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ORTHO VINYLATION OF ANILINES *VIA* CYCLOPALLADATION: A NEW ROUTE TO NITROGEN HETEROCYCLES

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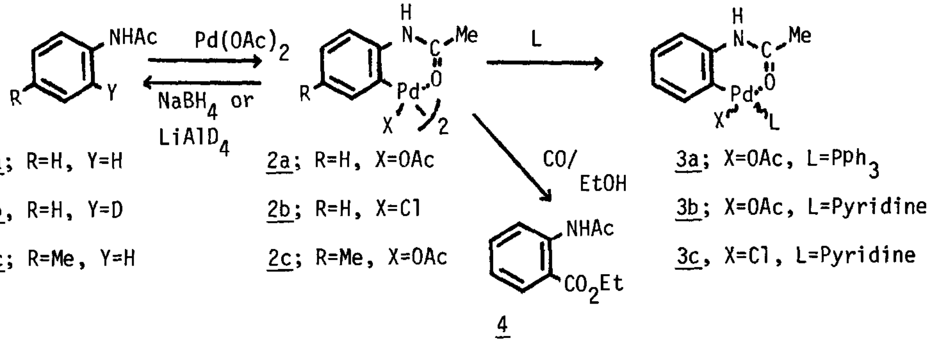
Summary: Preparation and chemical behaviors of cyclopalladated complexes of acetanilides were studied. Coupling reactions of these complexes with olefins afforded a variety of 2-substituted acetanilides which were subjected to intramolecular cyclization to quinolines.

Syntheses of heterocyclic compounds by utilization of transition metal complexes have been carried out by way of 2-halogeneted anilines.[1,2,3] Direct introduction of carbonyl group or vinylic moieties on the ortho position of anilines is also important to obtain the potential intermediates which can be converted into indoles, quinolines, and their related heterocyclic compounds.[4] Cyclopalladation of benzylidene aniline[5] and benzylamine derivatives[6] provided a new means of ortho substitution of aromatic ring in high selectivity. Rhodium-catalyzed quinoline synthesis from aniline was reported recently.[7] We report here a new ortho vinylation of anilines via cyclopalladation of acetanilides and its application to quinoline synthesis.

Treatment of acetanilide 1a with palladium acetate in refluxing toluene gave a yellow complex 2a,[8] dec., 199°, in 50 to 65% yields. Reduction of 2a with sodium borohydride or lithium aluminum deuteride afforded d_0- or d_1-acetanilide (1a or 1b). Addition of triphenylphosphine or pyridine to 2a produced monomeric complex 3a, creamy yellow, dec., 141-142°, or 3b, colorless, dec., 181°, respectively. Although the corresponding chloropalladium complex of acetanilide was reported by Cameron and Kilner,[9] the chemical behaviors of it were not examined. Attempted synthesis of the chloropalladium complex under their reaction conditions gave dichlorodianilinepalladium only.[10] Formation of chloropalladium complex 2b, greenish yellow, dec., 195° was achieved by stirring the mixture of 2a and lithium chloride in aqueous acetone. Addition of pyridine to 2b gave a colorless complex 3c, dec., 189°. Carbon monoxide reacted easily with

2a in ethanol to give N-acetylanthranilic ester 4, mp 66-68° (lit., mp 66°[11]) in a 84% yield. This is the first chemical evidence of the ortho palladated anilines.



1a; R=H, Y=H
1b, R=H, Y=D
1c; R=Me, Y=H

2a; R=H, X=OAc
2b; R=H, X=Cl
2c; R=Me, X=OAc

3a; X=OAc, L=PPh$_3$
3b; X=OAc, L=Pyridine
3c, X=Cl, L=Pyridine

The reaction of 2a with styrene (1.2 equivalent) in the presence of triethylamine (3.3 equivalent) was carried out in refluxing toluene for half an hour. The resulted mixture was filtered to remove metallic palladium, and the filtrate was evaporated in vacuo to give o-acetylaminostilbene 5a, mp 141-142° (lit., mp 140°[12]) in a 59.6% yield. The reactions of 2a with other olefins were run in the analogous way. Furthermore, the same vinylation of 2b was undergone. The palladium complex of acet-p-toluidide 2c, greenish yellow, dec., 201-202°, was prepared in a 44.6% yield, and the reaction of 2c with styrene or methyl vinyl ketone was carried out as shown in Table 1.

Acrolein diethyl acetal reacted with 2a to give the aldehyde 5e as well as quinoline 6a, which might be formed by the acidic components on silica gel column used in the course of purification.

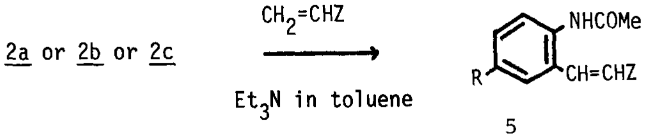
It is known that acid catalyzed cyclization of o-aminocinnamic acid produced carbostyril 6b.[13] Reduction of α-methyl-o-nitrobenzylidene acetone in the presence of zinc and hydrochloric acid was reported to afford quinaldine derivative.[14]

Reaction of 5e, 5f, and 5g with concentrated hydrochloric acid gave 6a (80.1%), 6b (54.5%), and 6c (71.0%) respectively.

5e or 5f or 5g

6a; Q=H
6b; Q=OH
6c; Q=Me

Table 1. Reaction of the complexes 2a, 2b, and 2c with olefins.



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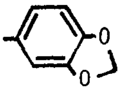
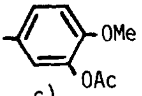
complex	olefin	product[a][g]	R	Z	yield (%)[b]	mp
2a	styrene	5a	H	-Ph	59.6	141-142°
2a	3,4-methylenedioxystyrene	5b	H		49.3	185-186°
2a	3-acetoxy-4-methoxystyrene	5c	H		86.9	135-137°
2a	acrylonitrile	5d	H	-CN[c]	45.7	171-172° (lit., 172-174°[e])
2a	acrolein diethyl acetal	5e	H	-CHO[c]	39.7[d]	163-164°
2a	methyl acrylate	5f	H	$-CO_2Me$[c]	49.3	136-137°
2a	methyl vinyl ketone	5g	H	-COMe[c]	82.8	126-127°
2a	vinyl acetate	5h	H	-OCOMe[c]	43.8	158°
2b	styrene	5a	H	-Ph	42.7[f]	
2b	methyl vinyl ketone	5g	H	-COMe[c]	63.0[f]	
2c	styrene	5i	Me	-Ph	57.0	159-160°
2c	methyl vinyl ketone	5j	Me	-COMe[c]	67.3	172-173°

a) Structures of all products are consistent with i.r. and n.m.r. spectra, and their analytical data. b) All yields refer to isolated materials. Yields are based on palladium complex. c) Reactions were carried out at lower temperature (bath temp. at 105°) with 3 to 5 equivalent of olefin and 3.3 equivalent of triethylamine. d) Quinoline was accompaied (37.8%) e) R. Pschon, Ber., 31, 1289 (1898). f) Reaction time was 10 min. g) Stereochemistry of the products 5 is assumed to be E-form by the coupling constants of olefinic protons. (J = 16 Hz in 5d, 5e, 5f, 5g, and 5i. J = 12 Hz in 5h.)

Meanwhile, the palladium catalyzed cyclization of 2-allylaniline to indole derivatives was reported recently.[1] Catalytic conversion of these 2-substituted acetanilides into various nitrogen heterocyclic compounds looks promising. Further studies on the preparation and chemical behaviors of analogous complexes, and their application to organic syntheses are in progress.

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