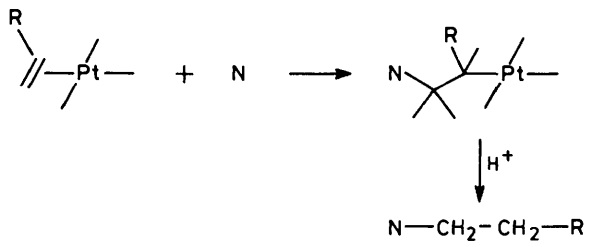
Platinum Complexes in Organic Synthesis: Catalytic *ortho*-Alkenylation of Anilines

Augusto De Renzi, Achille Panunzi,* Antonio Saporito, and Aldo Vitagliano
Dipartimento di Chimica, Università di Napoli, Via Mezzocannone 4, 80134 Napoli, Italy

Anilines, 3-substituted with an *ortho–para* activating group, undergo, after protection of the amino group by acetylation, electrophilic addition with platinum(II)-co-ordinated 1,1-dimethylallene. This alkenylation is regiospecific, affording *o*-isopentenyl derivatives. A similar reaction is also observed with diphenylamine. A catalytic process is described.

An olefinic bond, when co-ordinated to Pt^{II} in a square-planar arrangement, is activated [1] towards the addition of nucleophiles. Most of the reactions examined [2] so far are stoicheiometric processes, as the C–Pt σ bond formed shows a high stability or, more probably, a high kinetic inertness in these compounds. However, protolysis of this bond allows the organic moiety to



be recovered in quite satisfactory yields. Recently,[3] we found that an activated aromatic ring, *e.g.* a phenol, is an effective nucleophile when a Pt^{II} complex of 1,1-dimethylallene (DMA) is used as the substrate. This reaction appears to be of particular interest for two reasons: (i) only the carbon atoms *ortho* to the hydroxy group are involved in the addition; (ii) the organic product is released in the reaction medium by an intramolecular protolysis in a one-step process. Thus, a catalytic procedure was devised and *o*-isopentenylphenols were obtained in reasonable yields starting from phenols and DMA.

We have now examined the possibility of extending this reaction to other activated aromatic rings, in particular anilines.

Results and Discussion

The addition of an aniline to the Pt^{II}-co-ordinated double bond in the *cis*-$[PtCl_2(DMA)(PPh_3)]$ (**A**) complex can in principle occur by two different pathways (Scheme 1). To date, however, only type (**I**) products have been obtained and characterized [4] because the amino group is a much more powerful nucleophile than the aromatic ring. Nevertheless, type (**II**) species, or possibly related products, should be formed if the addition of the amino group is hindered by electronic and/or steric factors. Three *N*-substituted anilines, namely *N*-t-butylaniline (**1**), diphenylamine (**2**), and *N*,*N*-dimethylaniline (**3**), were allowed to react with complex (**A**) (1 : 1 molar ratio) in chloroform solution. In the first case, a type (**I**) compound (R^1 = H, R^2 = Bu^t) was obtained as white well-formed crystals that precipitated from the reaction medium. The structure of this alkenylammonium complex was established by analytical and ^1H n.m.r. data. The C–Pt bond showed a high resistance to the protolysis, cleavage occurring only on prolonged boiling with aqueous concentrated HCl. Under these experimental conditions, a mixture† of *N*-t-butyl-*N*-(3-hydroxy-3-methyl)butylaniline and *N*-t-butyl-*N*-(3-chloro-3-methyl)butylaniline hydrochlorides was isolated. The aniline (**2**) behaved differently, a slow precipitation of the orange complex $[PtCl_2(PPh_3)]_2$ occurring, and an *N*-phenyl-isopentenylaniline was isolated from the mother-liquor in very high yield with respect to the starting complex (**A**). This product conceivably results from the formation and subsequent rearrangement of a type (**II**) intermediate (R^1 = H, R^2 = Ph). The ^1H and ^{13}C n.m.r. spectra excluded the possibility that the alkenyl is *para* to the NH group. On the basis of the i.r. spectra and the similarities of this process with the reported [4] reactions between complex (**A**) and phenols, the hydrocarbon chain was located *ortho* to the amino group.

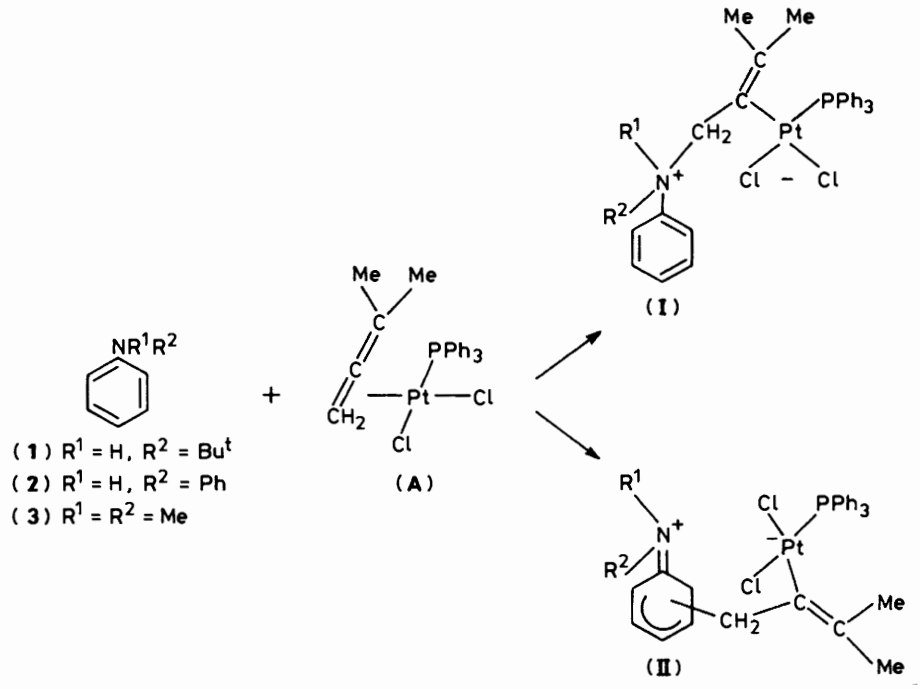
The difference in behaviour of compounds (**1**) and (**2**) seems to indicate that the electronic factors have a greater effect than the steric factors on the tendency for addition of secondary anilines to the co-ordinated DMA to occur at the nitrogen. In fact, the dissociation constant (K_a) [5] of the diphenylamine is 10^6 times higher than that of *N*-t-butylaniline, while the steric hindrance at the nitrogen atom of compounds (**1**) and (**2**) is comparable.

No reaction was observed when *N*,*N*-dimethylaniline (**3**) was used as the nucleophile. In this case the lack of addition at the tertiary nitrogen could be reasonably imputed to steric factors. The accompanying lack of the *C*-alkenylation can be attributed to the absence of an acidic proton on the nitrogen atom; this explanation is supported by our previous results [3] concerning the similar *C*-alkenylation of phenols, and no such reaction occurred with phenyl ethers.

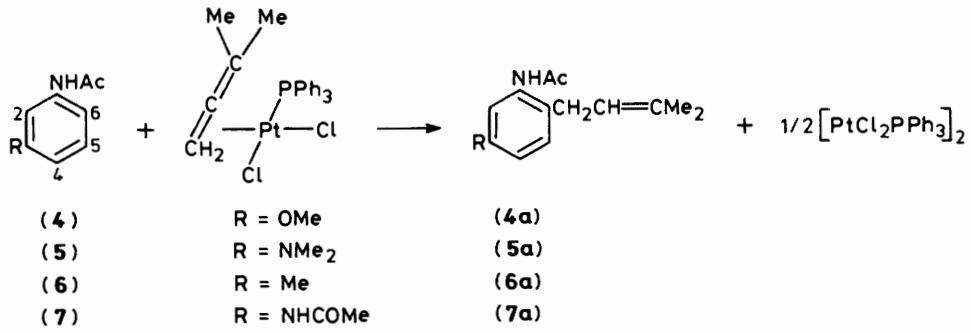
We therefore acetylated the nitrogen atom in order to reduce its nucleophilic character without losing the required NH group. Again no reaction was observed under our experimental conditions with *N*-acetylaniline as the nucleophile, probably owing to the weak activating effect of the NHAc substituent. Therefore, different *meta*-substituted *N*-acetylanilines [*m*-RC_6H_4NHAc] in which R is an *ortho–para* activating group, (**4**)—(**7**), were tested. In all cases a *C*-alkenylation took place. The reactivity order is as expected: (**5**) > (**4**) ⩾ (**6**) ≃ (**7**). In fact, when these acetanilides were treated with complex (**A**), the *N*′-acetyl-*N*,*N*-dimethyl-*m*-phenylenediamine (**5**) gave the *C*-isopentenyl derivative in almost quantitative yield, while with *N*-acetyl-*m*-toluidine (**6**) or *N*,*N*′-diacetyl-*m*-phenylenediamine (**7**) a 40—50% conversion was obtained.

As shown in Scheme 2, the reaction is highly selective, only the derivative in which the isopentenyl group is *ortho* to the acetylamino substituent being isolated. The structure was assigned on the basis of the ^1H n.m.r. spectra and n.O.e. experiments on the isolated organic products. Furthermore, it

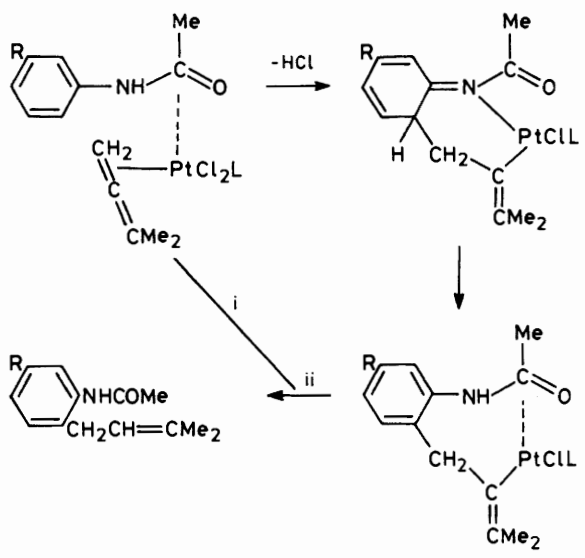
† The room temperature protolysis [4] of type (I) complexes with anhydrous HCl allows the alkenylammonium salts to be isolated without the occurrence of side reactions. When aqueous HCl is used, mixtures of hydroxy- and chloro-ammonium salts are always obtained (A. De Renzi, unpublished results).



Scheme. 1.



Scheme 2.



Scheme 3. *Reagents:* i, DMA; ii, HCl

was observed that steric factors direct the addition towards the less hindered *ortho* position. The other possible *ortho* derivative was only isolated and characterized in the case where R = OMe (**4b**) (*ca.* 8% of the whole reaction product). Trace amounts of a possibly similar by-product were observed with the acetanilides (**6**) and (**7**). Only those compounds in Scheme 2 were obtained when R = NMe_2. It is worth noting that in this case the organic reaction product is only partially released in the reaction medium. This may be because it reacts with the binuclear platinum complex *via* co-ordination of the dimethylamino group; however, the organic moiety can be completely recovered by treatment with cyanide or triphenylphosphine. The ^1H n.m.r. data of the reaction products and the starting acetanilides are reported in the Table.

The possible reaction mechanism illustrated in Scheme 3 agrees with our experimental results and shows very similar features to those supposed [3] for the phenol–DMA–Pt^{II} system. The lack of reactivity of the *N*-acetyl-*N*-methyl-*m*-anisidine (**8**) confirms that the presence of an acidic hydrogen on the Pt-anchoring group is necessary in this case as well as for phenols. It is questionable whether the first interaction between the starting acetanilide and the platinum complex occurs *via* the nitrogen or the oxygen atom of the acetylamino group. The latter route seems more reasonable in the light of the higher

Table. ^{1}H N.m.r. parameters of the starting *N*-acetylanilines and their alkenylation products[a]

Compound	NH	2-H	4-H	5-H	6-H	R	Ac	CH_2	CH	CMe_2
(**4**)	7.56br s	7.27s	6.65d	7.19t	6.97d	3.78s	2.15s			
(**4a**)	7.35br s	7.61s	6.64d	7.05d		3.78s	2.13s	3.25d	5.15t	1.82s, 1.79s
(**4b**)	7.3br s		6.69d	7.16t	7.54d	3.82s	2.11s	3.39d	5.08t	1.84s, 1.75s
(**5**)	7.53br s	7.07s	6.48d	7.15t	6.76d	2.95s	2.15s			
(**5a**)	7.4br s	7.52s	6.61d	7.04d		2.94s	2.11s	3.32d	5.20t	1.80s, 1.76s
(**6**)	7.44br s	7.35s	6.90d	7.18t	7.27d	2.32s	2.15s			
(**6a**)	7.4br s	7.68s	6.88d	7.04d		2.33s	2.13s	3.27d	5.19t	1.80s, 1.77s
(**7**)	7.57br s	7.84s		7.27br s (3 H)			2.20s			
(**7a**)	7.35br s	7.81s	7.58d[b]	7.12d[b]			2.13s	3.29d	5.19t	1.78s, 1.58s

[a] Chemical shifts are given as δ values. The numbering of the 3-R-acetylanilines is retained for all compounds, even where unsystematic, for ease of comparison. [b] These assignments could be interchanged.

basicity of the oxygen atom and of the previously[6] reported isolation of *ortho*-palladated acetanilides with Pd–O bonds in a closely related vinylation process.*

The finding that the metal is recovered as a binuclear phosphine complex prompted us to try catalytic runs. Diphenylamine and the reported *N*-acetylanilines were used as substrates. In all runs a 1:1 amine–DMA ratio and a 50:1 amine–Pt complex ratio were adopted. The complex *cis*-$[PtCl_2(C_2H_4)(PPh_3)]$ (**B**) was used as the catalyst. A few other platinum complexes were tested but appeared less effective in promoting the reaction. Diphenylamine was markedly more reactive, and after 6 h at 55 °C a conversion of greater than 90% was obtained. Only one product was isolated, identical with that characterized in the stoicheiometric reaction. With *N*-acetyl-*m*-anisine (**4**) 75% conversion had occurred after 24 h at 55 °C. The catalytic conversion of the other acetanilides under the same conditions gave lower yields (10—15%). In fact, a lower reactivity is expected for compounds (**6**) and (**7**) owing to the poor activation of the aromatic ring. The presence of the NMe_2 group in compound (**5**) should be responsible, as discussed above, for catalyst poisoning.

Conclusions

The above results show that anilines, like phenols and heterocycles,† are possible substrates for alkenylation with DMA promoted by d^8 ions. It must be noted that the regiospecific *ortho* functionalization of anilines by classical methods is fairly cumbersome.[7] Therefore the reported process represents a useful synthetic development. Although the aromatic substrate treated with the DMA must fulfil the requirements discussed in this paper, the following apply: (i) the process can, in principle, be applied to a fairly broad range of anilines; (ii) the reaction is very selective, only one product generally being observed, or the major product being obtained in more than 90% yield.

Experimental

Chromatographic separations were carried out with a Perkin-Elmer Series 2 liquid Chromatograph using Silica A or ODS columns and eluting with n-hexane–chloroform–methanol or water–methyl cyanide mixtures. Chromatographic analyses were performed with a Perkin-Elmer Sigma 3B gas chromatograph using a 4-m column of SE-30 on Chromosorb W. ^{1}H N.m.r. spectra were recorded on a Brucker WH 270 spectrometer in $CDCl_3$ solution with Me_4Si as internal reference. Elemental analyses were carried out by the Analytical Laboratories, Engelskirchen, West Germany.

All solvents and reagents were of analytical grade. The anilines were commercial products except for *N*,*N*-dimethyl-*m*-phenylenediamine[8] and *N*-t-butylaniline[9] which were synthesized according to literature methods. Acetylation of the anilines was accomplished by standard procedures.[10] *N*-Acetyl-*N*-methyl-*m*-anisidine was obtained by methylation[11] of *N*-acetyl-*m*-anisidine with MeI in the presence of NaH. *cis*-$[PtCl_2(DMA)(PPh_3)]$ and *cis*-$[PtCl_2(C_2H_4)(PPh_3)]$ were synthesized by known methods.[4]

Reaction between N-*t-Butylaniline* (**1**) *and Complex* (**A**).—To a chloroform solution (10 ml) of complex (**A**) (0.60 g, 1 mmol), *N*-t-butylaniline (0.15 g, 1 mmol) was added at room temperature. Within a few minutes white crystals began to precipitate. After 0.5 h at 0 °C, *dichloro*[1-(N-*t-butylammoniophenylmethyl*)-2-*methylprop*-1-*enyl*] *triphenylphosphineplatinum* (**II**) (R^1 = Bu^t, R^2 = H) (0.70 g, 93%) was isolated by filtration, m.p. 158—159 °C(decomp.)(Found: C, 53.3; H, 5.1; N, 2.0. $C_{33}H_{38}Cl_2NPPt$ requires C, 53.2; H, 5.15; N, 1.9%); δ_H($CDCl_3$–TFA) 0.45 (3 H, br s, =CMe), 1.53 (9 H, s, CMe_3), 1.74 (3 H, br s, =CMe), 3.40 (1 H, d, C*H*HN), 3.6 (1 H, m, CH*H*N), and 8.0—7.0 (21 H, m, ArH and NH).

To isolate the organic moiety, the complex (0.2 g) was boiled with aqueous concentrated HCl (10 ml) for 24 h. The aqueous solution was filtered and concentrated under reduced pressure. The residue was dissolved in aqueous KOH (2 ml) and the amine was taken up in diethyl ether. Acidification with HCl and concentration under reduced pressure afforded the amine hydrochloride as a white solid. ^{1}H N.m.r. and mass spectra of this material confirmed the presence of *N*-(3-hydroxy-3-methyl)butyl-*N*-t-butylaniline and *N*-(3-chloro-3-methyl)butyl-*N*-t-butylaniline in a 2:1 approximate ratio. The ^{1}H n.m.r. spectrum of the mixture of the free amines showed signals at δ_H 1.13 (br s, CMe_2), 1.30 (br s, CMe_3), 1.74 (t, CH_2COH), 1.82 (t, CH_2CCl), 3.6 (two superimposed t, NCH_2), and 7.3—6.5 (m, ArH). The mass spectrum showed peaks at *m*/*z* 235 (M^+) and 220 (M − Me) attributable to compound (**1a**) and 255—253 (2 peaks, M^+) and 240—238 (2 peaks, M − Me) attributable to (**1b**).

Reaction between Diphenylamine (**2**) *and Complex* (**A**).—To a chloroform solution (5 ml) of complex (**A**) (0.3 g, 0.5 mmol), diphenylamine (0.085 g, 0.5 mmol) was added at room temperature. The mixture was heated at 45 °C for 4 h. An orange crystalline solid precipitated {0.26 g, $[PtCl_2(PPh_3)]_2$}. The mother solution was concentrated under reduced pressure affording a yellow-green oil (0.13 g). Chromatography on silica

* However, a Pt ⋯N interaction, involving the tautomeric form of the amide group, cannot be excluded.

† Activated aromatic heterocycles can be alkenylated by Pt^{II}-coordinated DMA (A. De Renzi *et al.*, to be published). For instance, indole reacts with complex (**A**) to give a derivative bearing the alkenyl group in the β-position of the penta-atomic ring.

gel with n-hexane–ethyl acetate (95:5) as eluant yielded N-[2-(3-*methylbut*-2-*enyl*)*phenyl*]*aniline* (0.098 g, 82%) as a yellow oil (Found: C, 85.8; H, 8.0; N, 6.1. $C_{17}H_{19}N$ requires C, 86.05; H, 8.1; N, 5.9%); $\nu_{max.}$ (liquid film) 3 400 (NH), 750 and 700 cm^{-1} [CH(δ-bond)]; δ_H 1.74 (6 H, br s, $=CMe_2$), 3.29 (2 H, d, CH_2), 5.24 (1 H, t, =CH), 5.58 (1 H, br s, NH), and 7.3—6.8 (9 H, m, ArH); δ_C 17.8 and 25.9 [two q, $=C(CH_3)_2$], 31.3 (t, CH_2), 117.2, 119.0, 120.3, 122.0, 122.4, 126.9, 129.3, and 130.1 (eight d, 9 ArC and =CH), 131.5, 134.0, 141.5, and 144.2 (four s, 3 ArC and =C).

Reaction between the N-*Acetylanilines* (**4**)—(**7**) *and Complex* (**A**).—To a solution of complex (**A**) (0.6 g, 1 mmol) in chloroform (5 ml), was added an equimolar amount of the *N*-acetylaniline. The mixture was heated at 55 °C for 18 h, then the precipitated $[PtCl_2(PPh_3)]_2$ complex filtered off and weighed. The solution was concentrated and the *o*-isopentenylacetylanilines were isolated by h.p.l.c. In the reaction with the *N*-acetylaniline (**5**), the precipitation of the platinum complex was not quantitative, so a slight excess of PPh_3 was added to the mother liquor. $[PtCl_2(PPh_3)_2]$ complex formed on standing and was removed by filtration before purification by h.p.l.c. The following compounds were obtained: N-[2-(3-*methylbut*-2-*enyl*)-5-methoxyphenyl]acetamide (**4a**) (0.175 g, 74%), m.p. 76 °C (Found: C, 72.2; H, 8.1; N, 6.1. $C_{14}H_{19}NO_2$ requires C, 72.1; H, 8.2; N, 6.0%); N-[2-(3-*methylbut*-2-*enyl*)-3-*methoxyphenyl*]-*acetamide* (18 mg, 7.5%), m.p. 112 °C (Found: C, 72.3; H, 8.0; N, 6.2. $C_{14}H_{19}NO_2$ requires C, 72.1; H, 8.2; N, 6.0%); N-[2-(3-*methylbut*-2-*enyl*)-5-*dimethylaminophenyl*]*acetamide* (**5a**) (0.220 g, 89%), m.p. 96 °C (Found: C, 73.2; H, 9.0; N, 11.5. $C_{15}H_{22}N_2O$ requires C, 73.1; H, 9.0; N, 11.4%); N-[2-(3-*methylbut*-2-*enyl*)-5-*methylphenyl*]*acetamide* (**6a**) (0.082 g, 38%), m.p. 72 °C (Found: C, 77.5; H, 8.9; N, 6.6. $C_{14}H_{19}NO$ requires C, 77.4; H, 8.8; N, 6.45%); N,N′-[2-(3-*methylbut*-2-*enyl*)*phenylene*]-1,5-*bis-acetamide* (**7a**) (0.120 g, 46%), m.p. 206 °C (Found: C, 69.4; H, 7.7; N, 10.9. $C_{15}H_{20}N_2O_2$ requires C, 69.2; H, 7.75; N, 10.75%).

Compounds (**4a**), (**4b**), and (**6a**) were purified using a Silica A column with n-hexane–chloroform–methanol (86.2:13:0.8) as eluant. For compounds (**5a**) and (**7a**) a ODS column with water–methyl cyanide (1:1) as eluant was used.

Details of the ^1H n.m.r. spectra of the above products are given in the Table.

General Procedure for Catalytic Runs.—The catalyst $[PtCl_2(C_2H_4)(PPh_3)]$ (**B**) (0.056 g, 0.1 mmol), DMA (0.34 g, 5 mmol), and the appropriate amount of the aniline (5 mmol) were dissolved in chloroform (2 ml). The mixture was heated to 55 °C. Quantitative analyses of the reaction mixture composition were carried out by g.l.c. techniques. Reactions were stopped after 24 h.

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