The spectral data of our product correspond with those of ipsdienol recorded in the literature.[12,16,19,20,22]

f. Preparation of 3-Methyl-2-butenal. To a stirred solution of 0.200 mol of the $(CH_3)_2C{=}CHMgBr$ in 200 mL of THF—prepared from 20 g of magnesium and 0.200 mol of $(CH_3)_2C{=}CHBr$[8]—was added dropwise 0.240 mol of dimethylformamide. After this addition, which was carried out at −70 °C, the temperature was allowed to rise to −30 °C. The solution was then added over 15 min to a stirred mixture of 56 g of concentrated hydrochloric acid (36%) and 350 mL of an aqueous saturated NH_4Cl solution at −10 °C. The aqueous layer was extracted four times with diethyl ether. The combined solutions were dried over $MgSO_4$ after which the solvent was carefully removed at reduced pressure. The remaining crude product was warmed to 30 °C, and the pressure was reduced to 0.10 mmHg. The product was collected in an acetone/CO_2-cooled trap. This yielded 73% of 3-methyl-2-butenal: n^{20}_D 1.4525; lit.[19] bp 133 °C (760 mmHg); ^1H NMR δ 1.97 and 2.17 (2 CH_3, d, J = 1.2 Hz), 5.80 (HC=, dqq, J = 8 Hz, 2 J = 1.2 Hz), 9.96 (HC=O, d, J = 7.2 Hz).

Acknowledgment. This work was supported by The Netherlands Foundation for Chemical Research (SON) with financial aid from The Netherlands Organization for the Advancement of Pure Research (ZWO).

Registry No. **4**, 90753-25-6; **5** (R = $CH_3(CH_2)_4$), 110316-86-4; **5** (R = $CH_3(CH_2)_5$), 110316-87-5; **5** (R = cyclohexyl), 110316-88-6; **5** (R = $CH_3(CH_2)_3OCH_2$), 110316-89-7; **5** (R = $(CH_3)_2CHCH_2(CH_2O)CH$), 110316-90-0; **5** (R = $HOCH_2CH$), 110316-91-1; **5** (R = $HOCH(CH_3)CH_2$), 110316-92-2; **5** (R = $HOCH(Ph)CH_2$), 110316-93-3; **5** (R = $CH_3CH_2(HO)CH$), 110316-94-4; **5** (R = $(CH_3)_2CHCH_2(HO)CH_2$), 110316-95-5; **5** (R = $(CH_3)_2C{=}CH(HO)CH$), 110316-96-6; **5** (R = $Ph(HO)CH$), 110316-97-7; **5** (R = $(CH_3)_2(HO)C$), 110316-98-8; **5** (R = $CH_3CH_2(CH_3)(HO)C$), 110316-99-9; **5** (R = $(CH_3)_3C(CH_3)(HO)C$), 110317-00-5; **5** (R = 1-hydroxycyclohexyl), 110317-01-6; **5** (R = 1-hydroxytetrahydronaphthalyl), 110317-02-7; **5** (R = HOOC), 110317-03-8; **5** (R = CH_3CO), 110317-04-9; **5** (R = CH_3S), 110317-05-0; **5** (R = $CH_3(CH_2)_2S$), 110317-06-1; **5** (R = $HC{\equiv}CC(=CH_2)CH_2$), 110317-07-2; **5** (R = $HOCH_2(Ph)CH$), 110330-25-1; **9a**, 60894-96-4; **9b**, 54809-53-9; $PhSC{\equiv}CC(=CH_2)CH_3$, 35346-80-6; $Me_3SiC{\equiv}CC(=CH_2)CH_3$, 18387-60-5; $Me_3SiC{\equiv}CC(CH_3)CH_3$, 110330-26-2; $(CH_3)_2C(OH)C{\equiv}CC(=CH_2)(CH_2)_4CH_3$, 110317-08-3; $(CH_2)_5C(OH)C{\equiv}C(=CH_2)CH_2CH_3$, 110317-09-4; $(CH_3)_2C{=}CHMgBr$, 38614-36-7; $CH_3(CH_2)_4Br$, 110-53-2; $CH_3(CH_2)_5Br$, 111-25-1; $CH_3(CH_2)_3OCH_2Cl$, 2351-69-1; $(CH_3)_2CHCH_2(CH_3O)CHCl$, 86213-40-3; $CH_3CH_2CH{=}O$, 123-38-6; $(CH_3)_2CHCH_2CH{=}O$, 590-86-3; $(CH_3)_2C{=}CHCH{=}O$, 107-86-8; $PhCH{=}O$, 100-52-7; $(CH_3)_2C{=}O$, 67-64-1; $CH_3CH_2(CH_3)C{=}O$, 78-93-3; $(CH_3)_3C(CH_3)C{=}O$, 75-97-8; $(CH_3)_3N(CH_3)C{=}O$, 127-19-5; CH_3SSCH_3, 624-92-0; $CH_3SC{\equiv}N$, 556-64-9; $CH_3(CH_2)_2SC{\equiv}N$, 4251-16-5; bromocyclohexane, 108-85-0; oxirane, 75-21-8; methyloxirane, 75-56-9; phenyloxirane, 96-09-3; cyclohexanone, 108-94-1; tetralone, 529-34-0; isopropenylacetylene, 78-80-8.

Amidation of Chloroalkenes Catalyzed by Tertiary Phosphine Complexes of Palladium(0)

Paul P. Nicholas

BFGoodrich Research and Development, Brecksville, Ohio 44141

Received June 2, 1987

Tertiary phosphine complexes of palladium(0) catalyze the amidation of vinyl chloride (VCl) with carbon monoxide and amines. The reaction is surprisingly fast and gives high yields of the Michael adduct derived from the amine with the corresponding acrylamide. The high rate with VCl is unusual among monochloroalkenes, being orders of magnitude greater than all three of the chloropropenes. The reaction is also stereospecific, with *cis*- and *trans*-1-chloropropene giving the propenamides with retention of configuration and no adduct formation. Basicity of the amine, coordination stereochemistry of the ligand, and the concentration of carbon monoxide and amine all influence the reaction rate in ways that are sometimes unexpected, in both degree and direction. Like bromoalkenes and arenes, chloroalkenes undergo amidation through oxidative addition. This conclusion is based on the stereospecificity and the quantitative coupling of VCl to 1,3-butadiene when carbon monoxide is absent. Catalyst deactivation can occur and is mainly caused by the loss of ligand through conjugate addition with acrylamide. The rate of that reaction is controlled by the nucleophilicity of both the phosphine and the amine with which it competes. It is greatly suppressed in the presence of dimethylamine where amidation occurs with high catalyst turnover.

Introduction

Despite its low cost and abundant supply, the only commercial use of vinyl chloride (VCl) today is in the production of poly(vinyl chloride). Recently, we examined several hypothetical process concepts based on VCl. They included the preparation of acrylamide and N-substituted acrylamides by catalytic carbonylation with amines. Such an amidation process appeared to have commercial promise if it could be achieved with high rate, yield, and turnover.

There are only a few reports describing VCl carbonylation in the presence of alcohols. Saturated esters (propionate and 2-chloroprionate) are the main products when catalyzed by $Pd(PPh_3)_2Cl_2$.[1] Similarly, stoichiometric $PdCl_2$ in methanol gives methyl 2,2-dichloropropionate.[2] However, ethyl acrylate has been reported when $SnCl_2$ is used together with $Pd(PPh_3)Cl_2$, though large amounts of catalyst are required and few turnovers achieved.[1] Moreover, it is unclear if the acrylate forms directly or is an elimination product of the chloropropionate.

The classic studies by Heck, Schoenberg, and Bartoletti on the $Pd(PPh_3)_2X_2$-catalyzed amidation[3] and carbalkoxylation[4] of several halogen-substituted arenes and alkenes are the most comprehensive reported. Together with a complementary mechanistic study by Heck and Garrou[5]

(1) Knifton, J. U.S. Pat. 3 991 101, Nov. 9, 1976.

(2) Tsuji, J.; Morikawa, M.; Kiji, J. *J. Am. Chem. Soc.* **1968**, *86*, 4851.
(3) Schoenberg, A.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3327.
(4) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318.
(5) Garrou, P. E.; Heck, R. F. *J. Org. Chem.* **1976**, *98*, 4115.

0022-3263/87/1952-5266$01.50/0

Table I. Product Distribution from VCl Amidation with Amines Catalyzed by $Pd(PPh_3)_4$ under Selected Conditions[a]

amine	mol	T (°C)	yield (%) 1	2	3	4	5	6	R_a[b] (mmol min^{-1})	R_a (rel)	VCl turnover rate[c] (h^{-1})
ammonia	0.35	100	81	.2	16	.04			.50	1.6	26
	0.20	100	87	3	11	.8			.59	1.8	27
	0.12	100							1.4	4.4	101
	0.074	100	0	66	16	5.7			1.6	5.0	110
dimethylamine	0.12	100					94[d]		3.6	12.0	260
	0.12	90					100[d]		1.3		81
aniline	0.12	100						81	.32[e]	1.0	18[e]

[a] 0.36 mmol $Pd(PPh_3)_4$, 240 psi CO. [b] Amine consumption. [c] Mol VCl converted/mol catalyst·h. [d] 5·HCl present. [e] Average of three runs.

they are a rich source of chemistry. More recently, Ban and co-workers have applied this reaction to the synthesis of lactams,[6] while Yamamoto[7] and Sen[8] have reported double carbonylation of aryl halides to α-keto amides. However, only one example of chloroalkene amidation has been reported, that of 2-chloropropene with aniline to give the anilide.[3] However, the reaction is slow compared to bromides and iodides, despite the vigorous conditions used. This is, perhaps, not surprising considering that oxidative addition, the expected halogen activation step, is likely to be very slow. The resistance of monochloroalkenes and chloroarenes toward oxidative addition with zero-valent Ni, Pd, and Pt complexes is well-documented.[9] Nevertheless, we have found that the amidation of VCl is surprisingly fast compared to other monochloroalkenes and has proven to be preparatively useful. This report describes our study of this reaction and its chemistry.

Results and Discussion

VCl amidation is performed at elevated carbon monoxide pressures in liquid VCl, homogeneously catalyzed by tertiary phosphine complexes of Pd(0). The amine is the limiting reagent. Reaction rates are obtained by measuring its disappearance in the vapor phase. Since the amine concentration is low, rates measured as mole fraction against time will be essentially the same in both the vapor and liquid phases. Both phases are vigorously stirred to assure efficient vapor-liquid equilibrium. With aniline, the rate is determined by VCl conversion.

Product Distribution from VCl and Chloropropenes. In general, the main products of VCl amidation are Michael adducts of the amine with the corresponding acrylamide. With ammonia, the products are 3,3′,3″-nitrilotripropanamide (**1**), acrylamide (**2**), ammonium chloride, and the nitrilotripropanamide hydrochloride (**3**) (eq 1). Also formed are small amounts of (2-carbamoylethyl)triphenylphosphonium chloride (**4**), the adduct from the catalyst ligand (eq 2). Similarly, dimethylamine and

$$VCl + CO + NH_3 \xrightarrow[(L = t\text{-phosphine})]{PdI_n} \underset{\mathbf{1}}{N(CH_2CH_2CONH_2)_3} + \underset{\mathbf{2}}{H_2C{=}CHCONH_2} + \underset{\mathbf{3}}{ClHN(CH_2CH_2CONH_2)_3} + NH_4Cl \quad (1)$$

$$4H_2C{=}CHCONH_2 + PPh_3 + NH_4Cl \rightarrow \underset{\mathbf{4}}{ClPh_3PCH_2CH_2CONH_2} + 1 \quad (2)$$

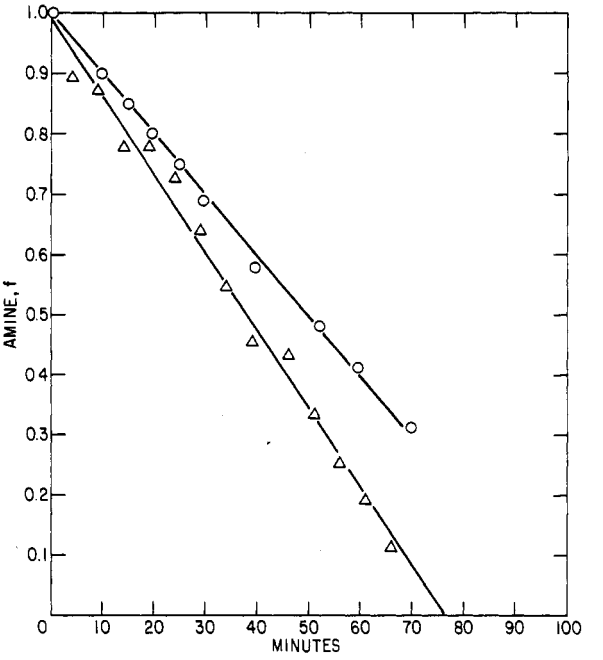


Figure 1. Disappearance of amine during VCl amidation, 0.36 mmol $Pd(PPh_3)_4$: (○) dimethylamine (90 °C, 0.059 mol, 240 psi CO); (△) ammonia (100 °C, 0.12 mol, 240 psi CO).

aniline give the Michael adducts **5** and **6** and the corresponding amine hydrochlorides. Yields, determined by ^1H NMR, are typically 80–100% (Table I). Like ammonia, dimethylamine can also produce the hydrochloride of the Michael adduct, in this case, **5**·HCl. The ^1H NMR spectrum of **5** undergoes a continuous change toward that of **5**·HCl, depending on the degree of protonation. This is most noticeable for chemical shift of the $(CH_3)_2N$ singlet. Therefore, while the exact distribution between **5** and **5**·HCl can sometimes be ambiguous, their combined yields are easily determined, and they are essentially quantitative.

$$\underset{\mathbf{5}}{(CH_3)_2NCH_2CH_2CON(CH_3)_2}$$

$$\underset{\mathbf{6}}{PhHNCH_2CH_2CONHPh}$$

The proportion of Michael adduct formed is markedly influenced by the amount of ammonia charged. At very low levels, acrylamide is the main product rather than the adduct **1**. This is caused by a marked acceleration in the rate of acrylamide formation and a reduction in the rate of adduct formation, thereby making amidation more competitive for available ammonia. This is discussed in more detail later.

Under the conditions described for the third entry of Table I, *cis*- and *trans*-1-chloropropene and 2-chloropropene react very slowly. However, small amounts of the corresponding propenamides **7**–**9** are obtained with retention of configuration, and no Michael adduct is formed.

(6) Ban, Y.; et al. *J. Org. Chem.* **1982**, *47*, 2456.
(7) (a) Yamamoto, A.; et al. *J. Am. Chem. Soc.* **1985**, *107*, 3235. (b) Yamamoto, A.; et al. *Organometallics* **1984**, *31*, 683.
(8) Chen, J. T.; Sen, A. *J. Am. Chem. Soc.* **1984**, *106*, 1506.
(9) (a) Fitton, P.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287. (b) Heck, R. F.; Patel, B. *Catal. Org. Synth. 7th* **1978** **1980**, 195. (c) Brunet, J.; Sidot, C.; Caubere, P. *J. Org. Chem.* **1983**, *48*, 1983. (d) Johnson, B. F. G.; Lewis, J.; Jones, J. D.; Taylor, K. A. *J. Chem. Soc., Dalton Trans.* **1974**, 34. (e) Bland, W. J.; Burgess, J.; Kemmitt, R. D. W. *J. Organomet. Chem.* **1968**, *15*, 217.

Yields are 66%, 51%, and 90%, respectively.

cis-$(CH_3)HC{=}CHCONH_2$ (7)

trans-$(CH_3)HC{=}CHCONH_2$ (8) $H_2C{=}C(CH_3)CONH_2$ (9)

Amidation Rate. The initial disappearance of amine during VCl amidation catalyzed by $Pd(PPh_3)_4$ is surprisingly constant, even through high conversions (Figure 1). However, the reaction is not zero order in amine since the rate changes with the amount of amine initially charged (Figure 2). Still another curious result is that the direction of change can differ depending on the amine used. Within the range of initial concentrations investigated, the rate slows with more ammonia while increasing with more dimethylamine. Carbon monoxide is like ammonia, though the rate passes through a maximum within the pressure range investigated (Figure 3). We believe these results are best explained in terms of competition among the reactants for coordination with palladium preceding a rate-controlling oxidative addition step (eq 3–5). "PdL_2"

$$\text{"}PdL_2\text{"} + VCl + CO + HNR_1R_2 \rightleftharpoons PdL_2(VCl) + PdL_2(CO)_x(HNR_1R_2)_y \quad (3)$$

$$PdL_2(VCl) \rightarrow ClPdL_2(HC{=}CH_2) \quad (4)$$

$$ClPdL_2(HC{=}CH_2) + CO + 2HNR_1R_2 \rightarrow \rightarrow \text{"}PdL_2\text{"} + H_2C{=}CHCONR_1R_2 + H_2NR_1R_2Cl \quad (5)$$

refers to either PdL_2, itself, or an operationally equivalent complex. There are several reports relating to dissociative equilibria involving zero-valent Ni, Pd, and Pt complexes,[10] their complexation with alkenes,[9d,e,11] and its importance to oxidative addition. On the basis of this interpretation, ammonia is a far more competitive ligand than dimethylamine, a difference that must originate from steric control. The coordinating ability of tertiary phosphines causes a similar effect. We find that most Pd(0) complexes of monodentate tertiary phosphines are active catalysts for VCl amidation with ammonia. But complexes of chelating diphosphines, such as 1,2-bis(diphenylphosphino)ethane (dppe) and 1,2-bis(diphenylphosphino)benzene (dppb), are essentially inactive (Table II).

The reactivity of aniline in VCl amidation is surprising. In Heck's studies, a weakly basic amine, such as aniline, was found to be unreactive unless a strongly basic tertiary amine was also present. However, aniline gives preparatively useful rates with VCl, though about an order of magnitude slower than dimethylamine (Table I). But considering that K_B for these amines differ by a factor of more than 10^6, we conclude that there is only a moderate overall sensitivity to basicity. Moreover, we find no primary deuterium isotope effect with ammonia-d_3. Together, these results suggested that base-induced deprotonation of a hydridopalladium chloride is not a kinetically important step in the catalytic process.

One of our greatest concerns when we began this study was the low rates expected for chloroalkenes. However, the amidation rate proved to be very sensitive to substitution on the chloroalkene, with VCl reacting orders of magnitude faster than all three of the chloropropenes. Under the conditions of the third entry in Table I, R_a(rel) for chloroalkene conversion, VCl/*cis*-1-chloropropene/*trans*-1-chloropropene/2-chloropropene, is 76:2:1:1.

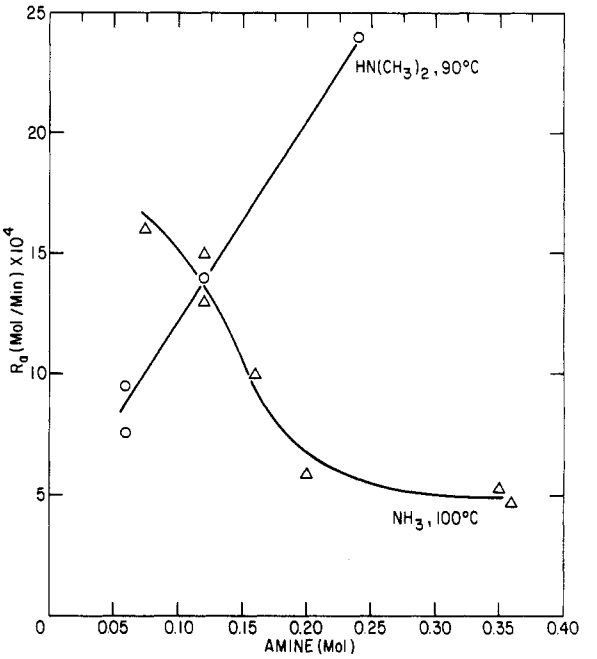


Figure 2. Influence of the initial amine charge on amidation rate (240 psi CO, 0.36 mmol $Pd(PPh_3)_4$).

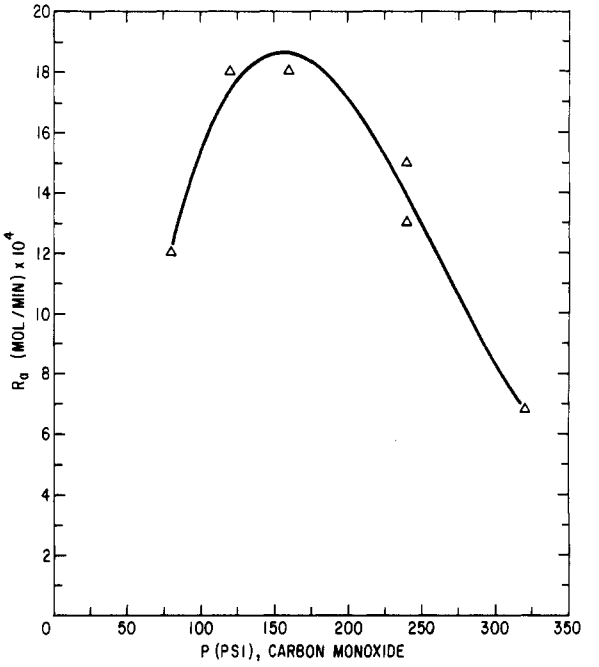


Figure 3. Influence of carbon monoxide pressure on amidation rate (100 °C, 0.12 mol ammonia, 0.36 mmol $Pd(PPh_3)_4$).

Table II. Influence of Tertiary Phosphine Structure in PdL_n on the Rate of VCl Amidation with Ammonia[a]

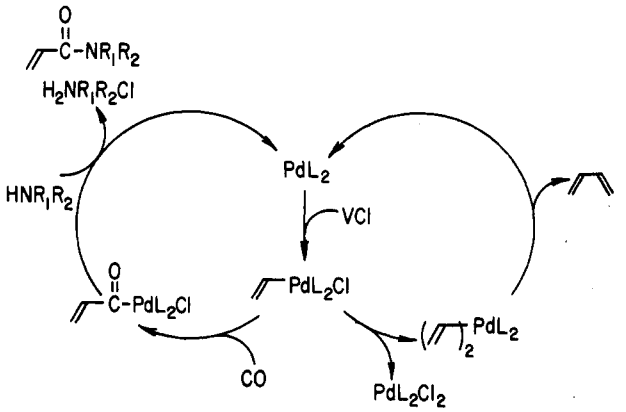
L	*n*	R_a (rel)	L	*n*	R_a (rel)
$P(p\text{-}C_6H_4CF_3)_3$	4	1.0	$P(p\text{-}C_6H_4CH_3)_3$	4	3.6
$P(p\text{-}C_6H_4F)_3$	4	1.1	$P(cyclohex)_3$[b]	4	4.9
$P(C_6H_5)_3$	4	1.7	dppe[b]	2	≤0.02
$P(C_6H_5)_3$	4	1.8	dppb[b]	2	≤0.01

[a] 240 psi CO, 0.12 mol NH_3, 100 °C. [b] Complex generated in situ from tris(tribenzylideneacetylacetone)tripalladium·($CHCl_3$) + ligand.

(10) (a) Tolman, C. A.; Seidel, W. C.; Gerlach, D. H. *J. Am. Chem. Soc.* **1972**, *94*, 2669. (b) Foa, M.; Cassar, L. *J. Chem. Soc., Dalton Trans*, **1975**, 2572. (c) Tolman, C. A.; Seidel, W. C.; Gosser, L. W. *J. Am. Chem. Soc.* **1974**, *96*, 53. (d) Kuran, W.; Musco, A. *Inorg. Chim. Acta* **1975**, *12*, 187. (e) Fauvarque, J. F.; Pfluger, F.; Troupel, M. *J. Organomet. Chem.* **1981**, *208*, 419.

(11) (a) Fitton, P.; McKeon, J. E. *J. Chem. Soc. D* **1968**, 4. (b) Burgess, J.; Hunt, M. M.; Kemmitt, R. D. W. *J. Organomet. Chem.* **1977**, *134*, 131. (c) Mukhedkar, A. J.; Green, M.; Stone, F. G. A. *J. Chem. Soc. A* **1970**, 947. (d) Tolman, C. A.; Seidel, W. C.; Gosser, L. W. *Organometallics* **1983**, *2*, 1391.

Scheme I



Though some rate acceleration would be expected with VCl for both electronic and steric reasons, the magnitude is surprising. Indeed, amidation with VCl is sufficiently rapid to be preparatively useful.

Carbon–Chlorine Bond-Activation Step. Retention of configuration during amidation of bromo- and iodoalkenes is the most compelling evidence supporting oxidative addition as the carbon–halogen bond-activation step.[3,5] Consistent with this, the amidation of *cis*- and *trans*-1-chloropropene occurs with retention of configuration. But there is a plausible alternative scheme that could accommodate stereospecificity, which we felt should be addressed. It involves the formation of a carbamoyl palladium complex **10** which could lead to acrylamides by an insertion/β-elimination route (eq 6–8). A wide variety

$$L_nPdCl_2 + CO + 2HNR_1R_2 \rightarrow \underset{\mathbf{10}}{L_nPdCl(CONR_1R_2)} + ClH_2NR_1R_2 \quad (6)$$

$$\mathbf{10} + VCl \rightarrow \underset{\mathbf{11}}{L_nPdCl(CH_2CHClCONR_1R_2)} \quad (7)$$

$$\mathbf{11} \rightarrow L_nPdCl_2 + H_2C{=}CHCONR_1R_2 \quad (8)$$

of transition metals form carbamoyl complexes according to eq 6.[12] Analogous carbomethoxy complexes are also known,[13] and they do undergo insertion with terminal alkenes.[14] Thus, overall retention during amidation could occur by cis insertion followed by trans elimination, and there is evidence supporting both stereochemistries.[15] Nevertheless, we believe that VCl undergoes amidation by an oxidative addition route. Our evidence is based on the fate of the adduct when carbon monoxide is absent. In this case, coupling occurs quantitatively to give 1,3-butadiene (eq 9). Since palladium-mediated coupling usually

$$Pd(PPh_3)_2 + 2VCl \rightarrow 1,3\text{-}C_4H_6 + Pd(PPh_3)_2Cl_2 \quad (9)$$

occurs by reductive elimination from dioroganopalladium intermediates,[16] these results indicate that disproportionation to a divinylpalladium occurs spontaneously under these conditions (Scheme I). Stille has similarly observed competition from 1,3-diene formation in the synthesis of ketones via carbonylation of vinyl palladium complexes at low carbon monoxide pressures.[16d] While coupling is

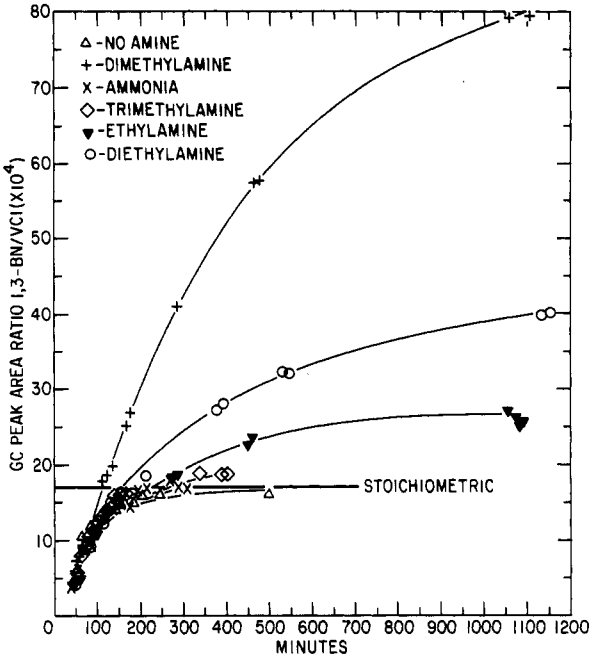


Figure 4. Coupling of VCl to 1,3-butadiene with $Pd(PPh_3)_4$ in the presence of amines, 70 °C.

Table III. Influence of PR_3 Nucleophilicity in $Pd(PR_3)_4$[a] on Rate and Phosphonium Salt Formation

R	time (min) to 80% NH_3 convn	ClR_3PCH_2C-H_2CONH_2 (% of PR_3 charged)
t-Bu	38	~100
p-Tol	102	70
phenyl	170	16

[a] Generated in situ from $Pd_3(TBAA)_3CHCl_3 + PR_3$; 0.36 mmol $Pd(PR_3)_4$, 0.20 mol NH_3, 240 psi CO, 90 °C.

stoichiometric in palladium when either ammonia or no amine is present, it becomes catalytic when an amine containing α-hydrogens is present (Figure 4). Thus, the amine must serve as a reducing agent for L_nPdCl_2, with the most effective ones being those having the greatest number of α-hydrogen atoms. The corresponding imine is likely the oxidation product, though we have made no attempt to characterize it. These results also explain why $Pd(PPh_3)_2Cl_2$ is equally effective as $Pd(PPh_3)_4$ in catalyzing amidation with dimethylamine, though it is inactive in amidation with ammonia.

In general, we find a declining rate of 1,3-butadiene formation with all three reducing amines (Figure 4). This does not originate from the consumption of VCl or amine because both are present in large excess over the palladium complex. The origin of this effect is unclear, though mass spectrometry has detected the phosphonium ions, $Ph_3PCH_2CH_2NR_2$(R = CH_3, C_2H_5) in coupling reactions with dimethylamine and diethylamine. Thus, at least some ligand is consumed during these coupling reactions, but we do not know if the amount is significant.

Catalyst Stability. The deactivation of $Pd(PPh_3)_4$ usually occurs within a few hundred turnovers during amidation with ammonia. This is accompanied by the formation of the phosphonium salt **4** and colloidal metallic palladium. The consumption of tertiary phosphine in this way causes palladium to cluster and precipitate. Though catalyst life can be extended with increasing PPh_3/Pd ratios (Figure 5), deactivation eventually occurs. Accordingly, complexes of more nucleophillic tertiary phosphines deactivate faster and form phosphonium salt more rapidly

(12) Angelici, R. J. *Acc. Chem. Res.* **1972**, *5*, 335.
(13) Stille, J. K.; Wong, P. K. *J. Org. Chem.* **1975**, *40*, 532.
(14) Heck, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 2712.
(15) (a) James, D. E.; Hines, L. F.; Stille, J. K. *J. Am. Chem. Soc.* **1974**, *96*, 1133. (b) Heck, R. F. *J. Am. Chem. Soc.* **1969**, *91*, 6707. (c) Henry, P. M. *J. Org. Chem.* **1972**, *37*, 2443.
(16) (a) Loar, M. K.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4174. (b) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirostu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158. (c) Murahashi, S. I.; Nasta, T.; Tanigawa, Y. *Org. Synth.* **1984**, *62*, 39. (d) Goure, W. F.; Wright, M. E.; Davis, P. D.; Labadie, S. S.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 6417. (e) Larock, R. *J. Org. Chem.* **1976**, *41*, 2241.

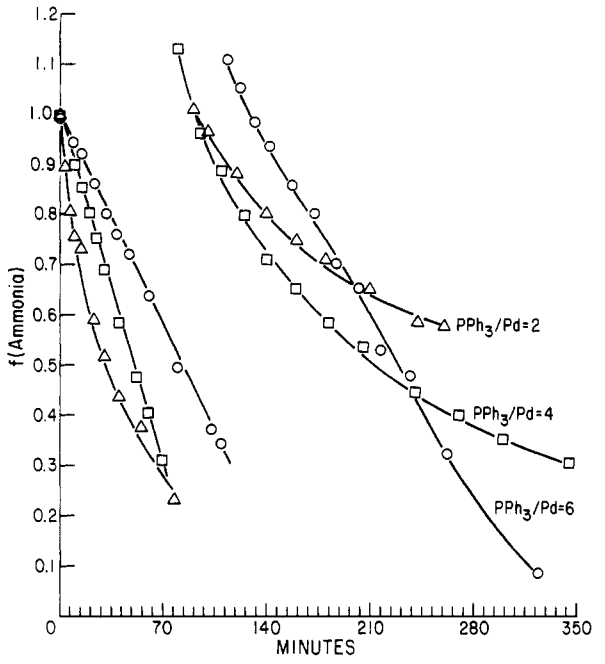


Figure 5. VCl amidation with ammonia at 100 °C catalyzed by $Pd(PPh_3)_n$ (240 psi CO, 0.36 mmol $Pd(PPh_3)_n$ derived from $Pd_3(TBAA)_3{\cdot}CHCl_3$ + PPh_3).

(Table III). When catalyst activity is prolonged with increased PPh_3/Pd ratios, small amounts of $Pd(PPh_3)_2Cl_2$ and 1,3-butadiene are detected among the products. Therefore, this slow side reaction is also able to make a measureable contribution toward deactivation during amidation with ammonia.

The type of amine used in VCl amidation can have a major influence on catalyst stability. Dimethylamine, for example, affords far greater catalyst stability than ammonia. We have, for example, achieved 1063 turnovers over a 6-day period with a quantitative yield of the Michael adduct **5**. Though the final rate is 27% of the maximum rate, this decline is difficult to interpret because of the large volume of product accumulated during this time. Since **5** is known to be thermally reversible, this process provides a route to *N,N*-dimethylacrylamide.[17]

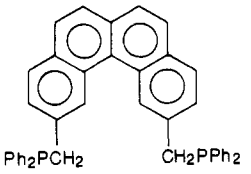
The greatly enhanced catalyst stability with dimethylamine originates from its ability to overcome the two identified causes of deactivation. First, the Michael addition of dimethylamine to *N,N*-dimethylacrylamide occurs much faster than phosphonium salt formation. ^{31}P NMR shows only an 11% yield of phosphonium salt, presumably $ClPh_3PCH_2CH_2CON(CH_3)_2$, during 1063 turnovers. Secondly, unlike ammonia, dimethylamine is able to rapidly reduce $Pd(PPh_3)_2Cl_2$ to the active catalyst, such that $Pd(PPh_3)_2Cl_2$ + $2PPh_3$ is catalytically equivalent to $Pd(PPh_3)_4$. Thus, to the extent that some coupling occurs and produces $Pd(PPh_3)_2Cl_2$, it is not a damaging side reaction with dimethylamine as it is with ammonia.

Influence of Coordination Stereochemistry. Cis- and Trans-Spanning Ligands. Coordination stereochemistry clearly plays an important role in the 1,1-reductive elimination of diorgano-Ni, Pd, and Pt complexes.[18] Since oxidative addition is usually stereospecific, it, too, is likely sensitive to coordination stereochemistry. We have examined the influence of coordination stereochemistry in PdL_n (L = monodentate and bidentate tertiary phosphine) on the overall amidation rate of VCl with dimethylamine. The three cases compared are the cis-spanning ligand, 1,2-bis(diphenylphosphino)ethane (dppe), n = 1, the trans-spanning ligand, 2,11-bis[(diphenylphosphino)methyl]benzo[*c*]phenanthrene (**12**) (transphos), n = 1, and the monodentate ligand, triphenylphosphine,

Table IV. Comparison of VCl Amidation Rates with Dimethylamine Catalyzed by Palladium Complexes of Cis- and Trans-Spanning Diphosphine Ligands, PdL_n[a]

L	n	rate(rel)	**5** (% yield)
dppe	1	1.0	98
12	1	8.1	87
PPh_3	4	18.0	100

[a] 0.36 mmol PdL_n, 0.12 mol dimethylamine, 240 psi CO, 90 °C.



12

n = 4. Transphos was first reported by Venanzi and coworkers and has been shown to be a trans-spanning ligand for several metals.[19] It has been used to successfully block 1,1-reductive elimination from dimethylpalladium complexes where cis stereochemistry is required.[18a] In all three cases, we generate the complex in situ from $Pd_3(TBAA)_3CHCl_3$ (TBAA = tribenzylidineacetylacetone) and the corresponding ligand. This method is reliable since amidation rates with either $Pd(PPh_3)_4$ or Pd(dppe) generated in this way are the same as those obtained with authentic $Pd(PPh_3)_4$ and $Pd(dppe)Cl_2$. The results show a pronounced stereochemical preference, with transphos giving rates eight times greater than dppe (Table IV). The reaction is faster still with triphenylphosphine. Possibly monodentate ligands can more easily comply with bond angle changes that occur through the transition state, not being constrained by a connecting group. The few $Pd(PR_3)_2$ complexes having bulky R groups that have been isolated are, indeed, nominally trans, e.g. $Pd[P(t\text{-}Bu)_2Ph]_2$ (176°) and $Pd[P(cyclohex)_3]_2$ (158°).[10d]

At this time, it is unclear which specific step (or steps is most influenced by coordination stereochemistry. A study of isolated reactions will likely be necessary to resolve this question.

Experimental Section

General Amidation Procedure and Analysis. All VCl amidation experiments were performed in an Autoclave Engineers 500-mL Zipperclave reactor. Important accessories included a proportioning controller with a custom-designed, full length heating mantel. The reaction was fitted with a thermowell and a full length internal glass liner providing ≤16 mL of dead volume between the liner and reactor wall. Stirring was performed with a Teflon-brand shaft and propeller blade having a second blade mounted on the shaft to stir the vapor space. A tachometer was used to control the stirring speed at 1000–1200 rpm. The reactor was also equipped with a heated gas sampling line having two bellows valves in series, a pressure gauge, a line to a vacuum

(17) (a) Matzner, M.; Robeson, L. M.; Wise, E. W.; McGrath, J. E. *Makromol. Chem.* **1982**, *183*, 2871. (b) Wiley, P. F. U.S. Pat. 2683741, July 13, 1954.

(18) (a) Gillie, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4933. (b) Tatsumi, K.; Nakamura, A.; Komiya, S.; Yamamoto, A.; Yamamoto, T. *J. Am. Chem. Soc.* **1984**, *106*, 8181. (c) Yamamoto, C. A.; Yamamoto, Y.; Komiya, S.; Ozawa, F. *Pure Appl. Chem.* **1984**, 1621.

(19) (a) De Stefano, N. J.; Johnson, D. K.; Lane, R. M.; Venanzi, L. M. *Helv. Chim. Acta* **1976**, *59*, 2674. (b) De Stefano, N. J.; Johnson, D. K.; Venanzi, L. M. *Ibid.* **1976**, *59*, 2683. (c) Johnson, D. K.; Pregosin, P. S.; Venanzi, L. M. *Ibid.* **1976**, *59*, 2690.

manifold, and a line to a U-tube used to condense and transfer amines to the reactor. The U-tube was also connected to a carbon monoxide cylinder through a shut-off valve in series with a metering valve. In this way, the amine was swept quantitatively into the reactor with carbon monoxide. Amines were condensed into the U-tube through a three-way valve.

In a general procedure, the glass liner was charged with catalyst and inserted into the reactor. It and all connecting lines were then evacuated to <0.2 mm. The reactor was then cooled with an ice bath and 63.4 g (1.01 mol) of VCl was condensed into it. The mixture was stirred as 800 mL of VCl vapor (2.0 g) was slowly vented through the sampling line to further assure an oxygen-free system. This VCl charge gives 53 mL of liquid VCl at 100 °C. The ice bath was then removed. The U-tube was evacuated, cooled in liquid nitrogen, and charged with ammonia or dimethylamine by vapor transfer. It was then heated with hot water (>90 °C) and the contents were transferred slowly to the reactor. The U-tube was then swept with carbon monoxide as the reactor was pressurized. The partial pressure noted for carbon monoxide is the difference between the combined pressure of amine/VCl and the final pressure. Pressurization is completed quickly and without stirring. When the stirrer is started, a pressure drop occurs due to the dissolution of gases. Carbon monoxide in aluminum cylinders should be used to avoid contamination by iron carbonyl. The warm-up period to the reaction temperature is reproducible, requiring about 38–39 min, and is designated as time zero. This period causes little uncertainty in the measurement of reaction rates because rates are slow below 80 °C. Moreover, the theoretical zero-point value in the rate curve is known from calibration.

The disappearance of amine is followed by gas chromatography using a $^1/_8$ in. × 6 ft silanized glass column packed with 80/100 Poropak PS operating at 60 °C for ammonia and 100 °C for dimethylamine. A 10 ft × $^1/_4$ in. glass column packed with Carbopak B/4% Carbowax/8% KOH (Supelco) operating isothermally at 30 °C was also used with dimethylamine. VCl is used as the internal standard. The amine peak is normalized by dividing its area by the are of the VCl peak. The mole fraction of amine (f) at any time is the normalized area divided by its graphically determined intercept value. Gas samples were taken by pressurizing the volume between the bellows values in the gas sampling line (2.0 mL). The line from the reactor to the bellows valves contains an annular $^1/_{16}$ in. stainless steel tube that extends into the vapor space in the reactor, and the entire line (including valves) is heated to ≥120 °C. Two successive samples were taken for each data point with the first discarded.

When desired, the amine can be recharged. With ammonia, this is accomplished in the usual way without interrupting the reaction. Following the recharging of ammonia, sufficient pressurization with carbon monoxide at the reaction temperature returns the system to the original total pressure. But the reaction must be interrupted with dimethylamine because its vapor pressure is relatively low. In this case, the reactor was first cooled in ice and then finally in dry ice/acetone to a pressure ≤170 psi. Dimethylamine was then charged in the usual way followed by a small amount of carbon monoxide to sweep out the U-tube. The reactor was then reheated and returned to the original total pressure with additional carbon monoxide.

At the conclusion of the reaction, the reactor is cooled in an ice bath and the contents are vented slowly to atmospheric pressure while stirring to prevent bumping. The reactor was then purged with nitrogen. The solid residue was extracted with 50–100 mL of D_2O, depending on conversion. Approximately 0.2 g of *tert*-butyl alcohol was added as an internal reference for quantitative ^1H NMR analysis, and the mixture was filtered. Analysis was performed with a Bruker XL200 spectrometer. VCl conversion was determined from an aliquot by potentiometric titration for Cl^- using aqueous silver nitrate and a chloride-specific electrode.

The identification of reaction products is based on the comparison of spectra with those of the following authentic materials.

3,3′,3″-Nitrilotripropanamide (1). Authentic **I** was prepared according to the procedure described by Marsh:[20] ^1H NMR (D_2O) δ 2.43 (t, 2, J = 7 Hz), 2.81 (t, 2, J = 7 Hz); ^{13}C NMR (D_2O) δ 33.05, 49.55, 179.99.

3,3′,3″-Nitrilotripropanamide Hydrochloride (3). The triamide 1 (1.19 g, 0.83 mmol) was dissolved in 4.0 mL of D_2O. Adding 1 drop of concentrated hydrochloric acid gave a downfield shift in the methylene triplets to δ 2.70 and 3.18 (J = 7 Hz), in excellent agreement with those observed in the amidation product (δ 2.73 and 3.21, J = 7 Hz).

(2-Carbamoylethyl)triphenylphosphonium Chloride (4). A three-neck, 50-mL flask fitted with a stirrer, nitrogen inlet, and a water-cooled condenser connected to a gas bubbler was charged with 40 mL of toluene, 1.73 g (6.60 mmol) of triphenylphosphine, and 0.43 g (6.0 mmol) of acrylamide. The system was stirred and swept with nitrogen. Anhydrous HCl (140 mL, 5.60 mmol) was slowly added with a syringe. The mixture was heated to 100 °C for 5 h, cooled to room temperature, filtered, and dried in a vacuum oven. The crude solid was crystallized from acetonitrile to give 1.06 g (2.87 mmol): 51.1% yield, mp 237.5–241 °C dec; ^{13}C NMR (D_2O) δ 19.25 (d, J = 56 Hz), 28.53, 118.92 (d, J = 87 Hz), 131.59 (d, J = 12 Hz), 134.71 (d, J = 9 Hz), 136.71, 175.2 (v. weak); ^1H NMR (D_2O) resonance for the 15 aromatic hydrogen atoms with peak at δ 7.82 is used for quantitation.

Anal. Calcd for $C_{21}H_{21}NPClO$: C, 68.2; H, 5.7; N, 3.79; P, 8.4; Cl, 9.59. Found: C, 67.9; H, 5.8; N, 3.81; P, 8.8; Cl, 9.91.

3-(Dimethylamino)-*N*,*N*-dimethylpropanamide (5) and 5·HCl. A 250-mL autoclave fitted with glass liner and magnetic stirrer was charge with 20.0 g (0.202 mol) of dimethylacrylamide, 43.5 g (0.240 mol) of 25% aqueous dimethylamine, and 0.2 g of 2,6-di-*tert*-butyl-*p*-cresol. The reaction was swept with argon, closed, and heated to 85 °C for 2.5 h. After cooling, the contents were purged with nitrogen overnight and distilled, giving 24.1 g (0.167 mol) of **5**, 83%, bp 92–94 °C (0.7 mm): mass spectrum (FAB) calcd for $C_7H_{16}N_2O$ 144.1262, found 144.1262; ^1H NMR (D_2O) δ 2.25 (s, 6), 2.65 (br s, 4), 2.94 (s, 3), 3.12 (s, 3). The broad singlet at δ 2.65 is converted to two triplets at δ 2.83 (J = 7 Hz) and 3.13 (J = 7 Hz) when completely protonated with HCl, while the singlet at δ 2.26 shifts to 2.67.

Tris(tribenzylideneacetylacetone)tripalladium·($CHCl_3$). This reagent was prepared according to the procedure described by Ishii.[21] We obtained a 48% yield of a dark purple crystalline solid, mp 128–131 °C dec [lit. mp 132–135 °C dec].

Amidation of VCl with Aniline. The reactor, charged with catalyst, was evacuated and then filled with nitrogen to a pressure slightly greater than 1 atm. A port at the reactor head was opened and nitrogen allowed to escape continuously as 11.0 g (0.12 mol) of aniline was charged with a syringe fitted with a long needle. The port was closed and the system evacuated to 5 mm. VCl and carbon monoxide were then charged in the usual way and the reaction mixture was heated to 100 °C. After 320 min, the reactor was rapidly cooled in ice water, vented, and purged with nitrogen. D_2O (100 mL) was injected and the contents were stirred at 50 °C for 1.5 h. The contents comprised a viscous, dark orange liquid and a D_2O phase, which were easily separated. The organic phase was rinsed with an additional 20 mL of D_2O and the extracts were combined. *t*-Butyl alcohol was then added for quantitative ^1H NMR, and we observed the aromatic protons of aniline hydrochloride. The solution was then titrated for chloride in the usual way to determine VCl conversion and VCl turnover rate (20 h^{-1}). Repeating this reaction for 105 and 376 min gave VCl turnover rates of 16 and 18 h^{-1}.

The organic phase was dissolved in 75 mL of THF and quantitatively removed from the reactor liner and stirrer. THF was evaporated and the residue dried under vacuum overnight to constant weight. ^1H NMR (DMSO-d_6) with *t*-butyl alcohol as an internal standard was used for quantitation. We observed the typical A_2B_2 pattern for NCH_2CH_2CON at δ 2.73 (J = 7 Hz) and 3.47 (J = 7 Hz), no vinyl groups, and an intense spectrum of aromatic hydrogen atoms. The FD mass spectrum showed the main component to have m/e 240, that expected for the anilide **6**.

Amidation of Chloropropenes. *cis*- and *trans*-1-chloropropene and 2-chloropropene were distilled from $NaHCO_3$ on a

(20) Marsh, J. T. *Text. Rec.* **1963**, *81*, 77.

(21) Ishii, Y.; Hasagawa, S.; Kimura, S.; Itoh, K. *J. Organomet. Chem.* **1974**, *73*, 411.

spinning band column to give collected fractions of ≥99.9% purity by GC. In three separate experiments, the reactor was charged with 0.41 g (0.36 mol) of $Pd(PPh_3)_4$, evacuated, and filled with argon. The chloropropene (48 g) was then charged with a syringe. Ammonia (0.12 mol) was condensed in the evacuated U-tube and transferred to the reactor followed by pressurization with 240 psi of carbon monoxide. The stirred reactor was then heated at 100 °C for 280, 288, and 270 min for *cis*- and *trans*-1-chloropropene and 2-chloropropene, respectively. After cooling and venting, the reactor was warmed with hot water and purged with nitrogen to remove residual chloropropene. The residue was then extracted with 25–30 mL of D_2O and analyzed by quantitative ^1H NMR (*tert*-butyl alcohol standard) and titration for chloride. Chloropropene conversions based on chloride analyses were 2.34, 4.37, and 2.15 mmol for *trans*- and *cis*-1-chloropropene and 2-chloropropene, respectively. The rate of ammonia consumption was too slow to accurately measure by GC.

The stereochemical assignments were based on the vinyl proton coupling constants obtained by matching computer-simulated spectra with the observed spectra (D_2O), as follows:

	$\delta(CH_3)$	$\delta(CH)$	$J_{H,H}$ (vinyl)	J_{H,CH_3} (gem)	J_{H,CH_3} (allyl)
7	2.00	5.92, 6.26	12	7.2	1.8
8	1.89	6.02, 6.86	16	7.0	1.7
9	1.96	5.54, 5.82	small		small

High Turnover Amidation of VCl with Dimethylamine. The reactor was charged in the usual way with 0.250 g (0.36 mmol) of $Pd(PPh_3)_2Cl_2$, 0.186 g (0.71 mmol) of triphenylphosphine, 63.4 g (1.01 mol) of VCl, 4.0 g (0.088 mol) of dimethylamine, and 240 psi of carbon monoxide. Amidation was performed at 90 °C and the disappearance of amine measured by GC using the 10 ft × $^1/_4$ in. Carbopak column described earlier. At 75% conversion, the reactor was recharged with 4.0 g (0.088 mol) of dimethylamine, as described earlier. Seven rechargings were performed over 3 days, with the reaction stopped overnight by cooling to room temperature. Because a large fraction of VCl had been converted during this period, the remaining VCl, carbon monoxide, and dimethylamine were vented, and fresh reagents were charged in the usual way to begin the fourth running day. After 12 rechargings over 6 days, the final rate of amine consumption was 0.54 mmol/min, 27% of the maximum rate of 2.0 mmol/min. The reactor was cooled, vented, and purged with nitrogen. D_2O (200 mL) was added slowly as gas evolution occurred. The reactor was reassembled and the mixture stirred for 1 h at room temperature. The mixture was filtered to give 307.9 g of clear, yellow-orange filtrate to which was added 1.07 g (14.4 mmol) of *t*-butyl alcohol as an internal standard for quantitative ^1H NMR.

Titration gave 0.389 mol of chloride and ^1H NMR showed 0.393 mol (100%) of the adduct **5**, based on the $(CH_3)_2N$ singlet at δ 2.34. The chloride titration was confirmed by the ^1H NMR analysis for dimethylamine hydrochloride (0.384 mol). This was determined from the singlet at δ 2.71 after subtracting the contribution of the four methylenic hydrogen atoms in **5**. ^{31}P NMR was required to analyze for the phosphonium salt since its concentration was very low. $Na_3PO_4 \cdot 12H_2O$ (0.0610 g) was added to 298.8 g of the D_2O extract as an internal standard. We observed a singlet at δ 22.3, 0.16 mmol (11%) based on the combined triphenylphosphine charged.

1,3-Butadiene from VCl. The reactor was charged with 0.82 g (0.71 mmol) of $Pd(PPh_3)_4$ and 63.4 g (1.01 mol) of VCl in the usual way. The stirred reactor was heated to 70 °C and the formation of 1,3-butadiene followed by GC using 0.05-mL gas samples with the Carbopak B column operating isothermally at 30 °C. The instrument had been calibrated with VCl as the internal standard. After 485 min, 0.69 mmol of butadiene (96%) was obtained. After cooling and venting the reactor, a yellow residue was recovered with ethanol, filtered, and washed with toluene and pentane. After drying in a vacuum oven, there remained 0.39 g (0.56 mmol), 78%, of $Pd(PPh_3)_2Cl_2$. This assignment was based upon its infrared spectrum which was identical with that of authentic material.

When the reaction was performed in the presence of amines, 0.118 mol of amine was condensed into the evacuated U-tube and transferred into the reactor by heating the U-tube with hot water (>90 °C). The residue of the reaction with dimethylamine was extracted with D_2O. Mass spectrometry (FAB) of the recovered solute showed $C_{22}H_{23}D_2NP$, *m/e* 336.1853 (theoretical 336.1850). Redissolving this solid in H_2O now gives an exchanged ion, $C_{22}H_{25}NP$, *m/e* 334. With diethylamine, the corresponding product recovered by H_2O extraction comprised $C_{24}H_{29}PN$, *m/e* 362.2032 (theoretical 362.2038).

Acknowledgment. My thanks to Thomas Barker for his excellent laboratory assistance. Thanks also to Richard Komoroski and John Shockcor for NMR spectra, to Robert Lattimer and Edward Harris for mass spectra, Richard Parker and Ronald Getts for the curve-fitting program, and to Gary Huvard, Angelo Magistro, and Professor John Fackler for helpful discussions. Finally, my thanks to Professor L. M. Venanzi, Technische Hochscule, Zurich, for his generous gift of transphos.

Registry No. **1**, 2664-61-1; **2**, 79-06-1; **3**, 104541-67-5; **4**, 110570-36-0; **5**, 17268-47-2; **5**·HCl, 110570-37-1; **6**, 79888-54-3; **7**, 31110-30-2; **8**, 625-37-6; **9**, 79-39-0; **12**, 61892-31-7; Ph_3P, 603-35-0; Me_2NH, 124-40-3; VCl, 75-01-4; $PhNH_2$, 62-53-3; $Pd(PPh_3)_4$, 14221-01-3; NH_3, 7664-41-7; $Pd(PPh_3)_2Cl_2$, 13965-03-2; $Ph_3P^+(CH_2)_2NMe_2$, 89207-39-6; $Ph_3P^+(CH_2)_2NEt_2$, 110570-38-2; $[P(p\text{-}C_6H_4CF_3)_3]_4Pd$, 105033-89-4; $[P(p\text{-}C_6H_4F)_3]_4Pd$, 105033-90-7; $[P(p\text{-}C_6H_4CH_3)_3]_4Pd$, 29032-56-2; $[P(cyclohex)_3]_4Pd$, 29032-55-1; $Pd(dppe)_2$, 31277-98-2; $Pd(dppb)_2$, 85318-49-6; $Pd_3(TBAA)_3 \cdot CHCl_3$, 54326-04-4; *t*-$Bu_3P$, 13716-12-6; *t*-$Bu_3P^+(CH_2)_2C(O)NH_2 \cdot Cl^-$, 110570-39-3; $(p\text{-}MeC_6H_4)_3P^+(CH_2)_2C(O)NH_2 \cdot Cl^-$, 110570-40-6; acrylamide, 79-06-1; *N,N*-dimethylacrylamide, 2680-03-7; *cis*-1-chloropropene, 16136-84-8; *trans*-1-chloropropene, 16136-85-9; 2-chloropropene, 557-98-2; 1,3-butadiene, 106-99-0.

Flavone-3-carboxylic Acids, Esters, and Related Compounds from β-Chloroarylidenemalonates

Osmo E. O. Hormi,* M. Riitta Moisio, and B. Christian Sund

Department of Organic Chemistry, Åbo Akademi, Akademigatan 1, SF-20500 Åbo, Finland

Received December 11, 1985

β-Chloroarylidenemalonates I have been transformed into β-(aryloxy)arylidenemalonates II. The ring closure of II in polyphosphoric acid leads to ethyl flavone-3-carboxylates and related compounds III. Hydrolysis of II gives β-(aryloxy)arylidenemalonic acids V, which on treatment with concentrated sulfuric acid or trifluoroacetic acid–trifluoroacetic anhydride give flavone-3-carboxylic acids and related compounds VI.

Synthetic utilization of the nucleophilic vinylic substitution (S_NV reaction) has provided an entry to many ring systems.[1] β-Chloromalonates I are of interest because they have an activated double bond for potential functionali-

0022-3263/87/1952-5272$01.50/0