalt-mediated hydroformylation products. Thus the formation of **16** does not involve the free primary



16

alcohol and requires the presence of both tertiary amine and chloride. Attempts to reduce other alcohols in the presence of triethylamine hydrochloride suspended in benzene have also been unsuccessful. Compound **12** gave a complex mixture of several products, the composition of which was not analyzed in detail. Again saturated cyclic ketones were definitely absent, and the expected unsaturated or chlorinated ketones and 2-pyrrolidinones appeared to be absent (<1%) as determined by GC/MS.

Finally, a direct test of our postulate in Scheme IV was completed by the preparation of acylcobalt species **2**, using $NaCo(CO)_4$. We first repeated Heck's experiment in Scheme II to establish our techniques. Then applying Heck's procedure, acid chloride **17** was added to an ethe-



17, X = Cl
18, X = $Co(CO)_4$

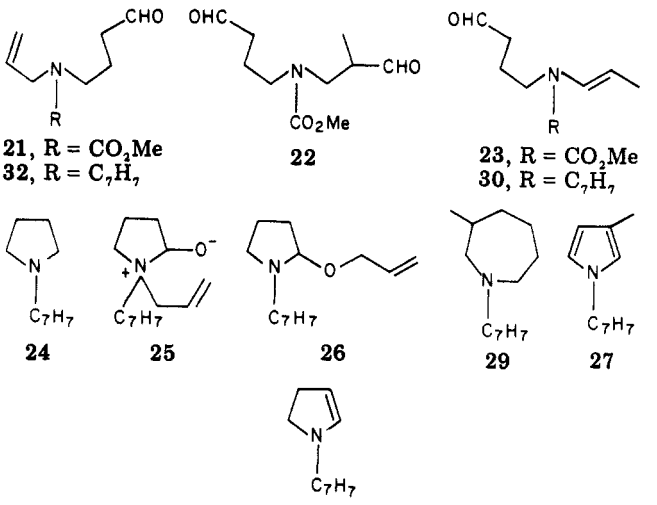
19

real solution of $NaCo(CO)_4$ under CO to give **18**. We had hoped, as previously discussed, that the carbamate nitrogen would act as a ligand to enable formation of the desired eight-membered ring. However, aqueous workup afforded the decarbonylation product **19** (~35% of the mixture) and recovered carboxylic acid (**20**) (~60% of the mixture). Olefin isomerization probably occurred via **18**. The decarbonylation generated $HCo(CO)_4$, which is known to disproportionate rapidly in ethereal solvents. From the formation of **19** we infer that **2b** or a related acylcobalt species prefers to decarbonylate rather than yield **2c**.

B. Rhodium. As indicated previously, literature precedent suggested that if monoaldehyde **2** were produced from **3** or **8**, then the desired rhodium-mediated hydroacylation might occur to give **1** (Scheme IV). Unfortunately, no ketones were produced under catalysis by Rh(I) and an atmosphere of 1:1 H_2/CO. All of the observed products were aldehydes or aldehyde derived. Apparently, if the cyclic acylrhodium species analogous to **2** was formed, reductive elimination to give an aldehyde was favored over olefin insertion to give ketone **1**.

Compound **3** (1 M) with $(Ph_3P)_3Rh(H)CO$ (15 mM) in benzene gave two products, **22** and **13**, in quantitative yield (3:1 ratio). Preparative HPLC afforded pure **22**. We have been unable to isolate **13**. Compounds **13** and **22** have similar structures as indicated by their GC/MS data. Examination of the crude NMR spectrum of **13** and **22** and of pure **22** left structure **13** as the only reasonable alternative. This spectrum of the mixture lacked additional methyl resonances and exhibited a greater intensity for the downfield aldehyde proton (9.75 ppm).

Under routine hydroformylation conditions, we have observed rhodium-catalyzed isomerization products which have constituted 0–10% of the product mixtures. Olefin isomerization has also been detected under two alternate sets of conditions. In the first of these, it was found that on increasing the $(Ph_3P)_3Rh(H)CO$ concentration to 55



21, R = CO_2Me
32, R = C_7H_7

22

23, R = CO_2Me
30, R = C_7H_7

24 **25** **26** **29** **27**

28

mM, a significant quantity of olefin aldehyde **23** was produced, as ascertained by spectral examination of a pure sample isolated by preparative GC. The reports by Sille[16] would suggest that **23** should afford hydroformylation adjacent to nitrogen, but this was not detected. In the other case, subjection of diallyl carbamate and $(Ph_3P)_3Rh(H)CO$ to an atmosphere of CO led to formation of a 90:10 mixture of starting material and **19** as verified by NMR inspection.

The aldehydes produced from amine **8**, on the other hand, were far more reactive and by further conversions gave rise to a complex mixture of which aldehyde(s) constituted only a small (<10%) portion. The major product (~30%) was *N*-benzylpyrrolidine (**24**), identified by comparison to an authentic sample.

One rationalization for the formation of **24** is based upon the following sequence of events initiated by the formation of **21**. After condensation of the amine and aldehyde functionalities of **21** to produce **25**, an N to O allylic migration of this zwitterionic species will afford **26**. This amino ether can eliminate allyl alcohol, producing an immonium ion which is readily reduced.

The formation of *N*-benzyl-3-methylpyrrole (**27**), a species constituting 6% of the crude mixture, is not readily rationalized. *N*-Benzylpyrrole might be expected to undergo hydroformylation at the α-position. On the other hand, pyrroline **28**, obtained from **26** via elimination and isomerization, should suffer hydroformylation at the β-position. Stille[16] has reported that the portion of hydroformylation occurring at the β-position of enamides increased as the *N*-acyl substituent becomes less election withdrawing. An enamine with only alkyl substituents on nitrogen represents the limiting case and would be expected to undergo hydroformylation at the β-position. However, this mechanism requires that the requisite immonium ion precursor to enamine **28** be a viable intermediate capable of isomerization to **28** in competition with reduction. Regardless of the mechanistic detail, the constitution of **27** was rigorously established by independent synthesis using *N*-(carboethoxy)3-methylpyrrole.[24]

The structure of amine **29**, a second major product formed in 17% yield, was also secured by independent synthesis. N-Benzylation of caprolactam (C_7H_7Br, NaH, THF), methylation of the amide enolate (LDA, MeI, THF, –78 °C), and amide reduction ($LiAlH_4$, THF) yielded **29**. The formation of **29** from **8** is envisioned to occur via **30**,

(23) Reference 8b, p 66, and ref 8c, p 58.
(24) Ichimura, K. *Chem. Abstr.* **1975**, *83*, 131448p.

formed by hydroformylation and olefin isomerization. Internal enamine aldehyde condensation of **30** and reduction of the resulting alcohol would yield **29**. Finally, the other major product **31** (15–20% yield) has the same structural formula as **29** and a similar NMR and mass spectra. Unfortunately we have only been able to obtain this product in 80% purity and cannot assign a definite structure.

Treatment of aldehyde **32** with $RhCl(PPh_3)_3$ under an atmosphere of ethylene[11] afforded a complex mixture of products which was not analyzed in detail. This mixture did not contain any of the expected amino ketones; the major products of this mixture were not **24**, **29**, or **31**.

Conclusions

The cobalt-catalyzed hydroformylation reaction of bisolefinic amine derivatives yields products which are dependent upon the cobalt reagent and the amine substitution. *N,N*-Diallylcarbamates with $HCo(CO)_4$ appear to yield products arising from initial hydroformylation at the secondary olefin carbon. For instance, **3** provides a 3-pyrrolidinone **4**. Other *N,N*-bisolefin carbamates afford products arising from reaction at several sites. Tertiary allylic amines, such as **8–12**, provide 8-acylcobalt compounds which undergo selective allyl group cleavage to yield 2-pyrrolidinones. Olefinic chlorine substituents in **10–12** have little effect on the directionality of the hydroformylation. When compounds **8–12** are compared with olefin **8**, the chlorinated moiety enhances bishydroformylation at the terminal carbon and gives a product which has undergone complete reduction to *N,N*-dibutylbenzylamine.

Under rhodium catalysis, *N,N*-diallylbenzylamine and *N,N*-diallylcarbamate first undergo hydroformylation primarily at the terminal olefinic carbon. The isolation of **23** suggests the possibility that dialdehyde **22** may arise from **23** rather than from **21**. The products obtained from *N,N*-diallylbenzylamine (**8**) can be rationalized as arising from aldehyde **32**.

Under hydroformylation conditions, cobalt-catalyzed reactions of diallylamines and rhodium-catalyzed reactions of both diallylamines and carbamates can yield terminally substituted acyl metal species as proposed in Scheme II. Unfortunately, these intermediates undergo several reactions other than the desired ring closure.

Experimental Section

General Procedures. Infrared spectra were recorded on a Beckman IR 18 AX spectrophotometer; bands yielding structural information are reported in reciprocal centimeters (cm^{-1}), using polystyrene calibration. Nuclear magnetic resonance spectra were recorded on a Varian EM 390 at 35 °C in deuteriochloroform and peak positions are reported in parts per million from tetramethylsilane internal standard, using multiplet (m), quartet (q), triplet (t), doublet (d), or singlet (s). Low-resolution mass spectra were obtained from an LKB 9000 at 70-eV and 16–20-eV ionizing voltage or from a Finigan 4021 GCMSDS system. High-resolution spectra were performed at the Bio-organic, Biomedical Mass Spectrometry Resource, A. L. Burlingame Director, University of California, Berkeley.

GC analysis was performed on a Varian 3700 gas chromatograph with FID detector and preparative GC on a Hewlet-Packard 5700 gas chromatograph with a TC detector. Both instruments were outfitted with a 6 ft × $^1/_4$ in. glass column containing 3% DEXIL 300 on 100/120 Supelcoport (Supelco, Inc.) or 3% on 100/120 Supelcoport.

The term "standard workup" means that the organic layer was washed with brine, dried over Na_2SO_4, and filtered and the solvent removed on a rotary evaporator at aspirator pressure. The term "base wash" means the organic layer was washed with saturated aqueous Na_2CO_3.

Reagents and Solvents. Tetrahydrofuran (THF) was distilled from sodium–benzophenone immediately prior to use. Benzene and toluene were distilled from sodium. Hexane was washed with sulfuric acid and distilled from calcium hydride. Dimethylformamide (DMF) was distilled from calcium hydride at reduced pressure. All amines were distilled from barium oxide and stored over molecular sieves under nitrogen. All metal catalysts were purchased from Alfa-Ventron. All other reagents and solvents were purchased from Aldrich Chemical Co. and Mallinckrodt Chemical Co., respectively, and were used as received after determination of purity by usual spectroscopic methods.

All reactions were magnetically stirred under a nitrogen atmosphere; balloons containing carbon monoxide or carbon monoxide–hydrogen were used for all hydroacylation reactions.

Amine Synthesis. All amines used in hydroacylation reactions were freshly distilled, exhibited appropriate spectra, and were homogeneous by GC. Amines **3** and **8** were prepared from diallylamine by the procedure of Hey and Ingold[26] and amines **9** and **11** by the alkylation of aniline or benzylamines. Amines **10** and **12** were prepared by the alkylation of N-benzylallylamine. Carbamate **6** was prepared from *N*-3-butenylallylamine, which in turn was prepared by the alkylation of allylamine with butenyl bromide. Carbamate **7** was prepared by N-alkylation of *N*-allylcarbamate.[27,28]

Carbamate 20. A suspension of 2.3 g (96 mmol) of sodium hydride in 50 mol of THF at 0 °C was treated with 8 g (94 mmol) of 2-pyrrolidinone. The suspension was stirred for 1 h and treated with 1.32 equiv of allyl bromide. The mixture was refluxed overnight and subjected to the standard workup to leave 88% of *N*-allyl-2-pyrrolidinone: NMR δ 1.80–2.16 (m, 2 H), 2.36 (t, 2 H), 3.32 (t, 2 H), 3.85 (d, 2 H), 4.97–5.26 (m, 2 H), 5.46–5.90 (m, 1 H); IR 1700–1640 cm^{-1}.

This amide was refluxed in constant boiling HCl for 12 h and then concentrated to a solid under vacuum. To 10 g (55.7 mmol) of this solid and 19.1 g (180 mmol) of Na_2CO_3 in 100 mL of H_2O was added with stirring 8.51 g of methyl chloroformate. The mixture was stirred overnight, acidified, and extracted with CH_2Cl_2 to give 4.38 g (39%) of the carbamate acid **20**: NMR δ 1.82 (2 H), 2.32 (t, 2 H), 3.24 (t, 2 H), 3.69 (s, 3 H), 3.83 (d, 2 H), 4.98–5.22 (m, 2 H), 5.50–5.95 (m, 1 H), 9.42 (br s, 1 H).

To 150 mg of the corresponding carbamate acid was added ca. 4 mL of oxalyl chloride. The mixture was stirred for 25 min. The remaining oxalyl chloride was removed in vacuo. The residue was Kugelrohr distilled (2 mm) to provide **21**: NMR δ 1.91 (q, 2 H), 3.91 (t, 2 H), 3.26 (t, 2 H), 3.71 (s, 3 H), 3.83 (d, 2 H), 4.95–5.18 (m, 2 H), 5.49–5.95 (m, 1 H); IR (neat) 1799 cm^{-1} (m).

Reaction of Stoichiometric Hydridocobalt Tetracarbonyl with Bisolefinic Carbamates: General Procedure. A modification of the procedure used by Orchin was employed.[29] In a typical experiment with diallylcarbamate **3**, the following conditions were used. To a 100-mL, three-neck, round-bottom flask equipped with two septae and a stirring bar was added 4.00 g (11.6 mmol) of $Co_2(CO)_8$ and ca. 30 mL of hexane. A balloon containing 50:50 H_2/Co was placed on a ground glass joint of the flask and the system was purged of air via needle in the septum. Then 10 mL of DMF was injected into the flask; the resulting mixture was stirred for 1 h, resulting in a clear two-phase system. At this time 10 mL of concentrated HCl was injected into the system, and the mixture was stirred for 15 min. The acid layer (dark blue) was withdrawn via syringe, ca. 25 mL of wash H_2O was added, and the mixture was stirred for 5 min. The water layer was withdrawn and 1.00 g of (6.45 mmol) of **3** was injected into the $HCo(CO)_4$ hexane solution. The reaction mixture was stirred overnight. The hexane was removed and the resulting residue was placed on a Florisil column and eluted with hexane followed by 100% ethyl acetate. In some cases evaporative distillation was required to remove the remaining traces of cobalt.

Carbamate **3** yielded a 1:1 mixture of **3** and **4** which was separated by preparative GC to afford analytical samples. Compound

(25) Trost, B. M.; Kunz, R. *J. Org. Chem.* **1974**, *39*, 2475.
(26) Hey, L.; Ingold, C. K. *J. Chem. Soc.* **1933**, 66.
(27) Nordlander, J. E., et al. *Tetrahedron Lett.* **1978**, 4987.
(28) We are grateful to Ms. V. Paul for determining that several other bases fail to effect this transformation.
(29) Kirch, L.; Orchin, M. *J. Am. Chem. Soc.* **1959**, *81*, 3597.

4 was formed in 45% crude yield: NMR δ 0.9–1.3 (m, 6 H), 1.8–2.0 (m, 2 H), 2.2–3.5 (m, 3 H), 3.7 (s, 3 H), 3.7–4.0 (m, 1 H); IR 1760 and 1710 cm^{-1}; mass spectrum (70 eV), *m/e* 185 (M^+), 183, 169, 157, 140, 131, 128 (base), 119 (base); high-resolution mass spectrum observed *m/e* 185.105232, $C_9H_{15}NO_3$ requires 185.10532.

Catalytic Hydroformylations: General Procedure. The reaction vessel used was a 0.75-in. swagelock cap connected via copper tubing to a tank containing a 50:50 mixture of H_2 and CO. The cap contained 3 mmol of substrate, 0.3 mmol of catalyst, and a spin bar in 3 mL of benzene or toluene. After attachment of the cap to the copper tubing the gas was let into the system from the tank (at ca. 1400 psi). The gas was released from the system, and the process repeated to purge the system of air. Finally the gas mixture was let into the system, and the tank valve was shut as well as a second valve lying between the tank and the reaction vessel. The initial pressure was thus presumed to be equal to the tank pressure. After completion of this degassing procedure, the stirred solution was placed in an oil bath at 90 °C for 4–5 h. The crude reaction products were analyzed by GC and GC/MS and then processed by filtration through a Florisil pad with EtOAC.

Reactions with $Co_2(CO)_8$. Aldehyde 13 from 3. Carbamate 3 and $Co_2(CO)_8$ afforded numerous products without any 3. Ketone 4, *N*-(carbomethoxy)-5-azacyclooctanone,[6] and *N*-(carbomethoxy)-2-methyl-4-azacycloheptanone were absent. The major component (28%) was identified dialdehyde 13.

***N*-Phenyl-2-pyrrolidinone (15).** Amine 9 and $Co_2(CO)_8$ yielded 15 (50%).

***N*-Benzyl-2-pyrrolidinone (14) from 8.** Amine 8 and $Co_2(CO)_8$ gave 8 and 14[31] in a 1:1 ratio in 90% yield.

14 and 16 from 10. Amine 10 and $Co_2(CO)_8$ afforded 14 (30%) and 16 in 40% yield.

14 and 16 from 11. Amine 11 and $Co_2(CO)_8$ afforded 14 (35%) and 16 (37%).

Preparation of $NaCo(CO)_4$. Reaction with *N*-Allyl-*N*-(carbomethoxy)-γ-aminobutyryl Chloride (17). A solution of $NaCo(CO)_4$ in ether was prepared as described by Orchin.[30] To a mixture of 150 g of 1% Na/Hg in 250 mL of hexane was added 5.4 g of $Co(CO)_8$. The sealed 500-mL round-bottom flask was flushed with N_2 (not with CO as originally described). The contents were stirred for 24 h. Water was then added to the mixture followed by separation and by evaporation of the hexane layer to give 5.35 g (62%) of $Hg[Co(CO)_4]_2$, having a melting point of 79–80 °C.

A solution of 0.217 g (0.40 mmol) of $Hg[Co(CO)_4]_2$ in dry ether was added to 50 g of 1% Na/Hg. The reaction mixture became colorless within 15 min. The IR showed a characteristic 5.3-μm band. The solution was then transferred via syringe to a 100-mL, three-neck, round-bottom flask under CO. The flask was placed on ice. To this stirring solution of $NaCo(CO)_4$ was added via syring 0.186 g (0.845 mmol) of distilled 17 in a small quantity of ether. Within 2 h the 5.3-μm band had disappeared, and the reaction mixture was taken off the ice and stirred overnight. The solvent was then removed and the residue chromatographed to remove the cobalt species.

The major product (with starting material, ~3:2 ratio) was *N*-(carbomethoxy)-*N*-allyl-(*E*)-1-propenylamine (19): NMR δ 1.64 (d of d, *J* = 7, 2.5 Hz, 3 H), 3.73 (s, 3 H), 4.10 (d, 2 H), 4.67–5.26 (m, 3 H), 5.50–5.93 (m, 1 H), 6.8 (d, *J* = 15 Hz, 1 H); mass spectrum (70 eV), *m/e* 155 (M^+), 140 (base).

Aldehydes 13 and 22 by means of $(Ph_3P)_3Rh(H)CO$. From 0.31 g (2.0 mmol) of 3 there was obtained 0.405 g (97%) of a mixture of two compounds in a 1:3 ratio (13 and 22): NMR δ 1.05 (d, *J* ~ 12 Hz, 2.2 H), 1.60–2.00 (m, 2 H), 2.30–3.00 (m, 1.7 H), 3.65 (s, 3 H), 3.10–3.60 (m, 4 H), 9.65 (d, *J* ~ 3 Hz, 0.6 H), 9.75 (t, *J* ~ 1 Hz, 0.75 H); IR (film) 1730, 1710 cm^{-1}; mass spectrum (70 eV) for 13, *m/e* 215 (M^+) and 22, *m/e* 215 (M^+). Preparative HPLC afforded the major isomer 22: NMR δ 1.05 (d, *J* ~ 12 Hz, 3 H), 1.60–2.00 (m, 2 H), 2.30–3.00 (m, 3 H), 3.10–3.60 (m, 4 H), 3.65 (s, 3 H), 9.65 (d, *J* ~ 3 Hz, 1 H), 9.75 (t, *J* ~ 1 Hz, 1 H); mass spectrum (70 eV), *m/e* 215 (M^+); high-resolution mass spectrum observed *m/e* 215.117296, $C_{10}H_{17}NO_4$ requires 215.1180.

In a separate experiment compound 23 was obtained by subjecting a mixture of 3 (1 M) and $(Ph_3P)_3Rh(H)CO$ (58 mmol) to the temperature and pressure conditions described above for a period of 20 h. A preparative GC sample of the resulting mixture contained pure 23 as the major product: NMR δ 1.6–2.1 (m, 5 H), 2.5 (t, *J* ~ 12 Hz, 2 H), 3.5 (t, *J* ~ 12 Hz, 2 H), 3.7 (s, 3 H), 5.0 (m, 1 H), 6.65 (m, 1 H), 9.85 (br s, 1 H); mass spectrum (70 eV), *m/e* 185 (M^+).

From 0.187 g of 8 there was obtained 0.168 g of a mixture 24, 27, 29, and one unidentified compound (31) as determined by GC. Isolated samples of 24 and 29 were identical with authentic samples as determined by GC coinjection, NMR, and GC/MS. Compound 27 and 31 were obtained as a mixture: NMR δ 0.7–1.0 (m, 3 H), 1.2–3.5 (m, 13 H), 2.1 (s, 1.5 H), 5.0 (s, 1 H), 6.0 (m, 0.5 H), 6.4 (m, 0.5 H), 6.55 (m, 0.5 H), 7.3 (5, 7.5 H); mass spectrum (70 eV), peak 1 *m/e* 171 (M^+) and peak 2 *m/e* 203 (M^+).

These data suggest that 31 is an isomer of 30.

***N*-Benzylpyrrolidine (24).** A solution of pyrrolidine (0.40 g), benzyl bromide (0.97 g), and potassium hydroxide (0.34 g) were stirred in EtOH for 12 h. Completion of the standard workup left 24: NMR δ 1.76 (m, 4), 2.53 (m, 4), 3.63 (s, 2), 7.29 (s, 5); mass spectrum (70 eV), *m/e* 161 (M^+), 91 (base).

***N*-Benzyl-3-methylazacycloheptane (30).** *N*-Benzylcaprolactam was alkylated by using the Trost procedure[25] in ca. 50% yield: IR 1629 cm^{-1}; NMR δ 1.16 (d, *J* ~ 7 Hz, 3 H), 1.4–2.0 (m, 6 H), 2.4–3.5 (m, 3 H), 4.5 (m, 2 H), 7.2 (s, 5 H); mass spectrum (70 eV), *m/e* 217 (M^+). A solution of this amide in THF was treated with excess $LiAlH_4$ and refluxed for 15 h under N_2. Usual workup left oily 29: NMR δ (d, *J* ~ 7 Hz, 3 H), 1.6 (m, 7 H), 2.6 (m, 4 H), 3.6 (s, 2 H), 7.3 (s, 5 H); IR 900, 720 cm^{-1}; mass spectrum (70 eV), *m/e* 203 (M^+), 91 (base).

3-Methyl-*N*-benzylpyrrole (32). According to the method of Ichimura,[24] a solution of 7.0 (78.6 mmol) of urethane in 300 mL benzene was cooled to 0 °C and successively treated with 9.35 g (78.6 mmol) of thionyl chloride and 12.42 g (157 mmol) of pyridine. To the resulting slush was added 5.4 g (77 mmol) of isoprene. The mixture was heated at reflux for 1 h. The flask was cooled, and the contents were filtered. The benzene was removed. The residue was dissolved in 200 mL of absolute ethanol and treated with 17.6 g (314 mmol) of potassium hydroxide. This mixture was refluxed for 1 h and subjected to the standard workup. Distillation of the residue afforded *N*-(carboethoxy)-3-methylpyrrole: bp <100 °C (4 mm); NMR δ 1.36 (t, *J* ~ 7 Hz, 3 H), 2.04 (s, 3 H), 4.33 (q, *J* ~ 7 Hz, 2 H), 6.03 (m, 1 H), 6.95 (m, 1 H), 7.10 (m, 1 H). The carboethoxy group was cleaved by refluxing 0.190 g of the carbamate and 4 g of potassium hydroxide in 25 mL of ethanol for 5 h. Completion of the standard workup provided ca. 0.070 g 3-methylpyrrole: NMR δ 2.11 (s, 3 H), 6.03 (m, 1 H), 6.51 (m, 1 H), 6.64 (m, 1 H).

N-Alkylation using oil-free potassium hydride and benzyl bromide in THF proceeded in abysmal yield to afford ca. 005 g of 32 identical by GC and GC/MS with the rhodium mixture. Further the proton shifts were very similar (within 0.05 ppm): NMR δ 2.1 (s, 3 H), 5.0 (s, 2 H), 6.0 (m, 1 H), 6.4 (m, 1 H) 6.55 (m, 1 H), 7.30 (s, 5 H); mass spectrum (70 eV), *m/e* 171 (M^+), 91 (base).

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(30) Dighe, S. V.; Orchin, M. *Inorg. Chem.* **1962**, *1*, 965.
(31) Purchased from Aldrich Chemical Co.