Tetrahedron Vol 37, pp. 173 to 177
© Pergamon Press Ltd., 1981 Printed in Great Britain

0040-4020/81/0101-0173 $02.00/0

PALLADIUM ASSISTED ORGANIC REACTIONS—II[1]

ORTHO-AMINOMETHYLSTILBENE DERIVATIVES

B. J. BRISDON* and P. NAIR
School of Chemistry, University of Bath, Bath BA2 7AY, England

and

S. F. DYKE*
Department of Chemistry, Queensland Institute of Technology, George Street, Brisbane 4001, Queensland, Australia

(*Received in UK* 10 *March* 1980)

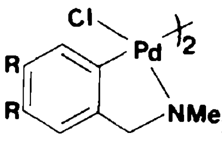
Abstract Di-μ-chlorobis(N,N-dimethyl-3,4-dimethoxybenzylamine-6-C,N)dipalladium (**1b**) reacts readily with a variety of styrenes to give good yields of the corresponding *o*-aminomethylstilbene derivatives.

Certain types of stilbene derivatives are of potential interest in the synthesis of 3-arylisoquinolines, protoberberines, benzo[c]phenanthridines, etc, and we were attracted by the possibility of utilising some organopalladium complexes to prepare them. Although the precise nature of the aryl-palladium intermediate is not known, the Heck reaction[2] seems to offer a useful route to stilbenes and we have employed it to prepare some 4-styrylisoquinoline derivatives,[1] although it does have certain disadvantages when either or both aromatic rings of the stilbene contain electron-donating substituents. No such problems are expected if cyclopalladated derivatives such as **1a** are used.[3-5] Holton[6] found that $\alpha\beta$-unsaturated ketones readily inserted into the Pd–C bond of both **1a** and **1b** yielding compounds **2a** and **2b** respectively, and in a review of C–C bond formation via Pd- complexes Tsuji[7] reported that complex **1a** reacted with styrene to give **3**, but no experimental details were given, and nothing further has been published on this reaction. There is an apparent similarity between these alkene insertion reactions of cyclic Pd- complexes and the Heck reaction, but the full scope of the former process has not been explored, nor has the usefulness of the products in further synthetic applications been examined in any detail.

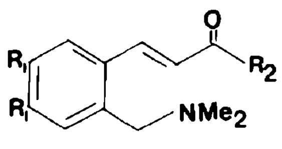
In this paper we describe the results obtained when **1b** was reacted with a series of eight styrene derivatives; the reactions with methyl vinyl ketone and with methyl acrylate are also included.

When an excess of 3,4-dimethoxy-N,N-dimethylbenzylamine was treated with Li_2PdCl_4, palladation occurred regiospecifically at C_6 in agreement with the observations of others.[6,8] The only other product isolated was the tetrachloropalladate salt of the protonated benzylamine derivative, and this was readily separated from the *ortho*-metallated product by chloroform extraction. Complex **1b**, obtained in high yield, seems to be stable indefinitely in the solid-state under normal storage conditions, and so provides a convenient starting material for the synthesis of *o*-substituted benzylic amines.

The ten α-alkenes listed in Table 1 readily inserted into the Pd–C linkage of **1b** under the appropriate experimental conditions, with subsequent formation of the products listed in Table 1, and deposition of metallic Pd. Both enones reacted in benzene solution at elevated temperatures to give high yields of products **2b** and **2c**, but none of the styrene derivatives would react under these conditions. However, changing to a more polar solvent system and cooling the reactants to 0° before mixing, resulted in generally high yields of the *trans*-stilbene derivatives **4a**–**4h**. In several reactions, small amounts of unreacted N,N-dimethyl-3,4-dimethoxybenzylamine were isolated, and in the reaction with *o*-chlorostyrene, small quantities of two isomeric derivatives (less than 5% of the total product) were indicated by tlc and spectroscopic examination, in addition to **4g**. Although the major product **4g** could be freed from the minor components by precipitation of the hydrochloride salt from ether, followed by recrystallisation from ethanol, attempts at separating and purifying the two minor components by chromatographic means were not completely successful. Both products were invariably contaminated with traces of the major *trans*-stilbene product, so preventing their complete characterisation. Nevertheless mass spectral and NMR evidence suggested that one minor product is the *cis*-stilbene **5a** in which C_6H (δ, 6.52 ppm) is shielded by the aromatic ring, and the *cis*-coupling of the olefinic protons is clearly seen in the doublet centred at 6.84 ppm (J = 8 Hz). The other constituent of the mixture appears to be the α-alkene (**6**). It too contains a shielded proton in the 6-position resonating at 6.63 ppm, and a quartet at 6.50 ppm in the spectrum is assigned to the =CH_2 group. Other absorbances [2.02 (6H, s, N$\underline{Me}_2$), 3.28 (2H, s, C$\underline{H}_2$N),



1a: R = H
1b: R = OMe



2a: R_1 = H; R_2 = Me
2b: R_1 = OMe; R_2 = Me
2c: R_1 = OMe; R_2 = OEt

Table 1. Analytical and NMR data on *o*-aminomethylstilbene derivatives

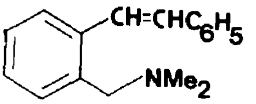
Alkene $CH_2{=}CHR$	Method	Yield (%)	Compound number	m.p.	Elemental Analysis Found (Calc.)			^1H NMR ($CDCl_3$, δ rel. to TMS, J[Hz])
					C	H	N	
R = -COMe	A	98	2b	83-84.5	67.95 (68.44)	8.00 (7.84)	5.42 (5.32)	2.23 (6H, s, $N\underline{Me}_2$); 2.36 (3H, s, $CO\underline{CH}_3$); 3.44 (2H, s, $\underline{CH}_2NMe_2$); 3.88 (6H, s, $O\underline{Me}$); 6.50 (1H, d[16], $\underline{CH}COCH_3$); 6.80 (1H, s, $C_3\underline{H}$); 7.08 (1H, s, $C_6\underline{H}$); 8.00 (1H, d[16], $Ar\underline{CH}$).
-COOEt	A B	85 93	2c	69.70	65.61 (65.53)	7.93 (7.85)	4.84 (4.78)	1.32 (3H, t[7], $OCH_2\underline{CH}_3$); 2.24 (6H, s, $N\underline{Me}_2$); 3.46 (2H, s, $\underline{CH}_2NMe_2$); 3.92 (6H, s, $O\underline{Me}$); 4.45 (2H, q[7], $O\underline{CH}_2CH_3$); 6.30 (1H, d[16], $CH{=}\underline{CH}CO$-); 6.90 (1H, s, $C_3\underline{H}$); 7.14 (1H, s, $C_6\underline{H}$); 8.20 (1H, d[16], -$\underline{CH}{=}CHCO$-).
$-C_6H_5$	B	94	4a	89-90	77.01 (76.77)	7.76 (7.74)	4.67 (4.71)	2.28 (6H, s, $N\underline{Me}_2$); 3.46 (2H, s, $\underline{CH}_2Ph$); 3.88 (3H, s, $O\underline{Me}$); 3.93 (3H, s, $O\underline{Me}$); 6.84 (1H, s, $C_3\underline{H}$); 6.88 (2H, d[16], $\underline{CH}Ph$); 7.15 (1H, s, $C_6\underline{H}$); 7.35 (5, m, $C_6\underline{H}_5$); 7.56 (1H, d[16], $\underline{CH}{=}CHPh$).
-p-$MeOC_6H_4$	B	76	4b	76.5-77.5	73.47 (73.40)	7.48 (7.65)	4.19 (4.28)	2.25 (6H, s, $N\underline{Me}_2$); 3.44 (2H, s, $\underline{CH}_2Ar$); 3.80 (3H, s, $O\underline{Me}$); 3.88 (3H, s, $O\underline{Me}$); 3.92 (3H, s, $O\underline{Me}$); 6.86 (1H, s, $C_3\underline{H}$); 6.90 (1H, d[16], $\underline{CH}C_6H_4OMe$); 7.18 (1H, s, $C_6\underline{H}$); 7.45 (1H, d[16], $\underline{CH}{=}CHC_6H_4OMe$); 6.85-7.45 (4H, m, $C_6\underline{H}_4OMe$).
-p-ClC_6H_4	B	94	4c	87.5-88	68.65 (68.76) and Cl, 10.66 (10.71)	6.68 (6.64)	4.35 (4.22)	2.26 (6H, s, $N\underline{Me}_2$); 3.45 (2H, s, $\underline{CH}_2Ar$); 3.90 (3H, s, $O\underline{Me}$); 3.93 (3H, s, $O\underline{Me}$); 6.87 (1H, d[16], $\underline{CH}C_6H_4Cl$); 6.85 (1H, s, $C_3\underline{H}$); 7.16 (1H, s, $C_6\underline{H}$); 7.30-7.55 (4H, m, $C_6\underline{H}_4Cl$); 7.56 (1H, d[16], $\underline{CH}{=}CHC_6H_4Cl$).

$-\underline{p}-NO_2C_6H_4$	B	> 75	4d	*260(d)	60.46 (60.24) and Cl, 9.38 (9.34)	6.18 (5.81)	7.40 (7.40)	2.26 (6H, s, $N\underline{Me}_2$); 3.46 (2H, s, $\underline{CH}_2Ar$); 3.88 (3H, s, $O\underline{Me}$); 3.92 (3H, s, $O\underline{Me}$); 6.84 (1H, s, $C_3\underline{H}$); 6.92 (1H, d[16], $\underline{CH}C_6H_4NO_2$); 7.16 (1H, s, $C_6\underline{H}$); 7.56 (2H, d[10], $C_2'\underline{H}$ and $C_6'\underline{H}$); 7.74 (1H, d[16], $\underline{CH}{=}CHC_6H_4NO_2$), 8.19 (2H, d[10], $C_3'\underline{H}$ and $C_5'\underline{H}$)
$-\underline{m}-ClC_6H_4$	B	61	4e	*246(d)	59.50 (61.96) and Cl, 19.29 (18.20)	5.91 (6.25)	3.72 (3.80)	2.24 (6H, s, $N\underline{Me}_2$); 3.44 (2H, s, $\underline{CH}_2NMe_2$), 3.86 (3H, s, $O\underline{Me}$); 3.90 (3H, s, $O\underline{Me}$); 6.79 (1H, d[16], $\underline{CH}C_6H_4Cl$); 6.83 (1H, s, $C_3\underline{H}$); 7.11 (1H, s, $C_6\underline{H}$); 7.15-7.40 (3H, m, $C_6\underline{H}_4Cl$); 7.44 (1H, s, $C_2'\underline{H}$); 7.52 (1H, d[16], $\underline{CH}{=}CHC_6H_4Cl$).
$-\underline{m}-NO_2C_6H_4$	B	80	4f	94-95	66.86 (66.67)	6.30 (6.43)	8.04 (8.19)	2.28 (6H, s, $N\underline{Me}_2$); 3.47 (2H, s, $\underline{CH}_2NMe_2$); 3.90 (3H, s, $O\underline{Me}$); 3.94 (3H, s, $O\underline{Me}$); 6.84 (1H, s, $C_3\underline{H}$); 6.92 (1H, d[16], $\underline{CH}C_6H_4NO_2$); 7.16 (1H, s, $C_6\underline{H}$), 7.70 (1H, d[16], $\underline{CH}{=}CHC_6H_4NO_2$); 7.40-7.85 (2H, m, $C_5'\underline{H}$ and $C_6'H$), 8.05 (1H, m, $C_4'H$), 8.32 (1H, m, $C_2'H$).
$-\underline{o}-ClC_6H_4$	B	> 61	4g	*238	62.35 (61.96) and Cl, 18.82 (19.30)	6.48 (6.25)	3.83 (3.80)	2.26 (6H, s, $N\underline{Me}_2$), 3.47 (2H, s, $\underline{CH}_2NMe_2$), 3.90 (3H, s, $O\underline{Me}$); 3.95 (3H, s, $O\underline{Me}$); 6.88 (1H, s, $C_3\underline{H}$); 7.15-7.45 (3H, m, $C_3'\underline{H}$, $C_4'\underline{H}$ and $C_5'\underline{H}$); 7.20 (1H, s, $C_6\underline{H}$); 7.30 (1H, d[16], $\underline{CH}C_6H_4Cl$); 7.56 (1H, d[16], $\underline{CH}{=}CHC_6H_4Cl$); 7.70 (1H, dd[8,2] $C_6'H$).
$-\underline{o}-NO_2C_6H_4$	B	32	4h	86	66.62 (66.67)	6.23 (6.43)	8.06 (8.19)	2.23 (6H, $N\underline{Me}_2$); 3.48 (2H, s, $\underline{CH}_2NMe_2$); 3.92 (3H, s, $O\underline{Me}$); 3.96 (3H, s, $O\underline{Me}$); 6.84 (1H, s, $C_3\underline{H}$), 7.16 (1H, s, $C_6\underline{H}$); 7.48‡ (2H, q[16], $-\underline{CH}{=}\underline{CH}-$); 7.28-8.00 (4H, m, $C_6\underline{H}_4NO_2$).

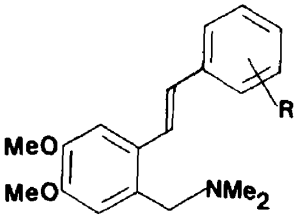
---

* Melting points and analytical data on the hydrochloride salts

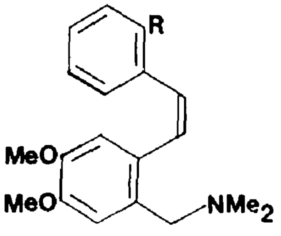
‡ Centre of AB quartet



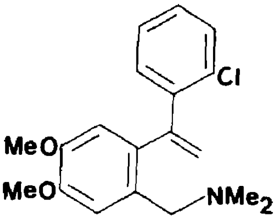
3



4a: R = H
4b: R = *p*-OMe
4c: R = *p*-Cl
4d: R = *p*-NO_2
4e: R = *m*-Cl
4f: R = *m*-NO_2
4g: R = *o*-Cl
4h: R = *o*-NO_2



5a: R = Cl



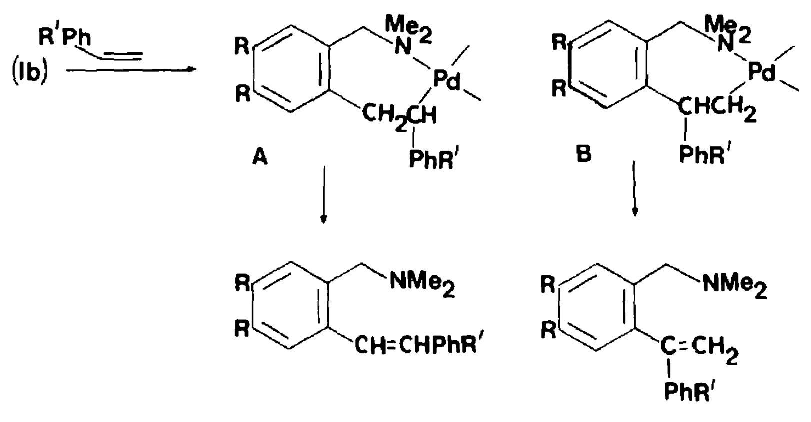
6

3.64 and 3.72 (6H, s, OMe), 7.00 (1H, s, C_3H) and 7.15–7.30 (4H, m, arom-H)] are little shifted from the corresponding band positions in the *cis*- or *trans*-stilbene derivatives. Surprisingly reaction of **1b** with *o*-nitrostyrene yielded only the *trans*-stilbene **4h**, with no evidence of any *cis*-isomer, or an α-alkene analogue of **6**. The anomolous reaction of *o*-chlorostyrene is of particular interest in a mechanistic context. The mechanism postulated for alkene insertion reactions into cyclometallated derivatives is basically similar to that for the Heck reaction,[9] in which insertion preceeds hydrogen elimination. There is now chemical and crystallographic evidence for the stability of some products of insertion reactions containing large ring systems closely related to (A),[10] and the β-hydrogen elimination reactions of Pd complexes are well documented. Such an elimination process can yield either the *cis*- or *trans*-stilbene, but in the absence of stabilising effects the *trans*-isomer is expected to predominate from a consideration of both the stereochemistry of the intermediate (A) and thermodynamic effects.

We suggest that the trace of **6** formed in the insertio reaction with *o*-chlorostyrene may arise from β hydrogen elimination from intermediate (B) in whic the alkene has inserted in such a way as to minimise th steric interaction of the bulky *ortho*-substituent wit the Pd atom.

EXPERIMENTAL

IR spectra were recorded on Perkin-Elmer 237 and 5 instruments. ^1H NMR spectra were measured with JEOL PS 100 spectrometer and are calibrated in parts p million (δ) downfield from TMS as internal standard. Ma spectra were recorded on an AEI MS 12 instrumen Microanalyses were performed by Dr. Strauss, Oxford. A m.ps are uncorrected. Pre-coated tlc plates (neutral alumin were used, the spots being detected by iodine vapour, a column chromatography was carried out on basic alumi (Brockman, grade 1). *p*-Nitrostyrene was prepared by methods,[11] the remaining styrenes were commercial available (Aldrich Chemical Co. Ltd.) and were used witho purification. N,N-dimethyl-3,4-dimethoxybenzylamine w prepared in 86% yield from veratraldehyde via N-methyl-3,



dimethoxybenzylamine according to standard lit. procedures,[12] and its physical and spectroscopic properties were in accord with lit. data on this compound prepared by an alternative method.[13]

Di-μ-chlorobis(N,N-*dimethyl-3,4-dimethoxybenzylamine-*6-C,N)*dipalladium* (**1b**). A soln of 2.0 g (10.3 mmol) of N,N-dimethyl-3,4-dimethoxybenzene in 10 ml dry MeOH was cooled in ice and stirred with 15.1 ml of a 0.34 molar methanolic solution of lithium tetrachloropalladate for 3 hr. The light-brown deposit was filtered off, washed with cold, dry MeOH and air dried. The crude product was extracted with $CHCl_3$ (5 × 25 cm^3) to remove traces of tetrachloropalladate salts and was isolated in 87% yield as a yellow powder, m.p. 160 (dec). (Found: C, 40.73; H, 4.75; N, 4.47. Calc. for $Pd_2Cl_2C_{22}H_{32}N_2O_4$: C, 39.30; H, 4.76; N, 4.47%). PMR (DMSO-d_6): 2.72 (6H, s, N$\underline{Me}_2$), 3.63 (3H, s, O$\underline{Me}$), 3.64 (3H, s, O$\underline{Me}$), 3.92 (2H, s, N$\underline{C}H_2$), 6.65 (1H, s, $\underline{H}C_2$), 7.32 (1H, s, $\underline{H}C_5$) Evaporation of the chloroform extract to low bulk yielded brown crystals of the tetrachloropalladate salt of the protonated base, m.p. 154 (dec). (Found: C, 40.78; H, 5.90; N, 4.32; Cl, 22.04. Calc. for $PdCl_4C_{22}H_{34}N_2O_4$: C, 41.22; H, 5.62; N, 4.37; Cl, 22.17). PMR (DMSO-d_6): 2.70 (6H, s, N$\underline{Me}_2$), 3.80 (6H, s, O$\underline{Me}$), 4.20 (2H, s, C$\underline{H}_2$N), 7.05–7.30 (3H, m, $\underline{H}C_2$, $\underline{H}C_5$, $\underline{H}C_6$), 10.5 (1H, br.s, $\overset{+}{N}\underline{H}Me_2$).

Two procedures were used to react the cyclometallated complex with the alkene derivatives. Both employed a five-fold excess of alkene and base. One example of each procedure is given below and any variations in reaction conditions for other reactants are noted in Table 1.

Procedure A. To 0.50 g (7.5 mmol) of the Pd complex in 15 ml dry benzene was added 0.6 ml NEt_3 and 0.32 ml (37.5 mmol) methylvinyl ketone. The soln was heated under reflux for 2 hr during which time a mirror of metallic Pd was deposited in the flask. The soln was cooled, filtered over celite and the residue washed with 5 ml 2M NH_4OH followed by 5 ml $CHCl_3$. The aqueous layer was extracted with 5 ml $CHCl_3$ and then discarded, and the combined $CHCl_3$ extracts evaporated leaving an oily residue. This residue and the benzene filtrate were combined and extracted with 2M HCl. The aqueous, acidic layer was washed with benzene and then basified with NH_4OH aq and extracted with 3 × 25 ml CH_2Cl_2. The extract was washed with water, dried over Na_2SO_4 and the solvent evaporated to yield the crude product. Final traces of metallic Pd were removed by filtering a CH_2Cl_2 soln of the product through a short column of basic alumina and eluting with CH_2Cl_2. Evaporation of the solvent and recrystallisation from Et_2O yielded 0.39 g (98%) of **2b**, as white crystals, m.p. 83–84.5 .

Procedure B. To 0.37 g (5.5 mmol) Pd complex in 15 ml of glacial AcOH/CH_2Cl_2 (3:1) was added 0.4 cm^3 of NEt_3 and the soln cooled to 0 . 0.24 ml, (27.5 mmol) styrene was added and the stirred mixture slowly allowed to warm up to room temp. After 48 hr the mixture was filtered over celite, and the residue washed with 10 ml 2M Na_2CO_3 aq, followed by 5 ml CH_2Cl_2. Both the aqueous and non-aqueous washings were combined with the original filtrate and basified with Na_2CO_3. The organic layer was separated, washed with water, and the solvent evaporated. The brown oil obtained was dissolved in 25 ml benzene and extracted with 3 × 25 ml 2M HCl aq. The aqueous layer was washed with benzene, basified with 2M NH_4OH aq and extracted with 3 × 30 ml CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4 and the solvent evaporated to yield the crude product as a yellow oil. Final traces of metallic Pd were removed as above and recrystallisation from a mixture of Et_2O/petroleum spirit gave colourless needle shaped crystals of **4a**, m.p. 89 90 yield 94%.

REFERENCES

[1] Part 1: S. F. Dyke and M. McCartney, *Tetrahedron*.

[2] R. F. Heck, *Accounts Chem. Res.* **12**, 146 (1979).

[3] A. C. Cope and E. C. Friedrich, *J. Am. Chem. Soc.* **90**, 909 (1968).

[4] For a review of cyclopalladation see S. Trofimenko, *Inorg. Chem.* **12**, 1215 (1973).

[5] For a review of cyclometallation see M. I. Bruce, *Angew Chem.* Int. Ed. **16**, 73 (1977).

[6] R. A. Holton, *Tetrahedron Letters* 355 (1977).

[7] J. Tsuji, *Accounts Chem. Res.* **2**, 144 (1969).

[8] R. A. Holton and R. G. Davis, *J. Am. Chem. Soc.* **99**, 4175 (1977).

[9] P. M. Maitlis, *The Organic Chemistry of Palladium*, Vol. 2, Chap. 1, Academic Press, New York (1971).

[10] A. Bahsoun, J. Dehand, M. Pfeffer, M. Zinsius, S-E. Bouaoud and G. Le Borgne, *J. Chem. Soc.* Dalton 547 (1979).

[11] R. H. Wiley and N. R. Smith, *J. Am. Chem. Soc.* **72**, 5198 (1950).

[12] R. N. Icke, B. B. Wisegarver and G. A. Alles, *Org. Synth. Coll.* **3**, 723 (1965).

[13] E. L. Elier, T. N. Ferdinand and M. C. Hermann, *J. Org. Chem.* **19**, 1693 (1954).