PALLADIUM(0) AND PHASE TRANSFER CATALYZED CONVERSION OF AZIRINES TO STYRYLINDOLES

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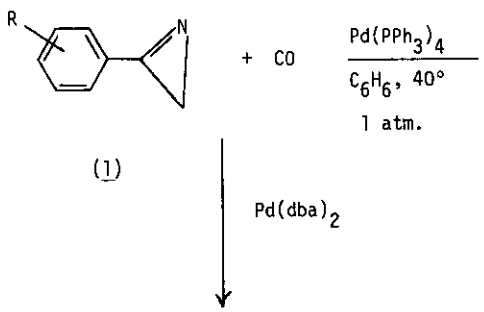
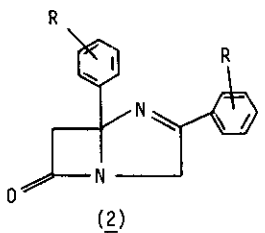
Abstract - 2-Styrylindoles were obtained in modest yields by the exposure of azirines to carbon monoxide, a palladium(0) catalyst, sodium hydroxide, benzene as the organic phase, and benzyltriethylammonium chloride as the phase transfer agent. The reaction is sensitive to the atmosphere used.

The chemistry of azirines has been extensively investigated in recent years[1,2]. The metal complex catalyzed ring opening of azirines has led to the development of several useful reaction processes[3]. Of particular note are palladium(0) catalyzed reactions, the course of which depends on the nature of the metal catalyst. When azirines (1) are exposed to carbon monoxide in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0), bicyclic β-lactams (2) are formed[4,5]. However, vinyl isocyanates (3) are obtained in a regiospecific manner using bis(dibenzylideneacetone)palladium(0) as the catalyst[5].

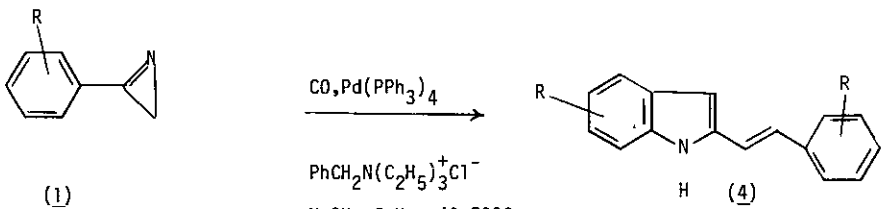




Phase transfer catalysis is a useful method for effecting a variety of valuable synthetic transformations catalyzed by transition metal complexes[6]. Examples include the regiospecific cobalt carbonyl catalyzed synthesis of butenolides from alkynes[7] and the palladium(0) induced conversion of vinylic dibromides to diynes, diacids or monoacids depending on the nature of the unsaturated halide, and the reaction conditions[8].

It seemed of interest to learn whether the palladium(0) catalyzed carbonylation of azirines, effected under phase transfer conditions, would afford the same (2, 3) or different products than the homogeneous reactions. We now report the results of this investigation.

Treatment of 2-phenylazirine [1, R=Ph, R'=H] with carbon monoxide, 50% sodium hydroxide, benzene as the organic phase, benzyltriethylammonium chloride as the phase transfer catalyst, and tetrakis-



(1) (4)

(triphenylphosphine)palladium(0) [10/1 ratio of 1/$Pd(PPh_3)_4$] as the metal catalyst, at 45°C for 1.5 h, afforded 2-styrylindole [4, R=H] in 29% yield of pure material. [See Table 1 for data]. Although the reaction should, in principle, proceed using a nitrogen instead of a carbon monoxide atmosphere, no reaction takes place under such conditions. However, the indole was obtained in 19% yield when carbon dioxide was used as the reaction atmosphere. The heterocycle 4 is not formed in the absence of the palladium(0) catalyst, but in the presence of carbon monoxide.

The conversion of 1 to 4 does occur in the absence of the phase transfer catalyst [i.e., as a biphasic process] but in lower yield (18%). Certain phase transfer agents are of no benefit and, in fact, are detrimental (dodecyltrimethylammonium chloride, tetrabutylammonium hydrogen sulfate). The concentration of base has little influence on the reaction since 4, R=H, was formed in 25% yield using more dilute sodium hydroxide (5N). It is noteworthy that the use of potassium carbonate as the base affords the β-lactam 2(R=H) in 35% yield, with 4(R=H) formed in 5% yield. This is the only instance where 2 was formed.

Increasing the proportion of palladium(0) [i.e., 5/1 ratio of 1/Pd(0)] results in a decrease in product yield. Bis[1,2-bis(diphenylphosphino)ethane]palladium(0) [$Pd(diphos)_2$] was a less useful catalyst than $Pd(PPh_3)_4$ while no reaction occurred using bis(dibenzylideneacetone)palladium(0) [$Pd(dba)_2$]. The palladium(II) catalyst, palladium acetate, afforded acetophenone in 41% yield

TABLE 1

Products of the Pd(0) and Phase Transfer Catalyzed Reactions of Azirines[a]

Azirine (1)	Reaction time, h	Temp. °C	$R_4N^+X^-$ [b]	Product	Yield[c] %
2-Phenylazirine	1.5	45	A	2-Styrylindole	29
	18	40	-	2-Styrylindole	18
	2.5	50	B	2-Styrylindole	20
	2.5	50	C	2-Styrylindole Acetophenone	6 5
	2.5	50	A	2-Styrylindole Acetophenone	18[d] 12
	18	50	A	2-Styrylindole Acetophenone	13[e] 3
2-p-Tolylazirine	2.5	50	A	2-p-Methylstyryl-6-methylindole	19
2-p-Methoxyphenylazirine	18	50	A	2-p-Methoxyphenyl-6-methoxyindole p-Methoxyacetophenone	15 23
2-o-Tolylazirine	2.5	50	A	2-o-Methylstyryl-4-methylindole o-Methylacetophenone	9 19
2,4-Dimethylphenylazirine	2.5	50	A	2(2,4-Dimethylstyryl)-4,6-dimethylindole 2,4-Dimethylacetophenone	6[f] 20

[a]Reaction using $Pd(PPh_3)_4$, CO, 50% NaOH, C_6H_6. [b]A=$PhCH_2N(C_2H_5)_3^+Cl^-$; B=$(C_4H_9)_4N^+HSO_4^-$; C=$C_{12}H_{25}N(CH_3)_3^+Cl^-$. [c]Yields are of analytically pure products, identified on the basis of analytical and spectral [ir, nmr(^1H, ^{13}C),ms] data. [d]Using 5:1 ratio of 1: $Pd(PPh_3)_4$. [e]Using benzene as the organic phse. [f]Yield of indole was 14% after a reaction time of 1 week.

from 2-phenylazirine (no indole). The substitution of other organic solvents for benzene, such as t-amyl alcohol or hexane, gives poorer yields of 4 (if formed at all). Pressure (350 psi) also inhibits the conversion of 1 to 4.

Modest yields of styrylindoles were also obtained from p-methyl- and p-methoxyphenylazirine, as well as from 2-methyl- and 2,4-dimethylazirine. The question arises as to the fate of the second nitrogen atom since two molecules of 1 are required to form 4. No nitrogen containing species was isolated as a by-product. It is conceivable that the nitrogen ends up as ammonium hydroxide. Styrylindoles have previously been obtained in much higher yields, from the homogeneous cobalt(0)[9] or rhodium(I)[10] reaction with azirines under a nitrogen atmosphere. Under carbon monoxide, vinyl isocyanates (3) are formed as in the case of $Pd(dba)_2$.

In conclusion, azirines are converted to styrylindoles by the palladium(0) and phase transfer catalyzed reaction of azirines. Neither β-lactams, nor vinyl isocyanates were detected in any of the Pd(0) phase transfer reaction. The different behavior, when compared to the homogeneous processes, is probably a consequence of the generation of anionic palladium conplexes under phase transfer catalysis.[8]

The following general procedure was used: a mixture of benzyltriethylammonium chloride [0.10g] in 50% NaOH (15 ml) and palladium(0) catalyst [0.34 - 0.43 mmol] in benzene (15 ml) was stirred for 1h at 40-50°C, under a carbon monoxide atmosphere. To this mixture was added, dropwise, 1, [3.4-4.3 mmol] in benzene (5 ml). The reaction was followed by thin layer chromatography and, when complete, was extracted with ether. The organic layer was washed with water, dried ($MgSO_4$), concentrated and then chromatographed on silica gel to give 9 on elution with ether-hexane. In some instances, additional 9 was obtained by ether extraction of the aqueous phase.

ACKNOWLEDGEMENT We are grateful to the Natural Sciences and Engineering Research Council of Canada for support of this research.

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Received, 16th May, 1983