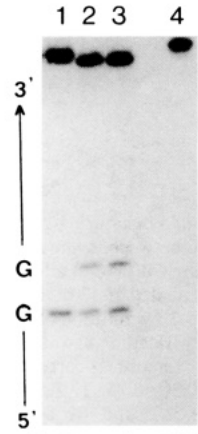

Figure 2. Autoradiogram of a denaturing 24% polyacrylamide gel of the products of the reaction between dimethyl sulfate and the starting product, the intermediate species, and the final product. After 4 h of reaction between cyanide ions and the platinated ds oligonucleotide (same conditions as in Figure 1, but the temperature was 17 °C), the products were separated by gel electrophoresis in a denaturing 24% polyacrylamide gel, eluted from the gel,[6] rehybridized, and then reacted with dimethyl sulfate according to the procedure of Maxam and Gilbert.[10] Lane 1 is relative to the intermediate species, lane 2 to the final product, lane 3 to Maxam–Gilbert specific reaction for the unplatinated ds oligonucleotide, and lane 4 to the starting product.

reaction of cyanide ions with the adducts.

The reaction between cyanide ions and the platinated ds oligonucleotide has been characterized by three sets of experiments. First, a kinetic study was performed at 17 °C. A good fit (not shown) between the experimental and the calculated relative concentrations of the three products was obtained, assuming that the scheme of the reactions is as follows:

$$\text{platinated ds oligonucleotide} \xrightarrow{k_1} \text{intermediate species} \xrightarrow{k_2} \text{unplatinated ds oligonucleotide}$$

The reaction rates $k_1 = 0.28 \pm 0.02$ h^{-1} and $k_2 = 0.27 \pm 0.03$ h^{-1} were calculated by Marquardt's least-squares procedure.

Then, the nature of the intermediate species was studied. The products eluted from the three bands were reacted with dimethyl sulfate according to the procedure of Maxam and Gilbert.[10] The results (Figure 2) show that (a) in the starting product, the two platinated G* residues do not react (the N7's are not accessible); (b) in the final product, the two G residues react; (c) in the intermediate species, the 5′G residue reacts but not the 3′G residue. Thus, in the reaction between cyanide ions and the platinated ds oligonucleotide, cyanide ions react selectively with the 5′G* residues. Within the resulting intermediate species, it is likely that the adduct is *cis*-[Pt(NH$_3$)$_2$(N7-dGuo)CN]$^+$.

Finally, we were interested to know whether subtle conformational changes in a double helix could influence the removal of a d(G*G*) adduct by cyanide ions. We have studied three platinated duplexes obtained by pairing the ss ^{32}P-labeled oligonucleotide containing a single d(G*G*) adduct respectively with the complementary strand and with the complementary strands in which either the 5′ or the 3′C residue complementary to the platinated G* residue was replaced by a T residue. The three platinated duplexes are named by their central two base pairs, i.e., d(G*G*/CC), d(G*G*/TC), and d(G*G*/CT). In the presence of cyanide, the qualitative behavior of the three duplexes was similar. Three bands were detected by gel electrophoresis under denaturing conditions (results not shown). However, the rates of removal of the bound platinum residues were different. At 37 °C, the half-lives of the starting products are 20, 30, and 70 min for the d(G*G*/CC), d(G*G*/CT), and d(G*G*/TC) duplexes, respectively. Recently, we reported that the mismatched T residues induce some distortions in the platinated ds oligonucleotides, the distortions being larger on the side of the mismatched residues.[5] The mismatched T residues paired with the 5′G* residues affect the kinetics more than the mismatched T residues paired with the 3′G* residues, which is in agreement with the selective reactivity of cyanide ions.

We have also compared the relative resistance of a d(A*G*) adduct using an experimental procedure similar to that described for the d(G*G*) adduct, the starting material being the ss oligonucleotide d(CTTCTCTTCTAGTCTTCTCT). By gel electrophoresis, two bands were detected with the ss oligonucleotide and three bands with the ds oligonucleotide (results not shown). The reaction was much slower with the ss oligonucleotide than with the ds oligonucleotide, the half-lives of the starting products being, respectively, 120 min and less than 10 min at 37 °C. Thus, the d(A*G*) adducts behave as the d(G*G*) adducts but are comparatively less stable to the action of cyanide ions.

In conclusion, the reactivity of cyanide ions with the two major adducts d(A*G*) and d(G*G*) depends strongly upon the DNA conformation. Experiments are in progress to determine, in ds natural platinated DNAs, the influence of the sequence on the relative stability of the major adducts in the presence of cyanide ions.

Acknowledgment. We are deeply indebted to Prof. J. C. Chottard, Prof. B. Lippert, Dr. J. M. Malinge, and Prof. M. Ptak for helpful comments. This work was supported in part by La Fondation pour la Recherche Médicale, La Fédération Nationale des Centres de lutte contre le Cancer, l'Association pour la Recherche sur le Cancer. One of us (M.S.) has received financial support from the Czech and French governments.

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Zwitterionic Rhodium Complexes as Catalysts for the Hydroformylation of Olefins

Ibrahim Amer and Howard Alper*

Ottawa-Carleton Chemistry Institute
Department of Chemistry, University of Ottawa
Ottawa, Ontario, Canada K1N 6N5
Received November 3, 1989

The homogeneous hydroformylation of olefins is a reaction that has attracted great interest, especially in terms of its synthetic utility, as well as studies probing the mechanism of this valuable industrial process.[1] Much of the recent effort has focused on the use of rhodium compounds as catalysts (usually containing phosphine ligands), since some complexes involving this metal exhibit high catalytic activity.[2,3] Despite the latter, the regioselectivity in many cases is not high, including synthetic approaches to commercially important compounds. For example, development of a mild, regiospecific method for the hydroformylation of *p*-isobutylstyrene to 2-(4-isobutylphenyl)propanal would be of significance since subsequent oxidation of the aldehyde[4] affords ibuprofen, one of the best, current, nonsteroidal antiinflammatory agents.[5]

Although numerous neutral and several cationic[6] rhodium complexes have been investigated, there have been no reports, to our knowledge, on the use of zwitterionic rhodium complexes as catalysts for the hydroformylation of olefins. It seemed conceivable that **1**, readily obtained from rhodium chloride, sodium tetraphenylborate, and 1,5-cyclooctadiene in aqueous methanol,[7] might

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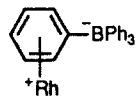

1

be a very useful hydroformylation catalyst. It was anticipated that the presence of a formal positive charge on the metal could direct the regiochemistry of the process and that cationic rhodium hydride and alkyl intermediates may be more susceptible to olefin coordination (and metal hydride addition) and carbonyl insertion, respectively. In addition, the anionic triphenylboron substituent attached to the coordinated arene ring may exert steric and/or electronic effects, subject to the stereochemistry of the intermediate which also has the olefin reactant bound to rhodium. We now report that **1** is of genuine use for the hydroformylation of a wide range of olefins under exceptionally mild conditions and that the process is highly regioselective, indeed in some cases regiospecific, for certain classes of alkenes (e.g., aryl olefins, vinyl ethers, and 1,1-disubstituted olefins).

Reaction of styrene in chloroform with a 1/2 mixture of carbon monoxide and hydrogen and a catalytic amount of **1** (54/1 ratio of styrene/**1**), at 47 °C and 200 psi for 22 h, resulted in 89% conversion to a 97.3/2.7 ratio of 2-phenylpropanal/3-phenylpropanal (eq 1). These results are superior to the results obtained

$$PhCH{=}CH_2 + 1/2\ CO/H_2 \xrightarrow[CHCl_3,\ 47\ ^\circ C,\ 200\ psi]{1,\ 22\ h} \underset{97.3}{PhCHCH_3}(CHO) + \underset{2.7}{PhCH_2CH_2CHO} \quad (1)$$

89% conversion

using many other rhodium complexes, including those with a phosphanonorbornadiene as the ligand, which effects lower conversion (46%) of styrene, affording 2-phenylpropanal/3-phenylpropanal in a 91/9 ratio.[8] In the case of **1**, use of a higher (4/1 or 2/1) or lower (1/9) CO/H_2 ratio results in appreciably lower conversion although the branched/linear ratio may be higher [2/1 CO/H_2; see Table I for data].

The hydroformylation reaction is essentially insensitive to electronic effects, as demonstrated by the results obtained for the reaction of a series of para-substituted styrenes (H, CH_3, *i*-Bu, F, Cl, Br, and OCH_3) with 1/2 CO/H_2 in chloroform at 200 psi and 47 °C for 22 h.[9] Although there was some variation in the percent conversion, the proportion of branched to linear aldehydes formed was remarkably similar in all cases (96.6–98.1 branched), except in the case of *p*-isobutylstyrene, which gave the branched and linear products in a 9/1 ratio. However, when *p*-isobutylstyrene was reacted at 500 psi for a shorter period of time (3 h), 2-(4-isobutylphenyl)propanal was formed as the exclusive product in quantitative conversion and isolated yield. The regiospecificity found here compares favorably with reports by others[10,11] using the same substrate and, as noted above, is of considerable potential as an efficient route to ibuprofen by oxidation of the aldehyde.[4]

Table I. Hydroformylation Reactions Catalyzed by Complex **1**[a]

substrate	pressure, psi	temp, °C	time, h	conversn, %	aldehydes[b] branched	aldehydes[b] linear
styrene	200	47	22	89	97.3	2.7
	200[c]	47	22	86	86.5	13.5
	200[d]	47	22	38	99.0	1.0
	200[e]	47	22	30	97.6	2.4
p-methylstyrene	200	47	22	90	98.1	1.9
p-isobutylstyrene	200	47	23	85	90.0	10.0
	500	50	3	100	100	-
p-fluorostyrene	200	47	22	91	98.0	2.0
p-chlorostyrene	200	47	22	73	98.6	1.4
p-bromostyrene	200	47	22	90	98.0	2.0
p-methoxystyrene	200	47	22	58	96.6	3.4
o-methylstyrene	200	47	22	61	95.0	5.0
3,4-dimethylstyrene	300	47	22	95	97.0	3.0
α-methylstyrene	200	60	43	75	-	100
p-isopropyl-α-methylstyrene	400	80	23	71	-	100
o-methoxy-α-methylstyrene	300	80	22	73	-	100
2-vinylnaphthalene	200	47	22	89	96.5	3.5
2-methyl-1-undecene	400	80	22	100	-	100
2,5-dimethyl-1,5-hexadiene	300	65	23	90	-	100[f]
1-heptene	200	47	20	89	48.0	52.0
3,3-dimethyl-1-hexene	200	60	22	69	-	100
phenyl vinyl ether	300	60	22	71	97.0	3.0
vinyl 2-naphthyl ether	300	55	22	96	96.0	4.0
vinyl *p*-*tert*-butylphenyl ether	300	55	22	84	90.2	9.8
vinyl 3,4-dimethylphenyl ether	300	60	21	85	90.0	10.0
vinyl acetate	300	55	22	76	94.5	5.5
methyl acrylate	300	60	22	46	30.0	70.0
methyl methacrylate	300	60	22	80	45.0	55.0
	400	70	22	64	43.0	57.0
allylbenzene	200	60	22	100	55.6	44.0
allyl phenyl ether	200	47	21	98	62.0	38.0
N-methyl-*N*-phenylallylamine	200	60	22	98	35.0	65.0

[a] All reactions effected by using chloroform, 1/2 CO/H_2, 1 mmol of substrate, and 0.0185 mmol of **1**. [b] The product ratio was determined by integration of the aldehyde proton signals (NMR) of the isomers and corroborated by gas chromatographic analysis. [c] CO/H_2, 1/9. [d] CO/H_2, 4/1. [f] No other products (e.g., unsaturated aldehydes) were formed.

Although the regioselectivities of reactions involving 3,4-dimethylstyrene and *o*- and *p*-methylstyrene are quite similar, the presence of a methyl group on the olefinic carbon atom bearing the aryl unit has a profound influence on the product distribution. Both aromatic [α-methylstyrene, *p*-isopropyl-α-methylstyrene, *o*-methoxy-α-methylstyrene] and aliphatic (2-methyl-1-undecene) 1,1-disubstituted olefins undergo hydroformylation affording the *linear* aldehyde as the only product. Of particular note are applications to carvone and *l*-(−)-limonene, which give the terminal aldehydes in excellent yields. Also, 2,5-dimethyl-1,5-hexadiene is cleanly converted to 3,6-dimethyloctane-1,8-dial in 90% yield. In addition, acenaphthylene reacts at lower pressure and affords acenaphthene-1-carboxaldehyde in higher yield (98%) than that reported for the reaction using chloro(dicarbonyl)rhodium(I) dimer and triphenylphosphine (100 atm, 100 °C, 79% product).[12] Some selectivity for hydroformylation at the benzylic position was observed when β-methylstyrene and indene were employed as reactants.

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(9) General procedure: A mixture of 1.0 mmol of olefin and 0.0185 mmol of **1** in chloroform (3 mL) containing 15 μL of an internal standard (*p*-xylene, cyclooctane, or *n*-octane; note that identical results were obtained in the absence of the internal standard) was heated in an autoclave using a 1/2 CO/H_2 mixture (see Table I for time, temperature, and pressure used in each case). The solvent was removed by rotary evaporation, and the residue was dissolved in benzene or ether and filtered through neutral alumina, which was then washed with additional solvent. The product mixture obtained by removal of the solvent was subjected to NMR and GC analysis. Further purification (e.g., separation of recovered starting material from aldehydes), if required, was effected by silica gel column chromatography using benzene as the eluant, or by distillation. Products were identified by comparison of physical and spectral data [IR, NMR, (^1H, ^{13}C), MS] with literature results, and with authentic materials (GC retention times) in some cases.
(10) Parrinello, G.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7122.
(11) Arakawa, M. Japan Pat. 77 97,930 (17 Aug 1977); *Chem. Abstr.* **1978**, *88*, 74208n. This reference describes the use of $[Rh(CO)_2Cl]_2$ at high pressure (100 kg/cm^2) for the hydroformylation of *p*-isobutylstyrene to the branched-chain aldehyde in 85% yield. The amount of linear aldehyde formed (i.e., up to 15%) was not specified.
(12) Raffaelli, A.; Rosini, C.; Dini, M.; Salvadori, P. *Synthesis* **1988**, 893.
(13) Exploratory investigations indicate the sequential generation of zwitterionic rhodium carbonyl and hydridocarbonyl complexes. A detailed study is in progress, and the results will be published in due course.

The zwitterionic complex is not a useful catalyst for the hydroformylation of simple monosubstituted olefins such as 1-heptene, since the branched/linear aldehyde ratio is near unity. However, if the substituent is bulky (e.g., 3,3-dimethyl-1-hexene), then regiospecific hydroformylation occurs leading to the linear aldehyde as the *only* product. In contrast, vinyl ethers (phenyl vinyl ether, vinyl 2-naphthyl ether, vinyl p-*tert*-butylphenyl ether, vinyl 3,4-dimethylphenyl ether) do undergo hydroformylation affording the branched-chain product in quite high regioselectivity.

While vinyl acetate undergoes hydroformylation with **1** to give principally the branched-chain aldehyde, isomeric methyl acrylate shows modest selectivity for the linear product. Unlike other 1,1-disubstituted olefins (above), methyl methacrylate affords aldehydes in low regioselectivity. The hydroformylation of allylic compounds (allylbenzene, allyl phenyl ether, *N*-methyl-*N*-phenylallylamine), while facile, are reactions of low regioselectivity. Finally, the carbon–carbon double bond of 2-cyclohexen-1-one is reduced under the usual hydroformylation conditions.

In conclusion, zwitterionic rhodium complexes display exceptionally high regioselectivity in the hydroformylation of vinylarenes and vinyl ethers to branched-chain aldehydes, while aliphatic or aromatic, 1,1-disubstituted olefins afford linear aldehydes in a regiospecific process. These reactions occur under remarkably mild conditions and are simple in both execution and workup.

Note Added in Proof. Rhodium complexes of trehalose-derived ligands (*not* zwitterionic) catalyze the hydroformylation of styrene in high regioselectivity. Unfortunately the naproxen precursor did not react in a regiospecific manner [95/5:b/l], and the ibuprofen precursor was not examined. We are indebted to Dr. John Brown for bringing this work to our attention [Brown, J. M.; Cook, S. J.; Khan, R. *Tetrahedron* **1986**, *42*, 5105].

Acknowledgment. We are grateful to British Petroleum and to the Natural Sciences and Engineering Research Council of Canada for support of this research. We are indebted to Karen Totland for experiments carried out with *p*-isobutylstyrene as reactant. We also are grateful to Johnson Matthey for providing a loan of rhodium chloride.

Novel Photorearrangements of Bridgehead-Substituted Dibenzobarrelene Derivatives in Solution and the Solid State

Phani Raj Pokkuluri, John R. Scheffer,* and James Trotter*

Department of Chemistry, University of British Columbia Vancouver, British Columbia, Canada V6T 1Y6

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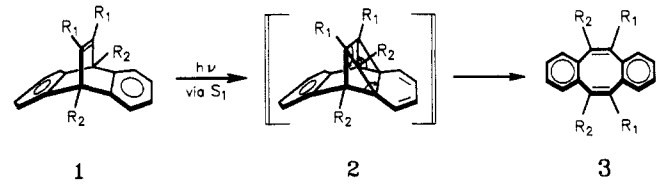
On the basis of an extrapolation from well-established benzo- and naphthobarrelene mechanisms,[1a-d] it has been assumed that the mechanism by which the analogous *di*benzobarrelene compounds rearrange photochemically to cyclooctatetraene (COT) derivatives involves initial intramolecular [2 + 2] cycloaddition through the singlet excited state followed by thermal reorganization of the resulting cage compound. This mechanism, outlined in Scheme I for the general dibenzobarrelene case, predicts the formation of dibenzocyclooctatetraenes with the substitutent pattern of structure **3**. We report in this communication that, for some bridgehead-substituted dibenzobarrelene derivatives, an alternative COT mechanism is followed, one that gives rise to a different labeling pattern in the derived dibenzocyclooctatetraenes.

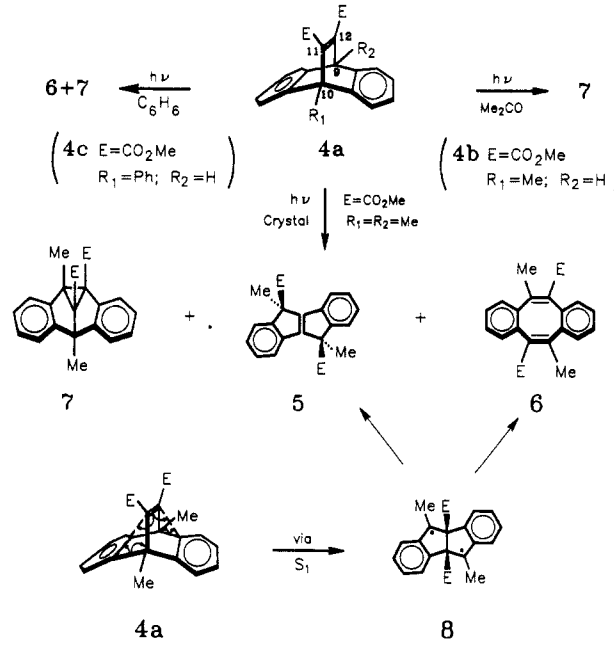
The clue that led to this discovery came from the isolation of an unusual and unexpected photoproduct in the *solid-state* irradiation of the dibenzobarrelene derivative **4a** (Scheme II).[2]

Scheme I



1 2 3

Scheme II



Photolysis of crystals of **4a** to low (≈5%) conversions afforded mainly (85%) the novel diester **5**, whose structure and stereochemistry were proved by X-ray crystallography;[3] small amounts of a COT derivative as well as the di-π-methane[4] photoproduct **7** were also formed. The structure of this latter material was assigned on the basis of its spectral data. Unsensitized *solution-phase* irradiation of **4a** gave approximately equal amounts of COT and **7**, and acetone-sensitized photolysis of **4a** gave **7** exclusively. Appropriate control experiments established that product interconversion was not occurring under the photolysis conditions.

It seems likely that the mechanism by which diester **5** is formed involves sequential carbomethoxy group migration in the bisbenzylic biradical **8** (Scheme II). This mechanism nicely rationalizes the stereochemistry of **5**, and such migrations, while rare, do have literature precedent.[5] The probable intermediacy of biradical **8** suggested that it might also be involved in COT formation through Grob-type fragmentation. This predicts the formation of a COT with C_2 symmetry rather than the C_s symmetry predicted by the mechanism of Scheme I. For this reason, a single-crystal X-ray diffraction study of COT **6** was undertaken.[3] The results of this study unambiguously establish that **6** has the unexpected, Grob fragmentation labeling pattern shown in Scheme II.[6]

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(2) Compounds **4a–c** were synthesized by Diels–Alder addition of dimethyl acetylenedicarboxylate to the appropriately 9-substituted or 9,10-disubstituted anthracene derivative. The structures of adducts **4a–c** were verified by X-ray crystallography.[3] The solution-phase photochemistry of compounds **4b** and **4c** has been reported, without, however, any mention being made of COT formation. (a) Iwamura, M.; Takuka, H.; Iwamura, H. *Tetrahedron Lett.* **1980**, *21*, 4865. (b) Paddick, R. G.; Richards, K. E.; Wright, G. J. *Aust. J. Chem.* **1976**, *29*, 1005.

(3) Full details on the crystal and molecular structures of compounds **4a–c**, **5**, and **6**, as well as the COTs from **4b** and **4c**, will be published separately.

(4) For a review on the di-π-methane photorearrangement, see: Zimmerman, H. E. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 3, Chapter 16.

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