Tetrahedron Letters,Vol.30,No.45,pp 6151-6154,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

A VERSATILE RHODIUM CATALYST FOR ACETALIZATION REACTIONS UNDER MILD CONDITIONS

J. Ott,[a] G. M. Ramos Tombo,[b] B. Schmid,[a] L. M. Venanzi,*[a]
G. Wang[a] and T. R. Ward[a]
[a]Laboratorium für Anorganische Chemie, ETH-Zentrum, CH-8092 Zürich
[b]Agricultural Division, Ciba-Geigy AG, CH-4002 Basel

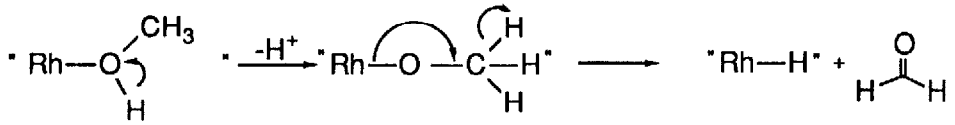
SUMMARY : Carbonyl compounds are readily acetalized under mild conditions in the presence of catalytic amounts of Rh(III)triphos moieties.

Acetals are one of the most widely used protecting groups for aldehydes and ketones.[1] Further, acetals have recently become important "tools" for the synthesis of enantiomerically pure compounds[2]. Although the formation of acetals is generally catalyzed by protons,[1b] several other Lewis acids, including a number of transition metal complexes, have been reported as being active catalysts for the acetalization reaction.[3] These, however have seldom shown major advantages over general acid catalysis.

We report here the use of several rhodium(III) complexes of the terdentate ligand $H_3CC(CH_2PPh_2)_3$, triphos, as catalyst precursors for the acetal formation and the trans-acetalization reactions. The herein described catalyst precursors have proven to be mild, demonstrate a high turnover rate, induce high diastereoselectivity and, have a high synthetic potential. These are : $[RhCl_3(triphos)]$,[4] A, $[RhCl_2(H_3CCN)(triphos)]^+$ $(CF_3SO_3^-)$,[5] B, $[RhCl(H_3CCN)_2(triphos)]^{2+}$ $(CF_3SO_3^-)_2$,[5] C, and $[Rh(H_3CCN)_3(triphos)]^{3+}(CF_3SO_3^-)_3$, [6] D. These complexes easily generate species with Lewis-acidic character and, thus, can be considered, at least in a formal sense, as "bulky protons". Some of the results obtained are summarized in Table 1. Typical substrates and reaction conditions for the formation of methyl-substituted acetals are listed in entries 1-5. A substrate:catalyst ratio of 2000:1 was used, although, in some cases, e.g., entry 1, the ratio 10000:1 could be used. Ethanol reacts more slowly, entry 6, and isopropanol does not react under the same reaction conditions. Catalyst precursors B, C and D give faster reaction rates as shown in entry 5. When cyclic acetals are to be formed, the water can be removed either by azeotropic distillation (entries 7, 11, 13) or by the use of isopropylorthoformate[7](entries 10, 12). For bulky substrates, complex D should be used (entries 11-15). Trans-acetalization reactions are carried out under mild and aprotic conditions (entry 8).

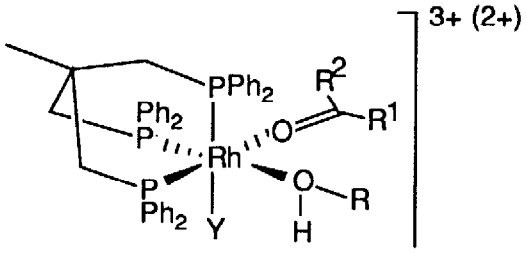
Further, methylorthoformate can be used as a source of methoxide (entry 14), as well as a water scavenger (entries1-5). Concerning diastereoselectivities, interesting ratios are obtained (entries 12,13, 15). For proton-sensitive substrates, the complex A should be preferentially used (entries 2-4). Since protons are formed upon reaction of complexes C and D with a primary or secondary alcohol (vide infra), one could suspect these to be the actual catalysts. Indirect evidence presented (entries 8 -no protons present-, 13 -no acetalization with 1/50 mol equivalent of acid-) suggests that the above complexes are active catalyst precursors.

Complexes D and C react with methanol, as shown by the formation of $[RhH(H_3CCN)_2(triphos)]^{2+}$ from D and $[RhHCl(H_3CCN)(triphos)]^{+}$ from C with liberation of a proton, by the following reaction sequence :



Therefore, it can be expected that the protons generated as described above can compete with the metal center for the acetalization reaction.

Concerning the reaction mechanism, it appears that two cis free coordination sites are required in the catalyst precursor. Both substrates, carbonyl and alcohol, can then be coordinated to the metal before coupling together. Further, the strong trans effect of the facial chelating tripodal phosphine activates all three cis positions equivalently. Complex A has also been prepared with the arsenic analog of triphos : triars $[H_3CC(CH_2AsPh_2)_3]$[8]. Its weaker catalytic activity confirms the above hypothesis : a strong trans effect activates the sites where catalysis is to occur.



[Y=solvent or (anionic ligand)]

Figure 1 : Coordination of both substrates to the metal center.

TABLE 1 : The Rh(III)triphos catalyzed acetalization of carbonyl compounds

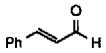
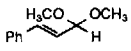
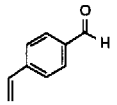
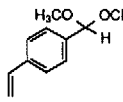
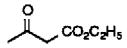
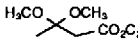
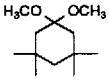
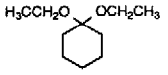
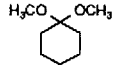
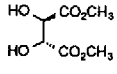
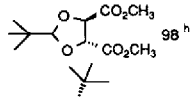
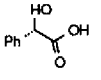
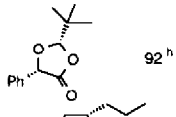
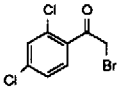
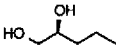
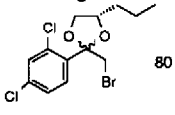
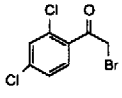
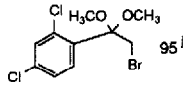
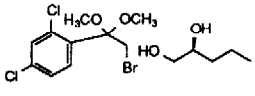
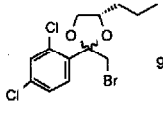
Entry	Substrates		Substr.[a] Ratio	Temp/ Time (h)	Desicc. Agent	Catalyst	Product	Yield (%)
1[k]		H_3COH	5.0	RT[f]/0.25	MOF[b]	A		85[h]
2[k]		H_3COH	5.0	RT/3.0	MOF	A		85[h]
3[k]		H_3COH	5.0	RT/0.25	MOF	A		89[h]
4[k]		H_3COH	5.0	RT/3.0	MOF	A		84[h]
5[k]		H_3COH	5.0	RT[i]	MOF	A-D		50[i]
6[k]		H_3CCH_2OH	5.0	RT/5	EOF[c]	A		86[h]
7[j]			1.0	RX[g]/2	AD[d]	A (D)		84[j] (100[j])
8[j]			3.0	RT/3	none	D		100[j]
9[j]			1.1	RT/3	none	D		87[j]
10[j]			1.05	RT/10	IOF[e]	D		100[j]
11[j]			0.66	RX/8	AD	D		98[h]
12[m j]			0.83	RT/8	IOF	D		92[h]
13[n j]			0.83	RX/70	AD	D		80[j]
14[j]		$HC(OCH_3)_3$	3.0	RT/8	none	D		95[j]
15[o j]			0.83	RX/24	none	D		95[j]

Table 1 : continued.

a) [Alcohol]/[ketone]; b) Methylorthoformate; c) Ethylorthoformate; d) Azeotropic Distillation; e) iso-Propylorthoformate; f) Room Temperature; g) Reflux; h) Isolated yield; i) Corresponds to the reaction time (minutes) required to obtain a 50% yield of the acetal. A : 7 min, B : 4 min, C : 2 min, D : 2 min; j) Yield determined by GC ; k) The alcohol was used as a solvent; l) Benzene was used as a solvent; m) The reaction affords only the cis product as proven by ^{1}H NMR; n) The proton catalyzed reaction with 1/10 mol equivalent of protons affords a cis/trans ratio of 6/4 when performed in refluxing toluene. The rhodium catalyzed reaction affords a cis/trans ratio of 1/2.5; o) Same diastereoselectivity as in n).

References and notes.

[1] a) T. W. Greene; Protective Groups in Organic Synthesis, John Wiley, New York 1981. b) F. A. J. Meskens, Synthesis (1981), 501.

[2] a) W. S. Johnson; C. A. Harbert; R. D. Stipanovic; J. Am. Chem. Soc. (1968), 90, 5279. b)W. S. Johnson; C. A. Harbert; B. E. Ratcliffe; R. D. Stipanovic; ibid. (1976), 98, 6188. c) P. A. Bartlett; W. S. Johnson; J.D.Elliott; ibid. (1983), 105, 2088. d) H. Yamamoto; A. Mori; J. Synth. Org. Chem. Jpn. (1987), 45, 944. e) A. Mori; H. Yamamoto; J. Org. Chem. (1985), 50, 5444. f) K. Narasaka; M. Inoue; T. Yamada, J. Sugimori, N. Iwasawa; Chem. Lett. (1987), 2409. g) D. Seebach; R. Imwinkelried; Th. Weber; Modern Synthetic Methods 1986, R. Scheffold, Springer Verlag Berlin, Heidelberg, New York, Tokyo, Vol. 4, 1986.

[3] a) W. Voelter; C. Djerassi; Chem. Ber. (1968), 101, 1154. b) B. H. Lipschutz; D. Pollart, J. Monforte, H. Kotsuki; Tet. Lett. (1985), 26, 705. c) R. V. Hoffman; Tet. Lett. (1974), 2415. d) J. F. Biellmann; M. J. Jung; W. R. Pilgrim; Bull. Soc. Chim. Fr.(1971), 7, 2720. e) C. A. 109 : 109880g. f) C. A. 98 : 215321q; JP 58 13,534 [83 13,534]. g) C. A. 100 : 85265w; EP 94,748. h) C. A. 108 : 21098b; JP 62,178,535 [87,178,535].

[4] a) J. Ott; L. M. Venanzi; C. A. Ghilardi; S. Midollini; A. Orlandini; J. Organomet. Chem. (1985) 291, 89. b) W. O. Siegl; S. J. Lapporte; J. P. Collman; Inorg. Chem. (1971), 10, 2158.

[5] J. Ott, Dissertation, ETH Zürich, 1986, number 8000.

[6] Synthesis of D : Silver trifluoromethanesulfonate (2.57 g, 10 mmol) was added to a stirred suspension of A (834 mg, 1 mmol) in 25 ml of acetonitrile. The solution was stirred for 15 minutes, then filtered through Celite to afford a slightly yellow solution. Ether (150 ml) was slowly added. The resulting white precipitate was filtered off, washed with ether and pentane and, dried under HV. Complex D (1.04g, 80%) thus obtained proved to be analytically pure. ^{1}H NMR (250 MHz, CD_3CN) : 7.6-7.3 ppm (m, P[C_6H_5]), 3.05 ppm (s broad, PCH_2); 2.05 ppm (q, ^{4}J (P, H) = 4Hz, CH_3); 1.95 ppm (s, H_3CCN).^{31}P NMR (101.3MHz, CD_3CN) : 17.0 ppm (d, ^{1}J (Rh,P) = 99Hz).

[7] R. H. Dewolfe; Synthesis (1974), 6, 153.

[8] S. Midollini; F. Cecconi; J. Chem. Soc., Dalt. Trans. (1973), 681. The complex with the triars ligand was prepared as complex A in Ref [4b].

(Received in Germany 31 July 1989)