Scheme I. Arrangement of the interturn hydrogen bonds in β helices with different sense of twist for generic Boc- and MeO-protected, DL-alternating heptapeptides (a) and octapeptides (b) having the same sequence as the oligopeptides considered in this work. β helices with 14- and 16-membered hydrogen-bonded rings (~4.4 residues per turn) are considered.





Figure 1. CD spectra of oligopeptides I-IV in cyclohexane solution: concentration, 0.2 mg/mL; T, 25 °C. The ellipticity values represent the molar ellipticities of the protected oligopeptides divided by the number of the residues.

at a non-H-bonded urethane NH. Thus the NMR data strongly suggest that the predominant sense of twist is lefthanded. Support for this assignment comes from Bayley's⁶ preliminary theoretical calculations of CD properties of β helices, where left-handed β helices with ~4.4 residues per turn have a negative ellipticity band near 200 nm and a positive one near 180 nm. The calculated positions relative to the signs of these bands coincide with those characterizing the CD spectra of Figure 1. Thus, we conclude that the predominant sense of twist of the β -helical conformations of the oligopeptides I-IV is left handed.

In the case of the alternating oligomers of DL-valine the preference for one sense of twist can only be determined by the sequence of the residues. Since the same left-handed helical sense is adopted predominantly by I and II, the preference for this particular helical sense must be related to the D residues' being in odd positions and the L-residues' being in even positions, these positions being numbered starting from the methoxy end group. It is possible that sequences of this type, with a D residue at the C-terminus, preferentially stabilize the left-handed sense, because there is one more interturn hydrogen bond for this sense than for the right-handed sense (Scheme I). III and IV have the same sequence pattern as I and II, and also favor the same handedness. Therefore, it appears likely that the sequence, and not the chirality of the side groups, is the determining factor for the preferential winding in the left-handed sense of the chains of III and IV. As long as the

nature of the side chains play only a minor role, if any, in the stabilization of a particular β -helical sense, any similarly protected DL-alternating oligopeptide having a D residue at the C-terminus should exhibit this preference for a left-handed sense for β helices in solution. Conversely, if the sequence of such oligopeptides terminates with an L residue, the righthanded sense should be favored. It is interesting to observe that a preference for the left-handed sense of twist has been proposed⁷ for the β -helical conformation of samples of poly(L-Glu(OBzl)-D-Glu(OBzl)), and can be inferred from the CD spectrum for the β -helical conformation attributed⁸ to poly(L-Ala-D-Val). Indeed, on the basis of the arguments of Heitz and Spach,⁷ the same type of relationship between sequence and the preferred sense of twist as that established for protected oligopeptides should also hold for nonprotected polypeptides.

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Reductions with Carbon Monoxide and Water in Place of Hydrogen. 1. Hydroformylation Reaction and Water Gas Shift Reaction

Sir:

When compared with the conventional method of performing the hydroformylation reaction, the Reppe modification of this process¹ reveals several features of interest and potential importance. In the normal process an olefin is converted to the next higher aldehyde or alcohol through reaction with carbon monoxide and hydrogen with use of a cobalt or rhodium carbonyl catalyst (eq 1). In the Reppe modification

8	324	

Table I

Expt ^a	Compd	Temp, °C	Mol of C4 aldehyde/ mol of catalyst	n-/isoaldehyde ratio	C_4 aldehyde/ C_4 alcohol	Water gas shift reaction, mol of H ₂ /mol of catalyst ^b
1	Fe(CO) ₅	110	5.2	1.0	4.5	5
2	$Rh_6(CO)_{16}$	125	300	1.4	40	1700
3	$Ru_3(CO)_{12}$	100	47	11.5	43	3300
4	$H_4Ru_4(CO)_{12}^d$	100	79	11.0	37	3400
5	$Os_3(CO)_{12}^e$	180	13	1.9	6.6	270
6	$H_2Os_3(CO)_{10}^{e}$	180	6	1.2	~300	270
7	$H_4Os_4(CO)_{12}^e$	180	9	1.4	~300	400
8	$Ir_4(CO)_{12}^{f}$	125	250	1.8	~300	300
9	$(Bu_4N)[Pt_3(CO)_6]_5^g$	125	0.5	1.9		700

^a All experiments run for 10 h in a 300-mL stirred autoclave containing 0.05 mmol of catalyst, 22 mL of 25% aqueous trimethylamine, 78
mL of THF, 350 psi of CO, and 150 psi of propylene. Small amounts of propane were formed in expt 2, 5, 6, 7, and 8. ^b Identical conditions
as in a except that the propylene is omitted; a temperature of 150 °C was used for expt 2 and 8. Optimum conditions for each catalyst system
have not been determined. c Reference 12. d Reference 14. e References 15 and 16. f Reference 13. g Reference 17.

$$CH_{2} = CH_{2} \xrightarrow{\text{covo}} CH_{3}CH_{2}C$$

the same conversion is achieved without the use of molecular hydrogen per se; the olefin is converted to the next higher alcohol through reaction with carbon monoxide and water, the catalyst now being iron carbonyl together with a Brønsted or Lewis base. Of special interest is in fact that $Fe(CO)_5$ is a very poor catalyst for the hydroformylation reaction when hydrogen is used, whereas, under Reppe's conditions with CO and H₂O, it is an active catalyst at relatively mild temperatures and pressures.^{2,3}

To understand the manner in which this catalyst system uses $CO + H_2O$ in place of H_2 , and with the expectation that such an understanding would be of value for the design of catalysts for other reductions using carbon monoxide and water, we have investigated the mechanism of the Reppe modification of the hydroformylation reaction further.

We have found that the formation of alcohols under Reppe conditions is strongly dependent on the pH of the solvent medium. When $Fe(CO)_5 (10.0 \text{ g})$ is heated in aqueous KOH (300 mL of a 3.3% solution) to 100 °C in a 1-L autoclave under a pressure of 200 psi of ethylene and 300 psi of carbon monoxide, the $Fe(CO)_5$ dissolves with formation of the anion 1 according to reaction 2.4,5 The pH of the solution is initially 12.06 and IR analysis indicates the anion 1 to be the only metal carbonyl species present. As heating is continued the pH of the solution decreases owing to the reaction of CO with hydroxide ion giving formate ion. However, only when the pH drops to the vicinity of 10.7 does the consumption of ethylene and the formation of propanol begin to occur. At this point the principal metal carbonyl anion present is the species 1, although the solutions are frequently red in color indicating the presence of at least trace amounts of the trinuclear anion $HFe_3(CO)_{11}$. The formation of propanol continues as the pH finally lowers to $\sim 8.0.7$ In an identical experiment, but with acetaldehyde added to the reaction mixture at pH 12.0, it is found that the acetaldehyde is immediately reduced to ethanol at the high pH, but, again, only when the pH drops to 10.7 does the ethylene react to form propanol.

$$Fe(CO)_{5} + OH^{-} \xrightarrow{-CO_{2}} HFe(CO)_{4}^{-} \xrightarrow{H_{2}O} H_{2}Fe(CO)_{4} \quad (2)$$

$$1 \qquad 2$$

These data indicate that, whereas the anion 1 is capable of reducing aldehydes, it is not capable of interacting with olefins; we conclude that at pH 10.7 the conjugate acid of 1, i.e., species 2, begins to be formed in significant concentration and this is the species which is required to undergo initial reaction with

the olefin. Consistent with this proposal we find that, when 1,5-cyclooctadiene is stirred with a solution of KHFe(CO)₄ in aqueous K₂CO₃ under an argon atmosphere at a pH initially of 12.0, and the pH then lowered by the addition of a stream of CO₂, only when the pH is lowered to 10.7 does the isomerization of 1,5- to 1,3-cyclooctadiene begin to occur. It is known that **2** is a powerful catalyst for double-bond isomerization contained the HFe₃(CO)₁₁ anion, no isomerization of 1,5-cyclooctadiene occurred in the pH range of 12.0-8.0. Although the trinuclear anion may be observed in the Reppe modification, it is not a catalyst under the reaction conditions.^{9,10}

Also consistent with the proposed role of 2 is the fact that, in the absence of olefins, basic solutions of the anion 1 under a pressure of CO begin to liberate molecular hydrogen when the pH is lowered to the vicinity of 10.7. The species 2 is known to decompose readily with liberation of H_2 .⁴ On the basis of these data, and by analogy with the mechanism of the normal reaction using HCo(CO)₄ as given by Heck and Breslow,¹¹ we propose that the mechanism of the Reppe modification involves reaction of an olefin with 2 to generate an alkyl metal carbonyl hydride followed by insertion of CO to give an acyl metal hydride derivative and the subsequent elimination of the aldehyde. The Fe(CO)₄ which is liberated reacts with CO to give Fe(CO)₅, thus completing the catalytic cycle. Depending on conditions the aldehyde may be further reduced to the alcohol.

The normal hydroformylation reaction and the Reppe modification of it are mechanistically closely related; the essential point in the latter process is that it is easier to form the species $H_2Fe(CO)_4$ from the reaction of $Fe(CO)_5$ and water plus a base than it is from $Fe(CO)_5$ and molecular hydrogen; for this reason the combination of water and CO provides a superior reducing system than does molecular hydrogen in this instance.

Directed by these conclusions we have now found other metal carbonyl systems which are much superior to $Fe(CO)_5$ in effecting the hydroformylation reaction using $CO + H_2O$ in place of H_2 . Because of the formation of CO_2 , one obvious requirement for a metal carbonyl to be a catalyst of practical value, in a catalytic cycle as given above for $Fe(CO)_5$, is that it must be capable of generating a metal hydride species through attack by a weak base. The base must be weak enough such that it can be regenerated from its carbonate salt upon moderate heating. Of the mononuclear metal carbonyls only $Fe(CO)_5$ appears to meet this requirement. However,- $Ir_4(CO)_{12}$ and $Rh_6(CO)_{16}$ are readily attacked by mild base to generate metal carbonyl hydride anions,^{12,13} and we have tested these and several other polynuclear carbonyls as hydroformylation catalysts with $CO + H_2O$. The pertinent data as applied to the reaction of propylene + $CO + H_2O$ to give n- and isobutyraldehyde are given in Table I, together with comparable data using $Fe(CO)_5$. (It should be noted that the exact nature of the catalyst species present under the reaction conditions has not yet been established.)

If the polynuclear carbonyls catalyze the reaction in a manner similar to that described for $Fe(CO)_5$, then, in the absence of olefin, they could also be catalysts for the generation of hydrogen via the water gas shift reaction; i.e., $CO + H_2O$ \rightarrow CO₂ + H₂. Hydrogen formation would be expected to occur via the steps given in eq 3. This catalytic generation of hydrogen is indeed observed; in the final column of Table I is given the efficiency of the generation of hydrogen under the same conditions as used in the hydroformylation reaction except for the exclusion of olefin.18

$$M \xrightarrow{CO} MCO \xrightarrow{OH^-} MH^- \xrightarrow{H_2O} MH_2 \rightleftharpoons M + H_2$$
 (3)

From Table I it is seen that catalysts which are efficient for the hydroformylation reaction are also efficient for the water gas shift reaction, but, not surprisingly, the converse is not always true.

Further studies directed at the development of catalysts for these and other reductions using $CO + H_2O$ in place of H_2 will be reported later.

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Regarding a Generalized Scale of Solvent Polarities¹

Sir:

We have recently developed a scale of solvent "polarities", π , based on the solvent-induced solvatochromic shifts of seven



Figure 1. π^* vs. dipole moment of the solvents. Closed circles are for select solvents, $\pi \equiv \pi_c^*$. Open circles are for other solvents; cf. footnote 24.

Table I. Select Solvents for Use in Solvent Polarity Studies with Eq 1

Solvent ^a	$\pi (\equiv \pi^*)^b$	Solvent ^a	$\pi (\equiv \pi^*)^b$
Hexane, heptane (1)	-0.081	Butanone (16)	0.674
Cvclohexane (2)	0.000	Acetone (18)	0.683
Triethylamine (3)	0.140	Ethyl chloroacetate (39)	0.704
Tri- <i>n</i> -butylamine (48)	0.162	Triethyl phosphate	0.715
Di- <i>n</i> -butyl ether (5)	0.239	Acetic anhydride	(0.747) ⁵
Diisopropyl ether (4)	$(0.271)^5$	Cyclohexanone (41)	0.750
Diethyl ether (7)	0.273	Cyclopentanone (51)	0.756
Butyl acetate (38)	0.460	Nitromethane (32)	0.848
Tetrahydropyran (40)	0.513	Acetonitrile $(50)^{c}$	(0.86) ⁵
Ethyl acetate (11)	0.545	γ -Butyrolactone (27)	0.873
Methyl acetate (52)	0.556	Dimethylformamide (25)	0.875
Methyl formate (55)	(0.596) ³	Dimethylacetamide (23)	0.882
Tetrahydrofuran (13)	0.576	Sulfolane (56)	(0.988)4
Tri- <i>n</i> -butyl phosphate (42)	0.653	Dimethyl sulfoxide (29)	1.000

^a The solvents are numbered as in ref 2 and Figure 1. ^b The π^* values are classified as in ref 2 primary values obtained from at least six different data sets, and secondary values in parenthesis, for which 3 to 5 π_i^* have been averaged (indicated by superscript). ^c The π value indicated for CH₃CN from χ_R , P, E_K , log k, and G values is 0.86 ± 0.02, and this value fits well on the correlation with μ , Figure 1. We have noted that H-bonding contributions are likely to be involved with $A_{\rm N}$ and $E_{\rm T}$ values for CH₃CN (giving apparent π^* 0.99). The smaller π^* value of 0.713 is unaccounted for at the present time.

different indicators.² It was shown that this scale gives a very satisfactory quantitative description of the solvent effects on more than forty $\pi \rightarrow \pi^*$ and $p \rightarrow \pi^*$ electronic transitions.

We have critically examined the π^* values in the light of other empirical solvent scales based upon a variety of spectroscopic and/or chemical reactivity data.³ Eight of the most widely used "polarity" scales have been chosen: Dimroth's E_{T} ,⁴ Brooker's $\chi_{\rm R}$,⁵ Lassau and Junger's log $k({\rm Pr}_3{\rm N} + {\rm MeI})_{20} \circ_{\rm C}$,⁶ Walther's $E_{\rm K}$,⁷ Knauer and Napier's $A_{\rm N}$,⁸ Allerhand and Schleyer's G,⁹ Taft's P,¹⁰ and Brownstein's S.¹¹ No general correlation of useful precision exists between these scales (Figure 3 of ref 2 illustrates a typical case).

We wish to report, however, that, for a group of selected solvents (Table I), all scales give very closely equivalent re-