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SUBSTITUTED TETRALIN FORMATION FROM *o*-PALLADATED SCHIFF BASES AND TWO EQUIVALENTS OF METHYL ACRYLATE

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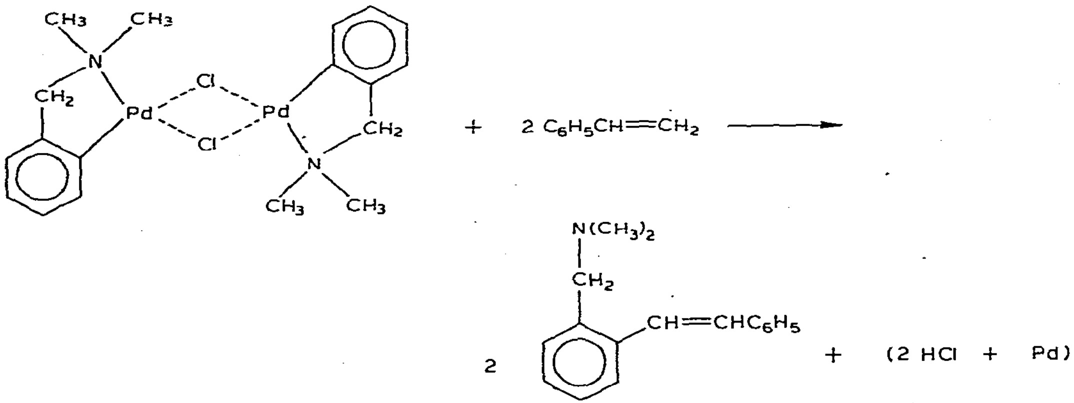
Summary

ortho-Palladated complexes of *N*-phenylbenzaldimine and *N*-phenyl-*p*-anisaldiimine reacted at 150°C with methyl acrylate by undergoing two successive methyl acrylate insertions followed by a cyclization to form tetralin derivatives in ca. 10% yield. The structure of the product from the *N*-phenylbenzaldimine complex was established by X-ray crystallography. The reactions appear to involve vinylic palladation as an intermediate step.

Many types of *ortho*-metallated aromatic complexes have been prepared in recent years and the chemistry of these derivatives is just beginning to be explored. Reactions with carbon monoxide, for example, have been studied in some detail [1]. To our knowledge, however, there are only two reports of reactions of one of these complexes with an olefin. Tsuji has reported the reaction of styrene with chloro-*o*-dimethylaminobenzylpalladium(II) dimer to form *o*-dimethylaminomethylstilbene but the yield and reaction conditions were not reported [2]. In the second example, Holton reported reactions of the same

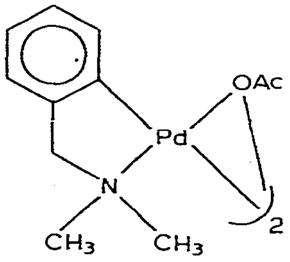


complex with α,β-unsaturated ketones [3]. Since the reaction of *ortho*-metallated aromatic complexes with olefinic compounds appeared to be potentially useful for the synthesis of various kinds of organic compounds we thought it worth investigating this reaction further.

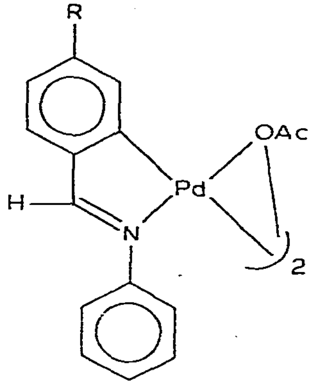
Results and discussion

Preliminary experiments with styrene and ethylene did not appear promising. However, methyl acrylate in acetonitrile solution did react and in two instances, at least, produced rather unusual products.

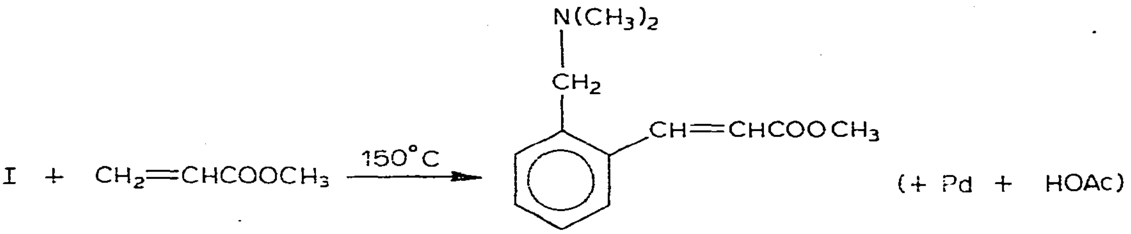
Methyl acrylate was clearly very much less reactive towards *ortho*-metallated complexes I, IIa, and IIb than was carbon monoxide [1]. Temperatures of 150° C were required to produce reactions with these complexes. Unfortunately, the high reaction temperatures required resulted in considerable decomposition in all cases and only relatively low yields of pure crystalline materials could be separated from the dark, viscous reaction mixtures. Complex I, when reacted with methyl acrylate at 150° C for 48 h, gave a mixture of products from which a 17.5% yield of *trans*-methyl-*o*-dimethylaminomethylcinnamate could be separated by column chromatography. Gas chromatography indicated a 39% yield.



(I)



(IIa) R = H
(IIb) R = OCH_3



Much more interesting were the products obtained from complexes IIa and IIb. The reactions required 62 h at 150° C to reach completion. Column chromatography separated a single crystalline product in each (IVa and b) in 10 and 11% yield, respectively. These products were shown by analyses, molecular weight measurements, and NMR spectra to contain two methyl acrylate units per Schiff base group. Reasonable structures for the products, consistent with these data, based on sequential insertion steps could be imagined. We initially thought tetrahydroisoquinoline compounds, IIIa and b, were formed but structure proof by X-ray crystallography showed the products to be tetralin derivatives.

Structure determination

The structure determination was made on IVa, the product from the palladated benzalaniline, IIa. A crystal was mounted on a glass fiber. Preliminary precession photographs indicated a triclinic space group ($P1$ or $P\bar{1}$). Unit cell dimensions derived from the observed 2θ values of thirty carefully-centered reflections are given in Table 1. Data collection was carried out on a Syntax $P2_1$ diffractometer using a $\theta/2\theta$ scan. The six standard reflections showed no significant fluctuation during data collection. Intensities were corrected for Lorentz and polarization effects, but not for absorption. The standard deviation of each intensity measurement, $\sigma(I)$, was estimated using the expression [4a] $\sigma(I) = [(\text{peak + background counts}) + (0.04)^2(\text{net intensity})^2]^{1/2}$. Wilson statistics indicated the presence of a center of symmetry and thus the probable space group is $P\bar{1}$ with two molecules per unit cell. An initial attempt to solve the structure with MULTAN [4b] and subsequent difference Fourier synthesis readily yielded 19 atomic positions that could be interpreted as forming a fragment of the suspected structure (IIIa). This fragment contained the tetralin core and some side chains. However, the remaining seven non-hydrogen atoms could not be located near their expected positions, and the R factor remained at a high value (~0.45). The partial model of 19 atoms was then used to calculate the phases of 100 reflections with large E values to generate "known" phases for input to MULTAN. The tangent refinement procedure yielded a new model (IVa) that contained the requisite number of atoms and appropriate

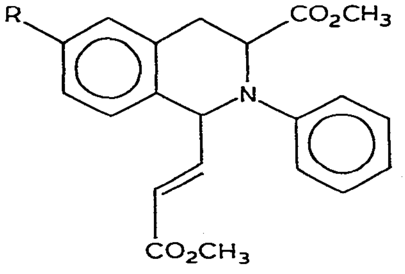
TABLE 1

SUMMARY OF CRYSTAL DATA, DATA COLLECTION CONDITIONS, AND REFINEMENT RESULTS FOR IVa

Formula	$C_{21}H_{21}NO_4$	space group	$P\bar{1}$ (triclinic)
Mol. wt.	351 g/mol	a	11.555 (5) Å
λ (Mo-$K\alpha$)	0.71069 Å	b	15.670 (11) Å
Temp.	ca. 20°C	c	5.270 (5) Å
$2\theta_{max}$	55°	α	93.64 (6)°
Total refl.	4628 (two hemispheres)	β	104.79 (4)°
Unique refl.	1769 ($I > 2\sigma$)	γ	90.98 (4)°
R from data averaging	0.038	V	920 Å^3
Average I/σ	14.7	Z	2
R^a	0.100	ρ_{obs}	1.3 g/cm^3
R_w^a	0.060	ρ_{calc}	1.26 g/cm^3
S^a	3.0	μ	0.75 cm^{-1}
$n_o/n_v{}^a$	7.53	Crystal size	0.45 X 0.45 X 0.15 mm

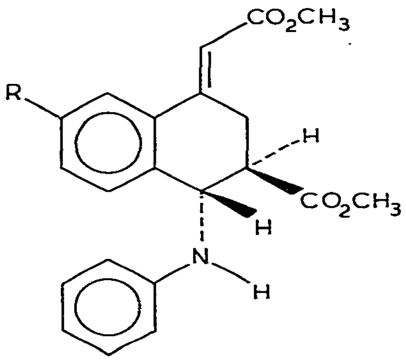
[a] $R = \Sigma|F_o - k|F_c||/\Sigma F_o$ $R_w = [\Sigma w(F_o - k|F_c|)^2/\Sigma wF_o^2]^{1/2}$, $S = [\Sigma w(F_o^2 - k^2F_c^2)^2/(n_o - n_v)]^{1/2}$, n_o = number of observations, n_v = number of variables.

molecular fragments. This structure was successfully refined * to the final agreement values $R = 0.100$ and $R_w = 0.060$ **. Other details of the refinement and the structure analysis are given in Table 1. A final difference Fourier map was essentially featureless, and gave no indication that the crystal is solvated. Selected interatomic distances and angles are given in Table 2. Listings of the final atomic parameters and the observed and calculated structure factors are available as supplementary material ***. The molecular structure is shown in the figure. All distances and angles are consistent with the structural assignment. The crystal is racemic, and thus contains both IVa and its mirror image.



(IIIa) R = H

(IIIb) R = OCH_3



(IVa) R = H

(IVb) R = OCH_3

Mechanism

The formation of product IVa can be rationalized in the following way. The first step would be the usual arylation of methyl acrylate [5] to form *trans*-methyl *o*-(*N*-phenylimidomethyl)cinnamate, V (see Scheme 1). The most reasonable second step would seem to be palladation of the beta (vinyl) carbon of the acrylate unit with a second palladium(II) species assisted by coordination of the palladium with the imine nitrogen, to form VI. Now a second acrylate insertion could occur followed by addition of the palladium—carbon group to the imine double bond to produce VII. The *trans* arangement of the carbomethoxyl and amine groups is probably favored for steric reasons. A final protonation of VII with acetic acid generated in the first step of the vinylic palla-

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* Major programs used in the structure analysis: ORFLS, by W.R. Busing and H.A. Levy, for least-squares refinement; CRYM, an amalgamated set of crystallographic programs by R.E. Marsh and co-workers, for Fourier map calculations; ORTEP, by C.K. Johnson, for molecular plots.

** The relatively high R factor is partly due to the fact that many weak high-angle reflections (up to $2\theta_{max} = 55°$) were included in the structure analysis. These data were retained, however, to yield more precise distances and angles. The fact that the value of R_w (the weighted R factor) is acceptably low indicates that the fit for the strong, low-angle reflections (whose weights are large) is quite good.

*** A listing of the final atomic positions and temperature factors and the table of structure factors have been deposited as NAPS Document No. 03454 (9 pages). Order from ASIS/NAPS, c/o Microfiche Publications, P. O. Box 3513, Grand Central Station, New York, N.Y. 10017. A copy may be secured by citing the document number, remitting $ 5.00 for photocopies or $ 3.00 for microfiche. Advance payment is required . Make checks payable to Microfiche Publications. Outside the U.S.A. and Canada add postage of $ 3.00 for photocopy and $ 1.00 for microfiche.

TABLE 2

INTERATOMIC DISTANCES AND INTERATOMIC ANGLES

Distances (Å)

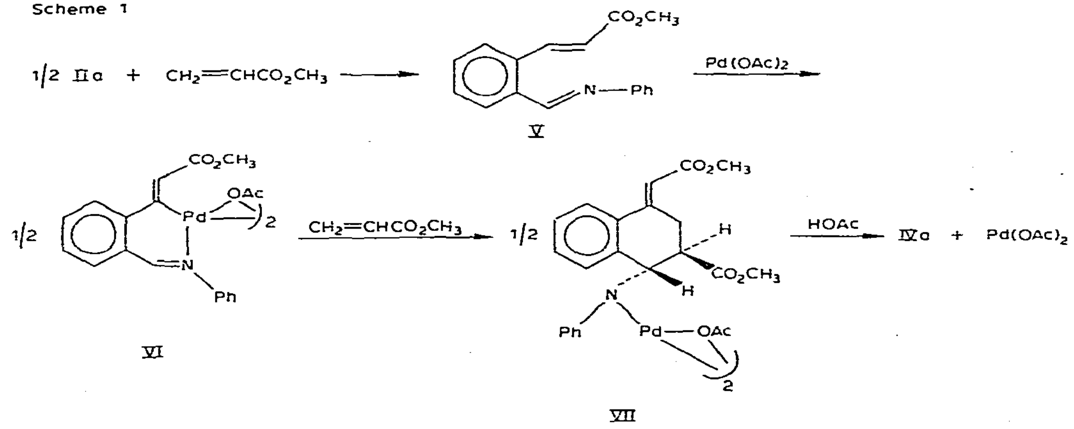
C(1)—C(2)	1.421 (6)	N(11)—C(12)	1.470 (5)
C(1)—C(6)	1.375 (6)	C(12)—C(13)	1.405 (6)
C(1)—C(10)	1.532 (6)	C(13)—C(14)	1.432 (8)
C(2)—C(3)	1.385 (7)	C(14)—C(15)	1.391 (8)
C(3)—C(4)	1.400 (7)	C(15)—C(16)	1.370 (7)
C(4)—C(5)	1.407 (7)	C(16)—C(17)	1.412 (7)
C(5)—C(6)	1.410 (6)	C(17)—C(120	1.367 (7)
C(6)—C(7)	1.480 (6)	C(18)—C(19)	1.471 (7)
C(7)—C(8)	1.501 (7)	C(19)—O(20)	1.334 (6)
C(7)—C(18)	1.366 (7)	C(19)—O(22)	1.180 (5)
C(8)—C(9)	1.557 (7)	O20()—C(21)	1.478 (7)
C(9)—C(10)	1.554 (6)	C(23)—O(24)	1.305 (5)
C(9)—C(23)	1.482 (6)	C(23)—O(26)	1.190 (5)
C(10)—N(11)	1.459 (6)	O(24)—C(25)	1.450 (6)

Angles (deg.)

C(2)—C(1)—C(6)	121.3 (4)	O(24)—C(23)—O(26)	121.2 (5)
C(2)—C(1)—C(10)	116.7 (5)	C(23)—O(24)—C(25)	117.7 (4)
C(6)—C(1)—C(10)	121.9 (4)	C(1)—C(10)—C(9)	109.8 (4)
C(1)—C(2)—C(3)	118.3 (5)	C(1)—C(10)—N(11)	114.2 (4)
C(2)—C(3)—C(4)	121.2 (5)	C(9)—C(10)—N(11)	106.8 (4)
C(3)—C(4)—C(5)	119.9 (5)	C(10)—N(11)—C(12)	124.2 (4)
C(4)—C(5)—C(6)	119.3 (5)	N(11)—C(12)—C(13)	122.0 (5)
C(1)—C(6)—C(5)	119.9 (4)	N(11)—C(12)—C(17)	117.1 (5)
C(1)—C(6)—C(7)	120.0 (4)	C(13)—C(12)—C(17)	120.9 (5)
C(5)—C(6)—C(7)	120.0 (5)	C(12)—C(13)—C(14)	117.0 (6)
C(6)—C(7)—C(8)	118.6 (5)	C(13)—C(14)—C(15)	122.0 (6)
C(6)—C(7)—C(18)	120.2 (4)	C(14)—C(15)—C(16)	118.7 (6)
C(8)—C(7)—C(18)	121.2 (4)	C(15)—C(16)—C(17)	120.8 (6)
C(7)—C(8)—C(9)	113.0 (4)	C(12)—C(17)—C(16)	120.5 (6)
C(8)—C(9)—C(10)	107.3 (4)	C(7)—C(18)—C(19)	124.3 (5)
C(8)—C(9)—C(23)	109.2 (4)	C(18)—C(19)—O(20)	109.8 (5)
C(10)—C(9)—C(23)	109.3 (4)	C(18)—C(19)—O(22)	128.6 (6)
C(9)—C(23)—O(24)	112.9 (4)	O(20)—C(19)—O(22)	121.6 (7)
C(9)—C(23)—O(26)	125.8 (5)	C(19)—O(20)—C(21)	117.6 (5)

dation would give IVa and regenerate the palladium(II) acetate needed for the vinylic palladation.

Scheme 1



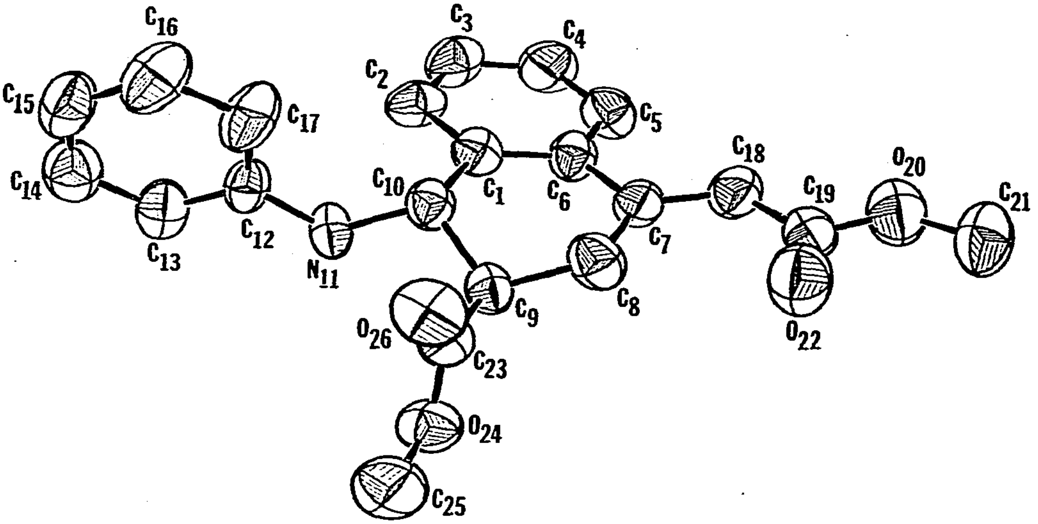


Fig. 1. The molecular structure of $C_{21}H_{21}NO_4$ (IVa). Atoms C(1)—C(6) and C(12)—C(17) define aromatic rings, and double bonds are situated between C(7) and C(18), C(19) and O(22), C(23) and O(26). The crystal is racemic, and contains both the molecule shown here and its mirror image.

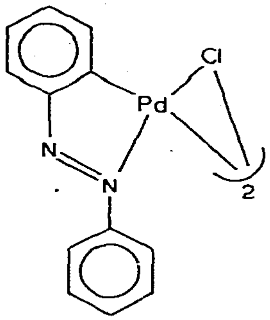
The catalytic amount of palladium acetate required for step 2 could arise from a reversal of the Schiff base palladation with acetic acid formed by decomposition reactions. The stereochemistry of IV is consistent with the expected *syn* addition of VI to methyl acrylate.

Attempts to obtain evidence to support the proposed mechanism have been unsuccessful so far. We have made several attempts to prepare *trans*-methyl *o*-(*N*-phenylimidomethyl)cinnamate from the aldehyde and aniline to react it with palladium acetate and methyl acrylate but we have not yet succeeded. Further attempts will be made.

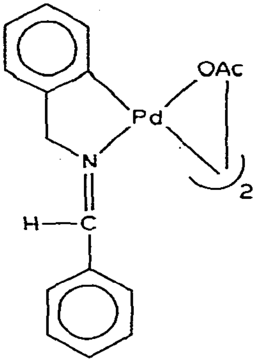
The structure of the product from the methoxy Schiff base complex IIb, by analogy and from the similarity of NMR spectra with that of IVa would be expected to be IVb.

Similar reactions carried out with other *ortho*-metallated complexes gave only trivial products or oily materials which could not be purified. The azobenzene complex, VIII, for example, reacted with methyl acrylate at 100°C to produce azobenzene in 6% yield and the cycloaromatization product of methyl acrylate, trimethyl 1,3,5-benzenetricarboxylate [6] in about 15% yield. Complexes IX, X, XI, and XII with methyl acrylate gave only dark, viscous oils which could not be purified.

The relatively low reactivity of the *ortho*-metallated aromatic palladium complexes towards methyl acrylate compared with carbon monoxide [1] or with similar reactions of non-chelated arylpalladium complexes [7] may be a result of an unfavorable, strained transition state being formed in the second methyl acrylate insertion. The formation of seven membered ring chelates is rare and it would be expected to be especially difficult in the above cases because the ring is probably planar except for the carboxyl bearing carbon and the preferred 90° bonding angle of square planar palladium(II) would be difficult to attain.



(VIII)



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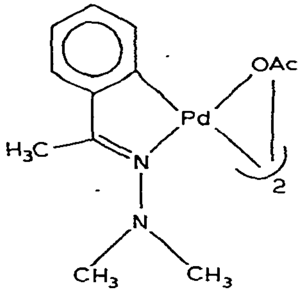
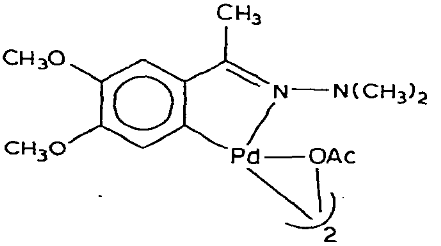
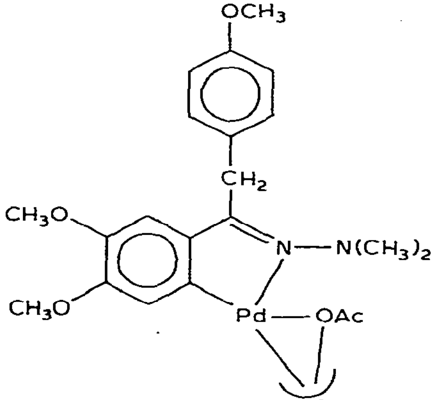


(X)



(XI)



(XII)

Experimental

Materials

Reagents and complexes I, IIa, VIII, IX and X were prepared as described previously [1].

General procedure for reactions of palladium complexes with methyl acrylate

Mixture of 5 mmol of the *ortho*-metallated complex, 4 ml of methyl acrylate, and 10 ml acetonitrile were heated in capped heavy-walled Pyrex tubes in an oil bath at 100—150° C until the starting complex had disappeared as judged from the NMR spectrum of a sample of the cooled reaction mixture. The cooled reaction mixtures were then concentrated under reduced pressure and chromatographed on silica gel.

Reaction of complex I with methyl acrylate

After reaction at 150° C for 51 h and isolation of the products as described above, chromatography gave 17.5% of liquid *trans*-methyl *o*-*N*,*N*-dimethylaminomethylcinnamate. The molecular weight found by mass spectroscopy was 219.123 and the calculated value was 219.125. The NMR spectrum in $CDCl_3$

was as follows: δ (ppm) 6.49 and 8.41 (both d, J 16 Hz, 2 vinylic protons); 7.45 (m, 5 aromatic protons); 3.83 (s, 3-methoxyl protons); 3.52 (s, 2 methylene protons); and 2.23 (s, 6 *N*-methyl protons).

Reaction of IIa with methyl acrylate

The crude reaction product was obtained as in the general procedure and chromatographed on silica gel. Benzene eluted the solid product. Recrystallization from methanol gave a 10% yield of compound IVa, m.p. 132—133° C. Molecular weight: found 351.134, calcd. 351.147. NMR ($CDCl_3$): δ (ppm) 6.45—7.75 (m, 9 aromatic protons and 2 vinylic protons); 5.00 (d, proton on C next to double bond); 4.02 (m, proton on C next to carbomethoxyl group); 2.85—3.20 (m, one methylene proton); 3.72 (s, carbomethoxyl group on double bond); 3.53 (s, other carbomethoxyl and second methylene protons).

Reaction of IIb with methyl acrylate

The crude products obtained by the general procedure yielded from the benzene eluate a colorless solid. Recrystallization from methanol gave 11% of compound IVb, m.p. 167—168° C. Molecular weight: found 381.158, calcd. 381.158. NMR ($CDCl_3$): δ (ppm) 6.45—7.58 (m, 8 aromatic and 2 vinylic protons); 4.93 (m, proton on C next to double bond); 3.57 (s, 3 protons of other carbomethoxyl group); 4.0 (m, proton on C next to carbomethoxyl group); 3.50 (m, one methylene proton); and 3.1 (m, second methylene proton).

Anal.: Found: C, 69.33; H, 5.86; N, 3.60. Calcd. for $C_{22}H_{23}NO_5$: C, 69.32; H, 6.09; N, 3.64%.

Reaction of complex VIII with methyl acrylate

The crude product was chromatographed as in the preceding reactions. Hexane eluted a 6% yield of azobenzene and benzene 14.5% of trimethyl 1,3,5-benzenetricarboxylate, m.p. 140—141° C (Lit. [5] 144° C). The NMR spectrum in $CDCl_3$ showed two singlets, one at δ 8.9 (3 aromatic protons) and one at 3.95 (9 carbomethoxyl protons).

Preparation of complex IIb

N-Phenylanisaldimine [8] (8.49 g, 0.041 mol) and 8.98 g (0.040 mol) palladium acetate in 100 ml of acetic acid were heated at reflux temperature for 1 h and cooled. Water was added and the yellow solid which precipitated was separated by filtration and washed several times with water. The solid was taken up in methylene chloride and dried over $MgSO_4$. Filtration and evaporation gave 12.7 g (74%) of the palladium complex, m.p. 215° C (dec.).

Anal.: Found: C, 51.26; H, 3.96; N, 3.67. Calcd. for $C_{32}H_{30}N_2O_6Pd_2$: C, 51.15; H, 4.02; N, 3.73%.

Preparation of complex XI *

A mixture of 4.48 g (0.040 mol) 3,4-dimethoxyacetophenone dimethylhydrazone [9] (m.p. 31° C, b.p. 128° C/0.65 mmHg), 4.57 g (0.040 mol) palladium acetate and 100 ml methylene chloride was heated at reflux temperature

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* Reaction was carried out by Mr. Evan Speck.

for 48 h. The resulting solution was concentrated and the product was precipitated by adding hexane. The yellow solid product, m.p. 226—228°C (dec.), was obtained in 58% yield. The NMR spectrum was consistent with the proposed structure.

Anal.: Found: C, 43.75; H, 5.19. Calcd. for $C_{28}H_{40}N_4O_8Pd_2$: C, 43.81; H, 5.47%.

Preparation of complex XII *

Desoxyveratroin *N,N*-dimethylhydrazone was prepared by the usual procedure [9] (m.p. 137—139°C). A mixture of 2.59 g (0.0072 mol) of the hydrazone and 1.66 g (0.0074 mol) palladium acetate dissolved in 50 ml of benzene was warmed to 40°C for 3 h. Decolorizing carbon was then added and the solution was filtered through Celite. The filtrate was concentrated under reduced pressure and the product was precipitated with pentane. A yellow powder (2.12 g, 57%) was obtained, m.p. 205°C (dec.). NMR ($CDCl_3$): δ (ppm) 6.54 (broad s, 5 aromatic protons); 4.05 (s, 2 methylene protons); 3.69 and 3.77 (2s, 12 methoxyl protons); 2.22 (s, 6 *N*-methyl protons) and 2.10 (s, 3 acetate protons).

Acknowledgment

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* Preparation carried out by Mr. Stephen Murdock.