(or computationally) derived index of selectivity, i.e., reactant-like or product-like character in terms of the response to energy perturbation, but it is not necessarily a measure of the structure of the TS even though it shows a normal magnitude. Selectivity and the structure of the TS are different matters. (3) The intrinsic barrier is in most cases not constant for a series of reactions but varies linearly with the change in endothermicity. α_A is controlled in large part by the variation of α_I and can be a TS index in a conventional sense only when $\Delta E_0^{\ddagger}$ is constant for a series of reactions. The α_I value is a measure of the tight–loose character of the TS of the symmetry reaction, provided that the arithmetic mean assumption holds. (4) The α_A value can be outside the normal range when the arithmetic mean assumption breaks down, which may occur due to a new interaction between the two reacting fragments in the TS.

Acknowledgment. We thank Professor Y. Kondo of Osaka University for critical discussions. Numerical calculations were carried out at the Computer Center of the Institute for Molecular Science, using the GAUSSIAN 80[12] and GAUSSIAN 82[13] programs in the Computer Center library package.

Registry No. HCH_3, 74-82-8; HCH_2CH_3, 74-84-0; $HCH(CH_3)_2$, 74-98-6; $HC(CH_3)_3$, 75-28-5; H·, 12385-13-6; Cl·, 22537-15-1.

Isoquinolinium Salt Syntheses from Cyclopalladated Benzaldimines and Alkynes

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Cyclopalladated, N-substituted benzaldimine tetrafluoroborates react with disubstituted alkynes in poor to good yields to form isoquinolinium tetrafluoroborates. The reaction is particularly useful for preparing N,3,4-trisubstituted products. Electron-donating substituents may be present at the 5, 6, 7, and 8 positions, as well. Methyl (*p*-benzoxyphenyl)propiolate adds to cyclopalladated *N*-methyl-3-benzoxy-4-methoxybenzaldimine tetrafluoroborate to form the 3-arylisoquinolinium salt. 3-Hexyne reacts with cyclopalladated *N*-phenylbenzaldimine chloro dimer at 150 °C to form the isoquinolinium chloride but at less than half (29%) the yield that is obtained from the corresponding tetrafluoroborate.

The presence of the isoquinoline ring system in many natural alkaloids has led to the development of a variety of methods for its synthesis. Of the many methods, however, only three are commonly employed: the Bischler–Napieralski, the Pictet–Pengler, and the Pomeranz–Fritsch reactions.[1] Both the Bischler–Napieralski and Pomeranz–Fritsch methods use strong acids in the ring closures limiting the procedures to acid-stable reactants. The Pictet–Spengler transformation often can be achieved under very mild conditions but a disadvantage of this method may be a tedious preparation of the starting material, an appropriately substituted phenylethylamine.

More recently a method based upon cyclopalladated *tert*-butylarylaldimines has been reported.[2] This synthesis, however, has as a final step a pyrolysis at 180–200 °C which also limits its utility. We have discovered a related, new synthesis of the isoquinoline ring system which occurs under mild, neutral conditions also starting with generally easily available aromatic imines. The method, which is modeled after our cinnolinium salt synthesis,[3,4] is very suitable for preparing polysubstituted and hindered derivatives.

Results and Discussion

Cyclopalladated arylaldimine tetrafluoroborates react with various disubstituted alkynes to form 3-, 4-, and N-substituted isoquinolinium tetrafluoroborates in low to good yields. Additional substituents may be present in

Table I. Isoquinolinium Salt Preparations

complex 1,[a] R^1 =	alkyne 2, R^2 =	temp (°C) and time of alkyne addition (h)	product 3, % yield
C_6H_5	C_2H_5	100, 2	80
C_6H_5	CH_3O_2C	100, 5	25
C_6H_5	$(C_2H_5O)_2CH$	100, 4	12
o-$CH_3C_6H_4$	C_2H_5	100, 2	60
o-$CH_3C_6H_4$	C_2H_5	25,[b]	5
$C_6H_5CH_2$	C_2H_5	100, 1	42
$C_6H_5CH_2$	C_2H_5	25,[b]	trace
$C_6H_5CH_2$	C_2H_5	100, 3	64
$C_6H_5CH_2$	C_6H_5	100, 1	34
CH_3	C_6H_5	100, 1	17[c]
CH_3	C_2H_5	100,[b]	~0
t-C_4H_9	C_6H_5	100, 2	27
CH_3[d]	C_6H_5	100, 1	48[e]
CH_3[d]	C_6H_5	70, 1	66[e]
CH_3[f]	C_2H_5	100, 1	45[g]
CH_3[f]	4-$PhCH_2OC_6H_4$ and CO_2CH_3	100, 1	54[g]
CH_3[f]	4-$PhCH_2OC_6H_4$ and CO_2CH_3	100, 4	53[g]
p-$CH_3C_6H_4$[i]	C_2H_5	100, 1	80[j,k]
p-$CH_3C_6H_4$[i]	C_6H_5	100, 2	75[k]

[a] All prepared in nitromethane solution from the dimeric chloro complexes and silver tetrafluoroborate and used without isolation. [b] Alkyne all present initially in methylene chloride solution. [c] Complex was unstable at 100 °C (see text). [d] Complex is the 3,6-dimethoxy derivative. [e] Product is the 5,8-dimethoxy derivative. [f] Complex is the 4-methoxy-5-benzoxy derivative. [g] Product is the 6-methoxy-7-benzoxy derivative. [h] Product is the 2-methyl-3-(*p*-benzoxyphenyl)-4-(methoxycarbonyl)-6-methoxy-7-benzoxyisoquinolinium tetrafluoroborate. [i] Complex is the 4-nitro derivative. [j] 60% of the complex was recovered. [k] Product is totally oligomers.

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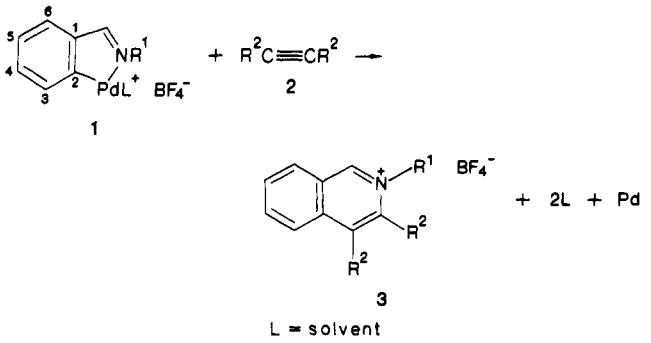


the benzene ring also and the two R^2 substituents need not be identical. Examples of the reaction are shown in Table I.

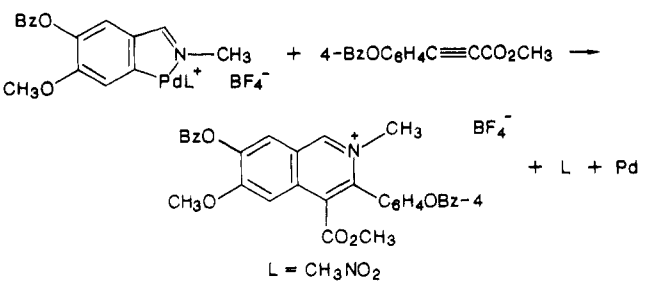
The required palladium reactants are obtained generally by warming the necessary imine with palladium chloride (or palladium acetate and allowing the cyclopalladated acetate to react with chloride ion) to form the cyclopalladated chloro dimers. These are then treated with silver tetrafluoroborate to form the solvated tetrafluoroborates. In most cases the tetrafluoroborates were not isolated but were generated in nitromethane solution since they were usually viscous liquids and in some cases unstable.

Fairly stable solvates were formed from at least some of the tetrafluoroborates. For example, the cyclopalladated tetrafluoroborate from *N*-methylbenzaldimine prepared in DMF solution afforded a disolvated product. A crystal structure of the compound showed the DMF molecules to be bound through oxygen. (See Figure 1, supplementary material, for the structure.) For another example, that of the cyclopalladated *N*-(*p*-tolyl)-*p*-nitrobenzaldimine tetrafluoroborate, the unsolvated salt in crystalline form was isolated from nitromethane solution. Unfortunately, it was not sufficiently stable to permit analysis or crystallographic characterization. The compound formed a monoetherate with diethyl ether. The last tetrafluoroborate complex (unsolvated) prepared was more stable than the others and did not insert alkynes. Instead, this complex formed only oligomers from the alkynes. The complex also dimerized styrene to the head-to-head dimer (70%) and isomerized allylbenzene to propenylbenzene (93%). The strongly electron-withdrawing influence of the nitro group in this complex must influence its behavior toward alkynes.

The reaction conditions for the alkyne insertion into the cyclopalladated salts are quite critical in most cases. The polar but poor coordinating solvent nitromethane has given the best results. If the alkyne is all added in a single portion or if it is added too rapidly to the palladium complex, a low yield of the isoquinolinium salt usually results because alkyne oligomerization occurs preferentially when the concentration of the alkyne is too high. It is best to add the alkyne slowly to the cyclopalladated complex over a period of 1 to 3 h at 70–100 °C. The rate of alkyne addition cannot be reduced indefinetely because, in most examples, thermal decomposition of the tetrafluoroborates becomes serious after a few hours. Thus, the reaction temperature and rate of alkyne addition should be investigated in each reaction in order to find the optimum conditions. The low yield of isoquinolinium salt from the reaction of the cyclopalladated *N*-phenylbenzaldimine with dimethyl acetylenedicarboxylate is probably due to the relative ease of oligomerization of this alkyne relative to the other ones we employed.

The nature of the N substituent present is an important factor in the reaction. As can be seen in Table I, *N*-phenyl, *N*-*o*-tolyl, and *N*-benzyl groups are comparable in the reaction with 3-hexyne while lower yields are obtained with the *N*-methyl and *N*-*tert*-butyl derivatives of the otherwise unsubstituted complexes. The low yield of the *N*-methyl product is due to the low thermal stability of the palladium complex. Palladium metal precipitation occurs slowly from solutions of this tetrafluoroborate in the absence of alkyne on standing at room temperature or more rapidly on warming. The low yield found with the *N*-*tert*-butyl complex may be due to steric problems. The *tert*-butyl group is totally lost from the product in the reaction and its presences in the reactant surely favors oligomerization more in this case than in examples where the N groups are smaller. The *N*-methyl complexes with electron-donating (alkoxyl) groups in the aromatic ring are more stable and afford better yields of the alkyne adducts.

Only one unsymmetrically disubstituted alkyne was examined. Methyl 4-(benzoxyphenyl)propiolate was added to cyclopalladated *N*-methyl-3-benzoxy-4-methoxybenzaldimine tetrafluoroborate. It was anticipated that the 4-arylisoquinolinium salt would be obtained since the closely related cyclopalladated azobenzene tetrafluoroborate and methyl phenylpropiolate interact to give the 4-arylcinnolinium product.[4] The structure of the isoquinolinium product, obtained in 54% yield, was determined by X-ray crystallography and the compound was found to be the 3-aryl isomer. (See Figure 2, supplementary material, for the structure.) The same regiochemistry



was observed by Pfeffer[5] in the addition of methyl phenylpropiolate to cyclopalladated *N*,*N*-dimethylbenzylamine. The results suggest that the addition to the azobenzene complex is sterically controlled while electronically the opposite regiochemistry is favored. This result contrasts with the regiochemistry observed in the addition of "phenylpalladium iodide" to methyl cinnamate.[6]

Attempts to simplify our isoquinolinium synthesis and make it catalytic with respect to palladium have not been successful. Attempts to bring about reaction of *N*-phenyl-2-bromobenzaldimine with diphenylacetylene using a $Pd(OAc)_2$–$P(o\text{-tol})_3$ catalyst at 100 °C in the presence of either triethylamine or sodium acetate as base led to the formation of viscous highly colored oils which contained little if any isoquinolinium product. The *N*-phenylbenzaldimine cyclopalladated chloro dimers were observed to react thermally, directly with 3-hexyne without first being converted to the tetrafluoroborate. However, this required temperatures of 150 °C and yields were significantly lower (29%) than when the tetrafluoroborate was used at 100 °C (80%). The same process employing diphenylacetylene gave only oligomers.

This isoquinolinium synthesis is best suited to the preparation of 3,4-disubstituted isoquinolinium salts with various N substituents and electron-donating (or H) substituents at the 6, 7, and/or 8 positions. Attempts to put

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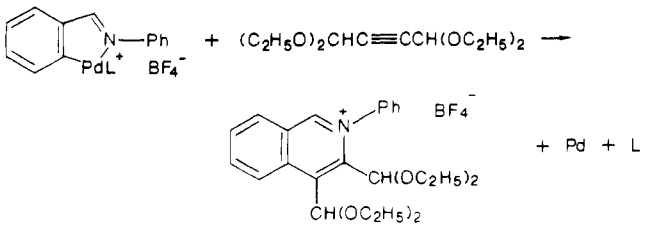
easily removable groups in the 3 and/or 4 positions have met with very limited success. Bis(trimethylsilyl)acetylene does not give isoquinolinium salts under our usual conditions and even dimethyl acetylenedicarboxylate adds poorly (25%). Arylpropiolate esters add well, however, and presumably the adducts could be decarboxylated to give 3-arylisoquinolines. Similar reactions should be possible with propargyl aldehyde derivatives. Unfortunately, yields of the adduct between the *N*-phenylbenzaldimine palladium complex and butynedial tetraethylacetal were very low (12%) but this may be largely a reflection of steric interactions in the product because of the three fairly large adjacent substituents in the pyridinium ring. This problem could be expected to inhibit the ring closure and favor alkyne oligomerization.



Many more examples of this reaction need to be examined in order to establish the scope of this useful, new isoquinolinium salt synthesis.

Experimental Section

General. Palladium chloride, palladium acetate, and silver tetrafluoroborate were used as received from Strem Chemicals, Inc. Dimethyl acetylenedicarboxylate (Aldrich), diphenylacetylene (Aldrich), and 3-hexyne (Chem Samples Co.) also were used without further purification.

3-Benzoxy-4-methoxybenzaldehyde. To a solution of 13 g (0.20 mol) of potassium hydroxide in 120 mL of ethanol were added 20 g (0.10 mol) 3-hydroxy-4-methoxybenzaldehyde (Aldrich) and 33.1 g (0.26 mol) benzyl chloride. The solution was heated under reflux for 6 h and then most of solvent was removed by distillation at reduced pressure. the residue was extracted with ether and the extracts were dried ($MgSO_4$) and concentrated. Distillation under reduced pressure gave 20.5 g (97%) of colorless liquid which crystallized on standing, mp 65–66 °C. The NMR spectrum is presented in Table 2 (supplementary material). The *N*-methylimine was prepared from this aldehyde by the general method described below.

Benzaldimines. The *N*-methylbenzalimines were prepared by heating 1 equiv of the aldehyde with about 2 equiv of methylamine as a 40% aqueous solution in methanol for 2 h. Alternatively, the reactions could be done in ether solution at room temperature. The products were isolated by concentration and vacuum distillation of the reaction mixtures. Other imines were prepared similarly in either methanol or ether solution. If after removal of the solvent the imines solidified, they were recrystallized rather than distilled. When employing methanol as a solvent for preparing imines, the amine should be added to the methanol before the aldehyde in order to prevent possible formation of acetals. The yields and properties of the new imines prepared are listed in Table 2 (supplementary material).

N-Phenylbenzaldimine,[3] *N*-*o*-tolylbenzaldimine,[7] *N*-benzylbenzaldimine,[4] *N*-methylbenzaldimine,[7] *N*-*tert*-butylbenzaldimine,[5] and *N*-*p*-tolyl-*p*-nitrobenzaldimine[6] have been reported previously.

Cyclopalladated Benzaldimine Chloro Dimers. Method A. The procedure of Widdowson[2] was used in which the imine in acetic acid is treated with $PdCl_2$ and an excess of sodium acetate at 60–80 °C. **Method B.** The cyclopalladated acetate dimer is first prepared from palladium acetate and the imine by the method of Pregosin.[10] The chloro dimers are then prepared from the acetate dimers by dissolving the acetates in methylene chloride and stirring the solutions overnight in the presence of a 2–5 M excess of lithium chloride dissolved in water or acetone. The *N*-methyl-2,5-dimethoxybenzaldimine and the *N*-(*p*-tolyl)-*p*-nitrobenzaldimine cyclopalladated chloro dimers were prepared by method B while all other chloro dimers were obtained by method A.

General Procedures for the Preparation of Isoquinolinium Tetrafluoroborates from Cyclopalladated Chloro Dimers and Alkynes. A mixture of 2 mmol of the cyclopalladated imine chloro dimer and 4.2 mmol of anhydrous silver tetrafluoroborate in 8 mL of nitromethane are stirred magnetically for several hours at 25 °C. The silver chloride formed is then separated by centrifuging and the clear tetrafluoroborate solutions are decanted. The residue is rinsed with 2 mL more of nitromethane and the solution is again separated. The original solution and the washings are placed in a 50-mL three-necked, round-bottomed flask equipped with a constant-rate addition funnel and a condenser. The solution is stirred magnetically and heated at 70–100 °C as indicated in Table I while a solution of 4.8 mmol of the alkyne in 5 mL of nitromethane is added from the dropping funnel over the period indicated in Table I. Heating is continued for another hour after completion of the addition. The mixture is cooled and a few grams of silica are added. The solvent is evaporated under reduced pressure and the powder remaining is poured on the top of a silica column and the products are separated by chromatography. The isoquinolinium products were generally eluted with a few percent methanol in methylene chloride. Recrystallization was usually possible from methylene chloride–ether or methanol–ether solutions. The products prepared by this procedure are listed in Table I. The properties of the products are given in Table 3 (supplementary material).

Methyl (*p*-Benzoxyphenyl)propiolate. To a solution of 20 g (0.30 mol) of potassium hydroxide in 400 mL of ethanol were added 25 g (0.20 mol) of *p*-hydroxybenzaldehyde and 50.6 g (0.4 mol) of benzyl chloride, and the solution was heated at reflux temperature for 5 h. Most of the alcohol was then removed by distillation and the residue was taken up in ether. After drying ($MgSO_4$) and concentrating to ca. 50 mL, the product crystallized from the solution. The product was isolated by filtration and dried at reduced pressure. There was obtained 32 g (77%) of *p*-benzoxybenzaldehyde.

A mixture of 69 g (0.20 mol) of carbon tetrabromide, 13.6 g (0.21 mol) zinc dust, and 55 g (0.21 mol) of triphenylphosphine in 300 mL of methylene chloride was stirred at room temperature (heat evolved) for 2 days. To this mixture was added 2 g (0.10 mol) of the *p*-benzoxybenzaldehyde, and the mixture was stirred at room temperature for 3 h. One liter of ether was added and the thick precipitate of salts was separated by filtration through Celite. Evaporation of the solvent left the crude 2,2-dibromo-*p*-benzoxystyrene. Purification was achieved by chromatography on silica gel. There was obtained 29 g of colorless product (79%).

A solution of 1.85 g (5.0 mmol) of the dibromide in 11 mL of dry THF under nitrogen was cooled to −78 °C. To the stirred, cold solution was added 6.7 mL of cold 1.6 M *n*-butyllithium (10.9 mmol) in hexane. The solution was kept at −78 °C overnight and then warmed to room temperature for 1 h. After recooling to −5 °C, 0.46 mL (5.5 mmol) of methyl chloroformate was added and the solution was left in the refrigerator overnight. After stirring at 25 °C for an hour, ether and water were added and the ether layer was separated and dried ($MgSO_4$). Evaporation of the solvent left an oil which crystallized on standing. Recrystallization from methylene chloride–hexane gave 0.80 g (60%) of colorless methyl (*p*-benzoxyphenyl)propiolate, mp 85–6 °C. Other data are listed in Table 2 (supplementary material).

Cyclopalladated *N*-(*p*-Tolyl)-*p*-nitrobenzaldimine Tetrafluoroborate. A suspension of 0.80 g (1.05 mmol) of the chlorodimer[10] in 25 mL of nitromethane was heated to 80 °C with magnetic stirring and 0.43 g (2.2 mmol) of silver tetrafluoroborate

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in 5 mL of nitromethane was added. The orange suspension turned yellow within a few minutes and after 1 h the solution was filtered through Celite. Removal of the nitromethane solvent at room temperature and reduced pressure afforded 0.87 g (~100%) of yellow crystals. The compound decomposed slowly at room temperature on standing. ^{1}H NMR (δ, ppm in $CDCl_3$): 8.16 (s, 1 H), 8.06 (dd, J = 2.1 and 8.3 Hz, 1 H), 7.82 (bs, 1 H), 7.65 (d, J = 8.3 Hz, 1 H), 7.23 (m, 4 H), 2.39 (s, 3 H).

When recovered from ether solution, a nicely crystalline monoetherate is obtained. ^{1}H NMR (CD_3OD): 8.30 (s, 1 H), 7.96 (dd, J = 2.1 and 8.3 Hz, 1 H), 7.65 (bs, 1 H), 7.63 (d, J = 8.3 Hz, 1 H), 2.53 (q, J = 7.4 Hz, 4 H), 2.27 (s, 3 H), 1.20 (t, J = 7.4 Hz, 6 H).

Cyclopalladated *N*-Methylbenzaldimine Tetrafluoroborate Bis(dimethylformamide solvate). A mixture of 0.80 g (1.5 mmol) of the cyclopalladated *N*-methylimine chloro dimer[7] and 0.75 g (3.9 mmol) of silver tetrafluoroborate was stirred in 10 mL of DMF at room temperature for 1 h. The solution was filtered through Celite and the solvent was evaporated under reduced pressure at 25 °C. The yellow crystals obtained were recrystallized from methylene chloride-ether to give 1.21 g (88%) of product, mp 147–8 °C dec. Figure 1 (Supplementary Material) shows the X-ray structure of this product.[12]

^{1}H NMR ($CDCl_3$, ppm): 8.01 (bs, 2 H), 7.83 (bs, 1 H), 7.25–7.22 (m, 1 H), 7.07–7.02 (m, 2 H), 6.79–6.75 (m, 1 H), 3.28 (s, 3 H), 3.14 (s, 6 H), 2.99 (s, 6 H). ^{13}CNMR ($CDCl_3$, ppm): 176.07, 167.10, 151.57, 146.12, 130.58, 129.75, 127.53, 125.18, 46.92, 38.31, 32.73. Anal. Calcd for $C_{14}H_{22}N_3O_2PdBF_4$: C, 36.74; H, 4.81; N, 9.18. Found: C, 36.74; H, 5.13; N, 8.79.

Dimerization of Styrene. A solution of 0.43 g (1.0 mmol) of the cyclopalladated tetrafluoroborate from *N*-(*p*-tolyl)-*p*-nitrobenzaldimine in 12 mL of styrene was heated at 100 °C in an oil bath for 19 h. Analyses by GLC showed less than 5% styrene remaining at this time. The mixture was dissolved in hexane and chromatographed on silica gel. There was obtained 7.0 g (70%) of nearly colorless, liquid 2,3-diphenyl-1-butene which was quite pure by NMR.[4]

Isomerization of 3-Phenyl-1-propene. This reaction was carried out as in the styrene dimerization above substituting 3-phenyl-1-propene for the styrene. Analyses of the reaction mixture by GLC showed the alkene was 93% isomerized after 19 h at 100 °C to a 89:4 trans to cis mixture of 1-phenyl-1-propenes.

Addition of 3-Hexyne to Cyclopalladated *N*-Phenylbenzaldimine Chloro Dimer. A solution of 0.65 g (1.0 mmol) of the chloro dimer[7] in 12 mL of DMF was magnetically stirred under nitrogen at 150 °C while 0.52 g (6.3 mmol) of 3-hexyne in 5 mL of DMF was slowly added over a 2.5-h period. After a further 30 min at 150 °C, the reaction mixture was cooled and the DMF was removed at 25 °C under reduced pressure. The residue was chromatographed on silica gel. Elution with methylene chloride–methanol gave 0.17 g (29%) of crude product for which the NMR spectrum was similar to that of the tetrafluoroborate. The chloride was very hygroscopic so it was converted to the known tetrafluoroborate by treating it with 0.12 g of silver tetrafluoroborate (0.62 mmol) in 7 mL of nitromethane. After being stirred for 1 h, the mixture was filtered through Celite with nitromethane rinsing. The filtrate was concentrated under reduced pressure and the residue was recrystallized from methanol–ether to give 0.12 g (63%) of off-white crystals for which the ^{1}H NMR and ^{13}C NMR spectra were identical with the spectra obtained from the compound prepared from the cyclopalladated tetrafluoroborate.

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Supplementary Material Available: Table of the yields and properties of intermediates prepared (Table 2) and the properties of isoquinolinium tetrafluoroborates (Table 3), Figures 1 and 2 showing the X-ray crystal structures of the cyclopalladated *N*-(*p*-tolyl)-*p*-nitrobenzaldimine bis(dimethylformamide) tetrafluoroborate and 7-benzoxy-3-(*p*-benzoxyphenyl)-6-methoxy-4-(methoxycarbonyl)-2-methylisoquinolinium tetrafluoroborate, respectively, and Tables 4, 5, 6, 7, and 8 giving crystallographic data for the isoquinolinium salt (13 pages). Ordering information is given on any current masthead page.

Hydrolysis of 2-Aminopurine Deoxyribonucleoside in Neutral Solution

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At various temperatures between 50 and 110 °C, 2-aminopurine deoxyribonucleoside is severalfold more prone to degradation in aqueous sodium cacodylate buffer, pH 6.9, than is its structural isomer, deoxyadenosine, as determined by HPLC analysis of hydrolysates. It is calculated that, at 37 °C, the rate of hydrolysis of 2-aminopurine deoxyribonucleoside is 5 times as large as the rate of hydrolysis of deoxyadenosine. The decomposition of 2-aminopurine deoxyribonucleoside is almost unaffected by changes in ionic strength or buffer concentration, but is clearly accelerated by increasing acidity in the range from pH 5.8 to pH 7.15. While deoxyadenosine decomposes to produce the corresponding free base, adenine, as the sole UV-absorbing product, 2-aminopurine deoxyribonucleoside yields primarily 2,4-diamino-5-formamidopyrimidine rather than 2-aminopurine. The latter compound is also formed during hydrolysis of 2-aminopurine deoxyribonucleoside, but it arises largely in a secondary reaction from 2,4-diamino-5-formamidopyrimidine. The increased propensity to depurination evinced by 2-aminopurine deoxyribonucleoside in comparison to deoxyadenosine as well as the alteration of the heterocyclic base occurring during the hydrolysis is of interest in view of the mutagenic activity of 2-aminopurine.

The *N*-glycosyl bond in 2-aminopurine 2′-deoxyribonucleoside (**1**, see Scheme I) is significantly more prone to cleavage in neutral or basic aqueous medium at elevated temperatures than are the glycosyl linkages in 2′-deoxyadenosine (**2**) and 2′-deoxyguanosine.[1] While this observation was initially used as the basis for an analytical procedure for the quantitation of 2-aminopurine moieties

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