tolylphosphine, 0.022 g (0.10 mmol) of palladium acetate, and 1.75 mL (12.5 mmol) of triethylamine was heated in a steam bath in a capped heavy-walled Pyrex tube for 2 days. At this time GLC showed all of the p-bromodimethylaniline had reacted. After cooling the reaction mixture was diluted with ether and filtered to remove the triethylamine hydrobromide. Evaporation of the filtrate followed by distillation of the brown residue under reduced pressure gave 0.93 g (57%) of a yellow liquid, bp 190 °C (0.4 mm), which solidified on standing. The NMR spectrum of the product was identical with that reported for p-(dimethylamino)acetophenone.[7]

***N*-2-(3',4'-Diacetoxystyryl)phthalimide (Ic).** A mixture of 2.37 g (10 mmol) of 4-bromocatechol diacetate, 1.82 g (10.5 mmol) of *N*-vinylphthalimide, 1.26 g (12.5 mmol) of diisopropylamine, 0.1824 g (0.6 mmol) of tri-o-tolylphosphine, 0.022 g (0.10 mmol) of palladium acetate, and 4 mL of acetonitrile was heated in a capped nitrogen-filled tube at 100 °C for 15 h. The cooled reaction mixture was diluted with 150 mL of cold water and the crude yellow product was filtered. The dried product was heated with 25 mL of acetic anhydride and 5 drops of pyridine for 1 h at 100 °C to reacetylate any hydrolyzed material. After cooling the mixture was poured into ice and the solid recovered by filtration. After air drying the product was recrystallized from benzene–heptane to give 2.5 g (68%) of the product as small yellow crystals: mp 162–164 °C. Anal. Calcd for $C_{20}H_{15}NO_6$: C, 65.75; H, 4.14. Found: C, 66.02; H. 4.30.

***N*-[2-(3',4'-Diacetoxyphenyl)ethyl]hexahydrophthalimide.** A mixture of 1.0 g (2.74 mmol) of *N*-[2-(3',4'-diacetoxystyryl)]-phthalimide, 0.21 g of 10% palladium on charcoal, and 20 mL of toluene was put in a 60-mL bomb and hydrogenated at 100 °C and 600 psi for 16 h. The reduction did not go to completion under milder conditions. The cooled reaction mixture was filtered through Celite and the solvent was distilled under reduced pressure. The colorless oil that remained was crystallized from methylene chloride–heptane to give 0.55 g (55%) of colorless crystals: mp 96–99 °C. NMR ($CDCl_3$) δ 7.1 (m, 3 H), 3.75 (t, 2 H, J = 6 Hz), 2.85 (m, 2 H), 2.25 (s, 6 H), 1.55 (m, 10 H). ^{13}C NMR 142.04, 140.90, 136.59, 127.09, 124.01, 123.42. Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.62; H, 6.48; N, 3.63.

Epoxidation of Ic. A solution of 1.0 g (2.63 mmol) of Ic and 0.679 g (3.95 mmol) of m-chloroperbenzoic acid in 10 mL of methylene chloride was stirred at room temperature for 43 h. The solution was then diluted with 25 mL more of methylene chloride and the solution was extracted with aqueous sodium bicarbonate. After drying the methylene chloride phase was concentrated under reduced pressure and the solid remaining was recrystallized from methylene chloride–hexane to give 0.78 g (77%) of epoxide IIIc: mp 205–207.5 °C. NMR (90 MHz, $CDCl_3$) δ 7.58 (m, 9 H), 5.32 (d, J = 1 Hz, 1 H), 4.85 (d, J = 1 Hz, 1 H), 2.3 (s, 6 H). Anal. Calcd for $C_{20}H_{15}NO_7$: C, 62.99; H, 3.96. Found: C, 62.77; H, 3.60.

Hydrogenation of Ia. A mixture of 0.56 g (2.25 mmol) of Ia, 0.21 g of 10% palladium on charcoal, and 20 mL of toluene was stirred under 1 atm of hydrogen at room temperature for about 1 h when gas absorption stopped. The mixture was then filtered through Celite, rinsing with toluene, and the filtrate was concentrated under reduced pressure. The solid residue was recrystallized from heptane to give colorless crystals: mp 131–132 °C (reported 131 °C).[8] NMR ($CDCl_3$) δ 8.05 (m, 4 H), 7.55 (s, 5 H), 4.1 (t, J = 6 Hz, 2 H), 3.1 (t, J = 6 Hz, 2 H).

Epoxidation of Ib. A mixture of 4.13 g (13.4 mmol) of Ib and 4.16 g (24.2 mmol) of m-chloroperbenzoic acid in 80 mL of benzene was stirred at room temperature for 20 h. After extraction of the solution with aqueous sodium bicarbonate and drying, the benzene was distilled under reduced pressure and the product was recrystallized from chloroform–heptane. There was obtained 3.15 g (70%) of colorless epoxide IIIb: mp 174–176 °C. NMR ($CDCl_3$) δ 7.6 (m, 8 H), 5.35 (d, J = 1 Hz, 1 H), 4.9 (d, J = 1 Hz, 1 H), 2.3 (s, 3 H). Anal. Calcd for $C_{18}H_{13}NO_5$: C, 66.87; H, 4.05. Found: C, 66.88; H. 4.10.

***N*-[2-(p-Acetoxyphenyl)-1-hydroxyethyl]phthalimide (Vb).** A mixture of 0.42 g of the epoxide of Ib and 0.1 g of 10% palladium on charcoal in 25 mL of ethyl acetate containing 2 drops of acetic acid was reduced at room temperature with 1 atm of hydrogen. In 2 h 1 equiv of hydrogen was absorbed. The solution was filtered through Celite and the solvent was removed under reduced pressure. The solid remaining was recrystallized from chloroform–heptane to give 0.162 g (39%) of colorless (impure) crystals: mp 220–233 °C dec. NMR ($CDCl_3$) δ 7.55 (m, 8 H), 5.95 (t, J = 7 Hz, 1 H), 4.3 (s, 1 H), 3.5 (d, J = 7 Hz, 2 H), 2.2 (s, 3 H). Anal. Calcd for $C_{18}H_{15}NO_5$: C, 66.46; H, 4.65. Found: C, 65.31; H, 3.66.

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Registry No.—Ia epoxide, 66374-02-5; IIIb, 66374-03-6; IIIc, 66374-04-7; IVb, 66374-07-0; Vb, 66374-06-9; *N*-[2-(3',4'-diacetoxyphenyl)ethyl]hexahydrophthalimide, 66374-05-8.

Supplementary Material Available: Table II listing melting points, molecular weights, and NMR spectra of the products prepared (2 pages). Ordering information is given on any current masthead page.

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Palladium-Catalyzed Synthesis of 2-Quinolone Derivatives from 2-Iodoanilines

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Several new examples of the use of 1,2-disubstituted olefins in the palladium-catalyzed vinylic substitution reaction have been studied. Stereochemical results are reported. This reaction was used with substituted acrylic acid derivatives and o-iodoanilines to form 2-quinolones in moderate to good yields.

The recent discovery that o-aminoaryl and hydroxyaryl halides underwent the palladium-catalyzed vinylic substitution reaction in good yields in several instances[1] suggested that quinolone and coumarin derivatives might be formed via these reactions. In the previous study monosubstituted olefins—methyl acrylate, acrylic acid, acrylonitrile, and styrene—were found *not* to undergo cyclization when reacted with 2-bromo- or 2-iodoaniline or the corresponding halophenols.

Palladium hydride elimination from the intermediate adduct (I, for example) must have been faster than ring closure. The elimination selectivity formed trans products which did not isomerize and cyclize under the reaction conditions

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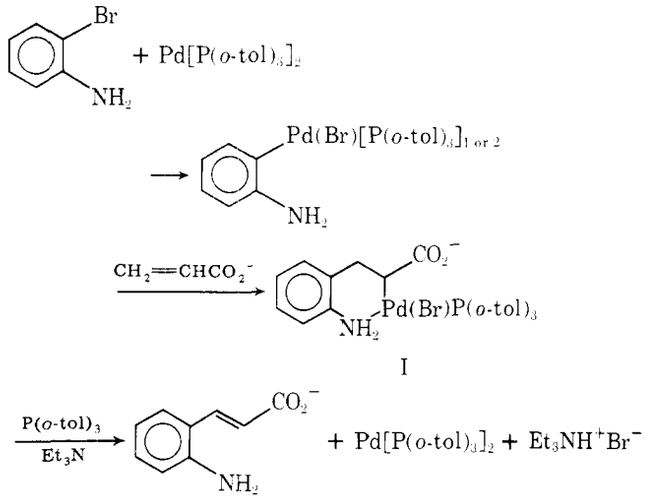
Scheme I



(Scheme I). Of course, various *trans*-*o*-amino- and hydroxycinnamic acid derivatives can be cyclized in various other ways, but it would be more useful if the cyclization could be achieved in one reaction without isolation of the cinnamic acid derivative.

1,2-Disubstituted olefins undergo the vinylic substitution reaction with triarylphosphine–palladium acetate catalysts, stereospecifically via a syn addition of the organopalladium intermediate followed by a syn "palladium hydride" elimination.[2] In the absence of a triarylphosphine, aryl iodides, but not bromides, reacted also, but with considerable loss of stereochemistry, presumably because of multiple palladium hydride readdition–elimination sequences before the "palladium hydride" was finally lost from the molecule. Evidence also indicated that isomerization occurred only from within the "palladium hydride" π complex and not from "palladium hydride" in solution.[2] Two approaches to the direct formation of cyclic products by the vinylic substitution were therefore possible. (1) (*Z*)-3-substituted acrylic acid derivatives could be reacted with haloanilines or halophenols and triarylphosphine-containing catalysts and the products should have the correct stereochemistry to cyclize directly. (2) Iodoanilines or iodophenols could be reacted in the absence of triarylphosphines with the hope that the intermediate palladium adduct of the olefin or its cis "palladium hydride" π complex would exist long enough to cyclize before the palladium hydride dissociated completely and was recycled.

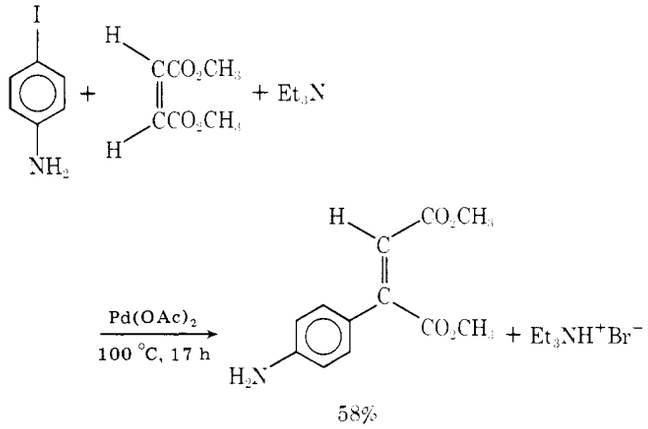
In addition to the stereochemical problem, we anticipated difficulty in getting the rather unreactive disubstituted olefins to react with the relatively unreactive ortho-substituted haloaromatics. Accordingly, we carried out experiments to see if these possible problems were significant. While the situation turned out to be somewhat more complicated than the above ideas suggested, we did find a generally useful, new synthesis for quinolone derivatives which will be the major subject of this report.

Results and Discussion

Relatively few 1,2-disubstituted olefins had been tried in the vinylic substitution reaction previously. Successful reactions had been reported only between bromo- or iodobenzene and (*E*)- and (*Z*)-propenylbenzene,[2] (*E*)-methyl crotonate,[3] and several allylic alcohols.[3] The range of reactions has now been extended considerably to include reactions of various aryl halides with dimethyl maleate, diethyl fumarate, (*E*)-methyl cinnamate, (*E*)-methyl *p*-carbomethoxycinnamate, cyclohexene, and (*E*)- and (*Z*)-3-hexene. The results of these reactions are summarized in Table I.

The results of a large number of vinylic substitution reactions indicate that monosubstituted olefins are more reactive than disubstituted ones, since when excess olefin is present the reaction does not give significant yields of diarylated products. However, a variety of disubstituted olefins will undergo arylation fairly easily. Aryl iodides generally react better than the bromides, but still the bromides are useful in some instances. The stereoselectivity of the additions vary widely with the reactants. Dimethyl maleate gave mixtures of (*E*)- and (*Z*)-phenylated products, along with minor amounts of biphenyl, in the reaction with iodobenzene. The highest selectivity was only a little better than 2:1 in favor of the *E* product using as catalyst triphenylphosphine–palladium acetate. The product ratio appeared to depend upon the strength of the base used in the reaction. Tri-*n*-butylamine gave much higher selectivity (*E*/*Z* = 1.75) than the more strongly basic triethylamine (0.61).

This result suggests that a (trans) base-catalyzed elimination of palladium hydride may be responsible, at least in part, for the formation of the *Z* product. Since the usual uncatalyzed palladium hydride elimination is syn and phenylpalladium complexes add in a syn manner to olefins,[2] the *E* product would have been expected. The possible base-catalyzed elimination cannot be the only source of the *Z* isomer, however, since the ratio of the *E* to *Z* products decreases with time. Examination of the excess olefin remaining after reaction of iodobenzene with dimethyl maleate revealed that about 60–70% of the excess had been isomerized to dimethyl fumarate. Since the fumarate and maleate esters react at roughly the same rates with iodobenzene and the tri-*o*-tolylphosphine catalyst, much or even all of the isomerized product could be coming from isomerized starting olefin. The tendency for isomerization to occur appeared even more serious in the reaction of 4-iodoaniline with dimethyl maleate, since only the *Z* product was found (58% yield).



58%

Diethyl fumarate and iodobenzene react much more selectively, since both the reactants and products are the more stable isomers. As observed previously, higher selectivity is achieved when phosphines are present. Thus, with a 2:1 tri-*o*-tolylphosphine–palladium acetate catalyst the *Z* product was obtained in 80% yield along with 6% *E* product and 11% biphenyl.

Attempts were made to react iodobenzene with three other related compounds—maleic acid (3 equiv of triethylamine were used), *N*-methylmaleimide, and maleic anhydride. In all cases the only identifiable product was biphenyl.

(*E*)-Methyl cinnamate and iodobenzene react rather slowly, but in 98 h under the usual conditions gave the expected methyl 3,3-diphenylacrylate in 67% yield. This product could also be obtained by diarylation of methyl acrylate with either bromobenzene (78% yield) or iodobenzene (70%). To achieve diarylation, an excess (250%) of the aryl halide was used over the methyl acrylate. Acrylonitrile did not diarylate under the

Table I. Vinylic Arylation of Various 1,2-Disubstituted Olefins[a]

olefin	registry no.	aryl halide	registry no.	PR_3	PR_3/Pd-$(OAc)_2$	temp, °C	time	product (% yield)	registry no.
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[b]	624-48-6	C_6H_5Br	108-86-1	P(*o*-tol)$_3$	4	100	6 days	(*E*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (10) (*Z*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (6)	29394-47-6 29576-99-6
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[b]		C_6H_5I	591-50-4			100	5 h	(*E*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (54) (*Z*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (39) Ph–Ph (5)	 92-52-4
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[b]		C_6H_5I		P(*o*-tol)$_3$	2	100	4 h	(*E*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (43) (*Z*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (36) Ph–Ph (11)	
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[c]		C_6H_5I		P(*o*-tol)$_3$	8	100	2 h	(*E*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (25) (*Z*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (41) Ph–Ph (14)	
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[c]		C_6H_5I		P(*o*-tol)$_3$	8[d]	100	44 h	(*E*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (42) (*Z*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (24) Ph–Ph (23)	
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[c]		C_6H_5I		PPh_3	8	100	2 h	(*E*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (51) (*Z*)-$CH_3OCOC(C_6H_5){=}CHCO_2CH_3$ (21) Ph–Ph (10)	
(*Z*)-$CH_3OCOCH{=}CHCO_2CH_3$[c]		4-$H_2NC_6H_4I$	540-37-4			100	17 h	(*Z*)-$CH_3OCOC(4\text{-}H_2NC_6\text{-}H_4){=}CHCO_2CH_3$ (58)	66416-69-1
(*E*)-$C_2H_5OCOCH{=}CHCO_2C_2H_5$[b]	623-91-6	C_6H_5I				100	30 min	(*E*)-$C_2H_5OCOC(C_6H_5){=}CHCO_2C_2H_5$ (19) (*Z*)-$C_2H_5OCOC(C_6H_5){=}CHCO_2C_2H_5$ (75) Ph–PH (5)	40746-94-9 5309-59-1
(*E*)-$C_2H_5OCOCH{=}CHCO_2C_2H_5$[b]		C_6H_5I		P(*o*-tol)$_3$	2	100	2 h	(*E*)-$C_2H_5OCOC(C_6H_5){=}CHCO_2C_2H_5$ (6) (*Z*)-$C_2H_5OCOC(C_6H_5){=}CHCO_2C_2H_5$ (80) Ph–Ph (11)	
(*E*)-$C_6H_5CH{=}CHCO_2CH_3$	1754-62-7	C_6H_5I				100	98 h[e]	$(C_6H_5)_2C{=}CHCO_2CH_3$ (67)	3461-34-5
(*E*)-$C_6H_5CH{=}CHCO_2CH_3$		4-$CH_3OCOC_6H_4Br$	619-42-1	P(*o*-tol)$_3$	4	150	53 h	(*E*)-(4-$HO_2CC_6H_4$)(C_6H_5)$C{=}CHCO_2H$ (52[f])	66416-70-4
(*E*)-4-$CH_3OCOC_6H_4$-$CH{=}CHCO_2CH_3$	52148-89-7	C_6H_5Br[g]		P(*o*-tol)$_3$	4	150	56 h	(*Z*)-(4-$HO_2CC_6H_4$)(C_6H_5)$C{=}CHCO_2H$ (77[f]) (*E*)-(4-$HO_2CC_6H_4$)(C_6H_5)$C{=}CHCO_2H$ (10[f])	66416-71-5
cyclohexene	110-83-8	C_6H_5Br		P(*o*-tol)$_3$	2	125	41 h	3-phenylcyclohexene (56)	15232-96-9
cyclohexene		C_6H_5I				100	15 h	3-phenylcyclohexene (72)	
cyclohexene		4-$HOCOC_6H_4Br$[i]	586-76-5	P(2,5-*i*-$Pr_2C_6H_3$)$_3$	4	125	40 h	4-(1′-cyclohexenyl)benzoic acid (16[j])	19920-83-3
(*E*)-$CH_3CH_2CH{=}CHCH_2CH_3$	13269-52-8	C_6H_5Br		P(*o*-tol)$_3$	2	100	112 h	(*E*)-$CH_3CH_2C(C_6H_5){=}CHCH_2CH_3$ (23) (*E*)-$CH_3CH_2CH(C_6H_5)CH{=}CHCH_3$[k] (23)	39857-50-6 51175-90-7
(*E*)-$CH_3CH_2CH{=}CHCH_2CH_3$[h]		C_6H_5I				100	15 h	(*E*)-$CH_3CH_2C(C_6H_5){=}CHCH_2CH_3$ (39) (*E*)-$CH_3CH_2C(C_6H_5)CH{=}CHCH_3$[k] (23)	
(*Z*)-$CH_3CH_2CH{=}CHCH_2CH_3$	7642-09-3	C_6H_5Br		P(*o*-tol)$_3$	2	100	5 days	(*E*)-$CH_3CH_2C(C_6H_5){=}CHCH_2CH_3CHCH_2CH_3$ (30[l]) (*E*)-$CH_3CH_2C(C_6H_5)CH{=}CHCH_3$[k] (15) unknown A (3) unknown B (2)	

[a] Reactants: 10 mmol of aryl halide, 11–12.5 mmol of olefin, 10 mmol of Et_3N, and 1 mol % of $Pd(OAc)_2$. [b] 4 mL of acetonitrile used as solvent. [c] Excess ester remaining after completion of the reaction was about 65% isomerized to dimethyl fumarate. [d] Tri-*n*-butylamine was used as the base in place of Et_3N. [e] 0.4 mol % of palladium acetate used as catalyst. [f] Hydrolyzed product, crude yield. [g] Reactants: 12.5 mmol of bromobenzene, 10 mmol of methyl *p*-carbomethoxycinnamate, 12.5 mmol of triethylamine, 0.1 mmol of $Pd(OAc)_2$, 0.4 mmol of tri-*o*-tolylphosphine, and 5 mL of acetonitrile. [h] 25 mmol of olefin with 10 mmol of organic halide was used. [i] 20 mmol of Et_3N was used. [j] 60% of unreacted *p*-bromobenzoic acid was recovered after the reaction. [k] Presumed isomer. [l] 46% Bromobenzene remained after the reaction stopped.

same conditions. Palladium metal was deposited very quickly and only monoarylation occurred.

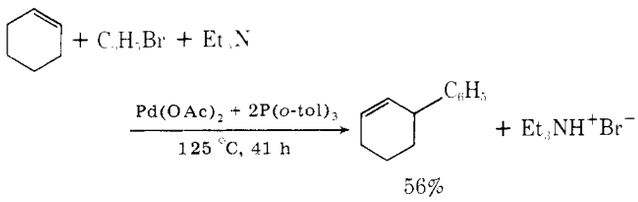
$$CH_2{=}CHCO_2CH_3 + 2C_6H_5Br + 2Et_3N \xrightarrow[100\ °C,\ 43\ h]{Pd(OAc)_2 + 4\ P(o\text{-}tol)_3} (C_6H_5)_2C{=}CHCO_2CH_3 + 2Et_3NH^+Br^-$$

78%

We looked briefly at the stereochemistry of the arylation of cinnamate esters. (*E*)-Methyl cinnamate was reacted with methyl 4-bromobenzoate at 150 °C and the product obtained was compared to the product obtained from the reaction of (*E*)-methyl *p*-carbomethoxycinnamate with bromobenzene. The first reaction should produce the *E* product and the second reaction the *Z* product. Both products were viscous liquids with very similar NMR spectra. Hydrolysis gave the diacids, which were conclusively shown to be, at least mainly, different compounds based upon the slight differences in the NMR spectra and melting points. While we cannot independently be sure of which isomer is which, we believe the reactions proceeded stereospecifically and that the structures of the major products formed can be assigned on the basis of the known stereochemistry of this reaction.[2]

Finally, three internal alkenes were reacted with bromo- or iodobenzene to determine the stereochemistry with these systems. With the usual 1 mol % of catalyst and bromobenzene as reactant these reactions generally stopped after only about 50% of the bromobenzene had reacted. Since little palladium metal precipitated, we presume the reactions stop because a stable organopalladium complex is being formed, probably a π-allyl complex. Iodobenzene with a palladium acetate catalyst gives much higher yields of products.

Cyclohexene and bromobenzene, with the tri-*o*-tolylphosphine catalyst, produced essentially pure 3-phenylcyclohexene



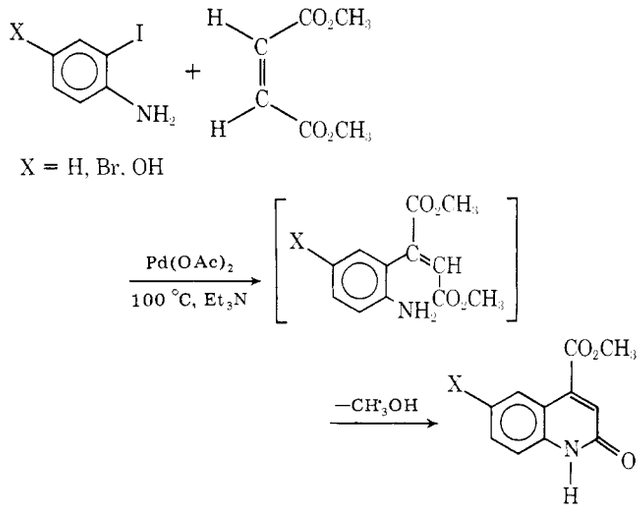
56%

in 56% yield. This is the product expected on the basis of a syn addition of the phenylpalladium complex to cyclohexene, followed by a syn elimination of the palladium hydride. Similar results were found previously when this reaction was carried out stoichiometrically with phenylmercuric acetate, palladium acetate, and various cyclic olefins,[4] although some isomerization occurred in some of these cases.

Application of this reaction to 4-bromobenzoic acid, however, led to only the 1-aryl olefin, presumably because the initially formed 3-aryl isomer isomerized under the reaction conditions (amine catalyzed?). The yield in this example was only 16%; however 60% of 4-bromobenzoic acid was recovered after completion of the reaction.

Both (*E*)- and (*Z*)-3-hexene gave the same two major products on reaction with bromobenzene: (*E*)-3-phenyl-3-hexene and 4-phenyl-2-hexene, probably also the *E* isomer. Two minor isomers were also formed, but not identified. The (*E*)-3-hexene reaction gave about a 1:1 ratio of the two major products (total yield 46%), while the *Z* olefin gave about a 2:1 mixture in favor of the conjugated isomer (total yield 45%). The absence of a significant amount of the (*Z*)-3-phenyl-3-hexene from the (*Z*)-3-hexene reaction suggests that the palladium hydride elimination may be giving largely the 4-phenyl-2-hexene–palladium hydride π complex initially, which then partially isomerizes to the (*E*)-3-phenyl-3-hexene.

Scheme II



Cyclohexene and (*E*)- and (*Z*)-3-hexene all gave incomplete reactions with the aryl bromides, presumably because the catalysts were gradually converted into stable π-allylic complexes during the reaction. The use of twice the usual amount of catalyst did not improve the yields. Better results were obtained with iodobenzene and palladium acetate as catalyst. In these reactions significant amounts of high boiling materials (diarylated products?) were formed under the usual conditions. The use of a 250% excess of olefin decreased the amount of higher boiling products and improved the yields of the monophenylated products from cyclohexene and (*E*)-3-hexene to 72 and 62%, respectively.

These results do not require modification of our previous conclusions about the mechanism of the olefin arylation reaction, but there are a variety of side reactions possible which can cause loss of stereoselectivity. The existence of these isomerization mechanisms, however, should make the formation of cyclic structures more favorable for reactions which would give open chain structures if isomerization could not occur.

Reactions of 2-iodoaniline or its derivatives with dimethyl maleate would be expected to form *Z* intermediate amino esters which would cyclize to quinolones. Indeed, this does occur in reasonable yields in the three examples we have studied. *o*-Iodoaniline, 4-bromo-2-iodoaniline, and 4-hydroxy-2-iodoaniline gave 71, 55, and 30% yields, respectively, of the expected quinolones in the reaction (Scheme II). The low yield from the 4-hydroxy compound is not unexpected in view of the low yields obtained in a variety of similar reactions when strongly electron-donating substituents were present in the aryl iodide.[1] The results of these and some related reactions appear in Table II.

The reaction of *o*-iodoaniline with diethyl fumarate could give the *E* intermediate amino ester, which should not cyclize without first isomerizing. This reaction also gives the quinolone, but only in 47% yield along with 20% aniline. None of the possible *E* amino ester was found. Clearly either isomerization occurs fairly easily or the σ-bonded palladium intermediate cyclizes readily in this reaction.

4-Phenyl-2-quinolone was obtained in 66% yield by reacting *o*-iodoaniline with (*Z*)-*N*-phenylcinnamamide[5] (Scheme III). Again the stereochemistry is correct for direct cyclization, but as in the above case the use of (*E*)-*N*-phenylcinnamamide instead of the *Z* isomer also gives the quinolone, but only in 15% yield. The rest of the product is an intractable dark viscous oil.

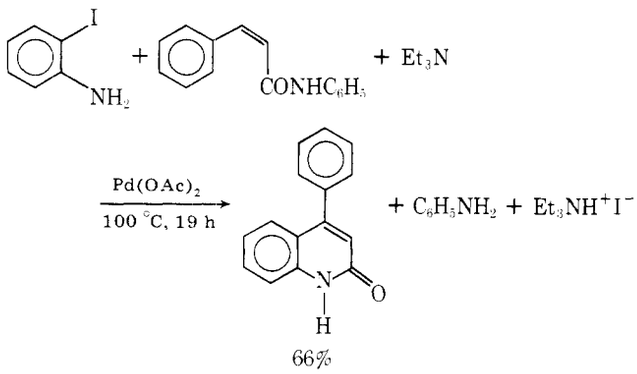
An alternative route to 4-phenyl-2-quinolone, in which the intermediate with the presumed most desirable stereochem-

Table II. Quinolone Derivatives Prepared by the Olefinic Substitution Reaction[a]

organic halide	registry no.	olefin	registry no.	reaction time, h	product (% yield)	registry no.
2-iodoaniline	615-43-0	dimethyl maleate		2	4-carbomethoxy-2-quinolone (72)	39497-01-3
4-bromo-2-iodoaniline	66416-72-6	dimethylmaleate		3.5	6-bromo-4-carbomethoxy-2-quinolone (55)	66416-74-8
4-amino-3-iodophenol	66416-73-7	dimethyl maleate		45	4-carbomethoxy-6-hydroxy-2-quinolone (30)	66416-75-9
2-iodoaniline		diethyl fumarate		48	4-carboethoxy-2-quinolone (47) aniline (20)[b]	5466-27-3 62-53-3
2-iodoaniline		(*Z*)-*N*-phenylcinnamamide	52393-67-6	19	4-phenyl-2-quinolone (66)	5585-57-2
2-iodoaniline		(*E*)-*N*-phenylcinnamamide	25775-89-7	31	4-phenyl-2-quinolone (15)	
iodobenzene		(*E*)-2-aminocinnamic acid	22469-15-4	27	4-phenyl-2-quinolone (71)	
2-iodoaniline		(*E*)-methyl crotonate	623-43-8	30	4-methyl-2-quinolone (55)[c] aniline (22)	607-66-9
2-iodoaniline		methyl methacrylate	80-62-6	42	3-methyl-2-quinolone (24)[d]	2721-59-7

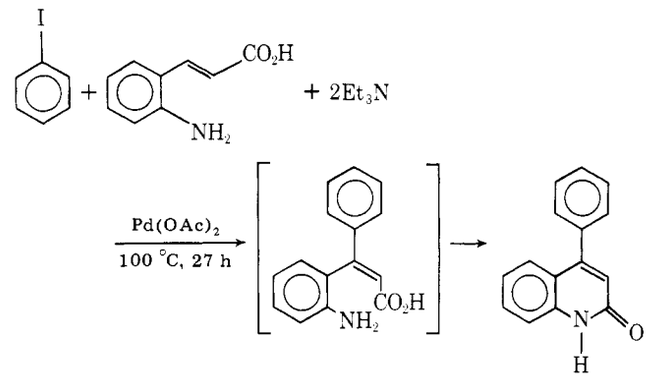
[a] Reactions carried out with 10 mmol of aryl halide, 12.5 mmol of olefin, 10 mmol of Et_3N, 1 mol % of $Pd(OAc)_2$, and 4 mL of acetonitrile at 100 °C. [b] GLC yield. [c] When this reaction was carried out with the addition of 2 mol % of PPh_3 the yield was 19%. [d] After sublimation.

Scheme III



66%

Scheme IV



71%

istry should be attained, is the reaction of (*E*)-2-aminocinnamic acid (or esters or amides) with iodobenzene. This variation works well. A 71% yield of the quinolone was obtained (Scheme IV).

A third example of cyclization with reactants which should yield the wrong stereochemistry for direct cyclization occurred in the reaction of (*E*)-methyl crotonate with *o*-iodoaniline. The reaction produced 4-methyl-2-quinolone in 55% yield along with 22% aniline. As expected, the reaction of 4-iodoaniline with (*E*)-methyl crotonate gives a high yield, 76%, of (*E*)-methyl 2-methyl-4-aminocinnamate under similar conditions. Presumably (*Z*)-methyl crotonate and *o*-iodoaniline would give a higher yield of cyclized product than the *E* ester did, but we did not carry out this reaction.

Since *o*-iodoaniline and acrylic acid react to form only (*E*)-*o*-aminocinnamic acid in 72% yield and no significant amount of 2-quinolone,[1] it was of interest to see if α-substituted acrylate esters would cyclize. Accordingly, methyl methacrylate and *o*-iodoaniline were reacted. This reaction apparently gave a mixture of open-chain product, presumably the *E* amino ester, and 3-methyl-2-quinolone. These were difficult to separate, so the mixture was sublimed to convert the open-chain ester into the cyclic product also. The quinolone was then isolated in 24% yield.

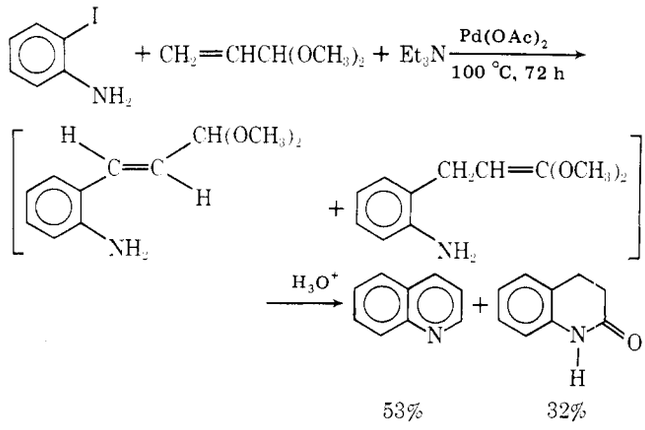
Attempts to react two trisubstituted olefins, methyl 2-cyclohexenecarboxylate and (*Z*)-*N*-phenyl-2-ethylpentanamide,[5] with *o*-iodoaniline under our usual conditions were unsuccessful presumably because of steric congestion.

Thus, even though the yields are not always high, the synthesis of 2-quinolone derivatives by the olefin arylation reaction is a very simple, one-step procedure. Since the starting materials are readily available, in most instances, this reaction provides a convenient method for preparing a variety of 2-quinolones.

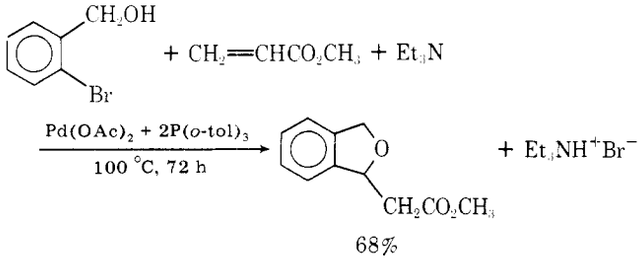
We briefly investigated the preparation of quinoline from 2-iodoaniline and acrolein dimethyl acetal. From previous work we knew that the acetal rather than free acrolein had to be used.[6] No attempt was made to isolate the presumed acetal intermediate in the reaction, but the crude product was treated with aqueous acid to cyclize it. As anticipated from the previous work, two products were obtained. The major product was quinoline, obtained in 53% yield, and the minor product was dihydroquinolone, obtained in 32% yield (Scheme V). The minor product is likely formed from the ketene acetal formed when palladium hydride elimination in the intermediate occurs to the acetal carbon rather than the benzylic carbon.

An obvious extension of the 2-quinolone preparation is to *o*-iodophenol to produce coumarins. However, in spite of many tries, we have had no success in obtaining cyclic products directly. *o*-Iodophenol and methyl acrylate react in 95% yield to form (*E*)-methyl *o*-hydroxycinnamate,[1] but *o*-iodophenol and dimethyl maleate or methyl cinnamate produce only phenol in over 80% yield under the same conditions. Even *o*-iodophenyl acetate and methyl cinnamate do not give a

Scheme V



significant yield of a single product. We did achieve a clean cyclization in the reaction of *o*-bromobenzyl alcohol with methyl acrylate, however, according to the following equation.



2-Bromobenzylamine did not yield an analogous product under the same conditions.

We also looked at the possibility of forming 2-aminoquinoline derivatives from *o*-iodoaniline and acrylonitrile. This reaction produced 53% (*E*)-2-aminocinnamonitrile,[1] 6% of the *Z* isomer, and no cyclic product. Apparently cyclization is much more difficult in this case. 2-Aminocinnamonitrile and iodobenzene reacted to form five or six products and clearly cyclization, if it occurred, was not a particularly favorable reaction.

Experimental Section

Reagents. With the exceptions noted below the reagents and solvents employed were the same as those used previously.[1,2] (*E*)-Methyl 4-carbomethoxycinnamate was prepared as previously described.[2] The procedure of Dains et al. was used for the preparation of 4-bromo-2-iodoaniline[7] and 4-hydroxy-2-iodoaniline was made by the method of Kvalnes.[8] The preparation of (*E*)-*o*-aminocinnamic acid was described in a previous paper.[1]

General Procedure for Arylation of 1,2-Disubstituted Olefins. Mixtures of 10 mmol of the aryl halide, 11–12.5 mmol of olefin, 10–12.5 mmol of triethylamine, 4–5 mL of acetonitrile, 0.10 mmol of palladium acetate, and the appropriate amount of a triarylphosphine, if one was used, were heated in capped Pyrex tubes at 100–125 °C as indicated in the tables until GLC analyses indicated the aryl halide had all reacted or that the reaction had stopped. An internal standard for GLC analyses of naphthalene, benzophenone, or methylnaphthalene was sometimes used. Reactions at 150 °C were done in a 60-mL stainless steel bomb. In some examples the products crystallized from the reaction mixtures and on cooling were filtered, washed with acetonitrile, and recrystallized. In other examples the reaction mixtures were diluted with cold dilute hydrochloric acid and the products were extracted with ether or methylene chloride. Evaporation of the solvent then gave crude products which were either distilled, sublimed, or recrystallized. This is essentially the same procedure we used previously.[2] Some specific examples are given below. The properties of the products prepared, melting points, NMR spectra, molecular weights, and other properties are given in Table III, which will only appear in the microfilm edition of this paper. (See note on Supplementary Material at the end of this article.)

Diethyl Phenylmaleate. In a heavy-walled Pyrex tube equipped with a stirring bar were placed 1.1 mL (10 mmol) of iodobenzene, 2.15 g (12.5 mmol) of diethyl fumarate, 22.4 mg (0.10 mmol) of $Pd(OAc)_2$, 60.8 mg (0.20 mmol) of tri-*o*-tolylphosphine, 1.4 mL (10 mmol) of triethylamine, 4 mL of acetonitrile and 334 mg (2.61 mmol) of naphthalene as an internal standard. The reaction tube was flushed with argon and capped. It was then stirred in the steam bath at 100 °C for 2 h. At the end of this time GLC analyses showed that all of the halide had reacted and that the yields of products were 80% diethyl phenylmaleate, 6% diethyl phenylfumarate, and 11% biphenyl.

Methyl 3,3-Diphenylacrylate. A capped bottle containing 25.5 g (125.0 mmol) of iodobenzene, 4.3 g (50 mmol) of methyl acrylate, 12.8 g (0.125 mmol) of triethylamine, 0.0560 g (0.25 mmol) of $Pd(OAc)_2$, and 20 mL of acetonitrile was stirred at 100 °C under a N_2 atmosphere for 21 h. Analyses of a portion of the reaction mixture by GLC showed a 70% yield of methyl 3,3-diphenylacrylate and a 20% yield of methyl cinnamate had been obtained. Also present was 14.5 mmol of biphenyl. The reaction mixture was poured into 500 mL of cold 1 N HCl. An oil separated. It was extracted with CH_2Cl_2 and the extracts were dried with sodium sulfate, filtered, and concentrated. The dark oil was distilled, yielding 7.2 g (61%) of colorless liquid: bp 135–149 °C (0.5 mm) [lit. 130–132 °C (0.01 mm)].[9] NMR ($CDCl_3$) showed absorption bands at δ 3.6 (s, 3 H), 6.4 (s, 1 H), and 7.3 (s, 10 H).

(*E*)-3-(*p*-Carboxyphenyl)-3-phenylacrylic Acid. In a 60-mL stainless steel pressure vessel was placed 2.36 g (11 mmol) of methyl *p*-bromobenzoate, 1.62 g (10 mmol) of methyl cinnamate, 1.25 g (12.5 mmol) of triethylamine, 0.0224 g (0.1 mmol) of palladium acetate, 0.1216 g (0.4 mmol) of tri-*o*-tolylphosphine, and 5 mL of acetonitrile. The closed vessel was heated in an oil bath at 150 °C for 53 h. After cooling the contents of the bomb was diluted with 100 mL of 1 M hydrochloric acid and the product was extracted with methylene chloride. The extracts were dried and concentrated to a viscous oil. Since the oil could not be crystallized, it was boiled with methanolic sodium hydroxide for 2 h to hydrolyze the ester groups. Dilution of the hydrolysis mixture with cold dilute hydrochloric acid precipitated the product. After air drying, 1.4 g (52%) of crude diacid, mp ~262 °C dec, was obtained. The product was sublimed at <1 mm pressure and 220 °C and recrystallized twice from aqueous methanol to give 0.24 g (9%) of pale yellow pure acid: mp 268–273 °C dec. The NMR spectrum of the crude acid showed it to be at least 80% pure.

(*Z*)-3-(*p*-Carboxyphenyl)-3-phenylacrylic Acid. A mixture of 1.96 g (12.5 mmol) of bromobenzene, 2.2 g (10 mmol) of methyl 4-carbomethoxycinnamate,[2] 1.25 g (12.5 mmol) of triethylamine, 0.0224 g (0.1 mmol) of palladium acetate, 0.1216 g (0.4 mmol) of tri-*o*-tolylphosphine, and 5 mL of acetonitrile was heated at 150 °C for 56 h in a 60-mL stainless steel bomb. The product was isolated and hydrolyzed, giving 2.33 g (87%) of crude diacid, mp 217–225 °C dec. The NMR spectrum of the crude acid was very similar to that of the *E* isomer, but at 90 MHz a mixture of the two showed a double set of peaks, confirming that they were different compounds. Sublimation and recrystallization of this product led to the isolation of 10% of the *E*-diacid: mp 268–273 °C dec. We could not determine from the NMR spectrum if this minor amount of material was present in the crude acid or whether it was formed in the 220 °C sublimation.

Preparation of 3-Phenylhexenes. In a 200-mL heavy-walled Pyrex bottle were placed 31.4 g (200 mmol) of bromobenzene, 21.1 g (251 mmol) of *cis*-3-hexene, 0.5 g (2.2 mmol) of palladium acetate, 1.3 g (4.2 mmol) of tri-*o*-tolylphosphine, and 25.4 g of triethylamine. The bottle was flushed with argon and capped and the reaction mixture was heated at 100 °C on a steam bath for 5 days. The cooled reaction mixture was diluted with water and the products were extracted with ether. The ether extract was then dried with magnesium sulfate, filtered, and concentrated to a red oil. Distillation gave a 49% yield of a 2:1 mixture of 3-phenyl-3-hexene (*E* isomer?) and 4-phenyl-2-hexene (*E* isomer?). Also present in this mixture were two minor isomers present in 2 and 3% yields. The major components were separated by preparative GLC and their identities confirmed by mass spectroscopy and NMR and UV analyses.

Hydrogenation of the 3-Phenylhexene Isomers. The above isomeric mixture (2 g) was placed in a heavy-wall Pyrex bottle with 0.1 g of 5% Pd/C, 10 mL of 95% ethanol, and a stirring bar. After capping, the bottle was flushed several times with N_2 and evacuated. The bottle was then pressurized with H_2 to 30 psi and stirred vigorously at room temperature. After 18 h hydrogen absorption stopped. The reaction mixture was filtered through a glass frit and the filtrate was distilled. There was obtained an 87% yield of 3-phenylhexane: bp 92 °C (17 mm). This product was a single material as judged by GLC analyses.

Methyl 6-Bromo-2-quinolone-4-carboxylate. In a heavy-walled Pyrex tube equipped with a stirring bar were placed 2.84 g (10 mmol) of 2-iodo-4-bromoaniline, 1.8 g (12.5 mmol) of dimethyl maleate, 22.4

mg (0.10 mmol) of $Pd(OAc)_2$, 1.4 mL (10 mmol) of triethylamine, and 4 mL of acetonitrile. The tube was then flushed with argon, capped, and placed in the steam bath and stirred at 100 °C for 3.5 h. At the end of this time GLC analysis showed that all of the halide had reacted. The reaction tube was filled with a solid. The solid was filtered and washed with CH_3CN. Recrystallization from a large volume of benzene gave a 55% yield (1.56 g) of light tan needles: mp 275–278 °C.

Quinoline from Acrolein Dimethyl Acetal. In a heavy-walled Pyrex tube equipped with a stirring bar were placed 2.19 g (10 mmol) of 2-iodoaniline, 1.25 g (12.5 mmol) of acrolein dimethyl acetal, 22.4 mg (0.10 mmol) of $Pd(OAc)_2$, 1.4 mL (10 mmol) of triethylamine, and 4 mL of acetonitrile. The tube was flushed with argon and capped. It was then placed in the steam bath and stirred at 100 °C for 72 h. At this time GLC analysis showed that all of the halide had reacted. The products were isolated by evaporating the acetonitrile under reduced pressure and treating the residue with 10% HCl. An ether extraction of the acidic solution removed the 2-quinolone. Evaporation of the ether gave a 32% yield of product: mp 161–162 °C. The acidic solution was then basified with $NaHCO_3$ and extracted with ether. Evaporation of the ether and distillation, bp 115–117 °C (0.25 mm), gave quinoline in 53% yield.

Methyl 1,3-Dihydrobenzo[*c*]furan-1-ylacetate. In a heavy-walled Pyrex tube were placed 1.87 g (10 mmol) of *o*-bromobenzyl alcohol, 1.12 mL (12.5 mmol) of methyl acrylate, 22.4 mg (0.10 mmol) of $Pd(OAc)_2$, 60.8 mg (0.20 mmol) of tri-*o*-tolylphosphine, and 5 mL of triethylamine. The tube was flushed with argon, capped, and placed in a steam bath for 72 h. At this time the reaction mixture was filtered to remove amine salt. The salt was washed with ether and the filtrate was diluted with water. The ether layer was separated, dried over $MgSO_4$, filtered, and concentrated. Distillation of the residual oil afforded the product in 68% yield: bp 115 °C (2 mm).

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Registry No.—3-Phenylhexane, 4468-42-2; acrolein dimethyl acetal, 6044-68-4; methyl 1,3-dihydrobenzo[*c*]furan-1-ylacetate, 66416-76-0.

Supplementary Material Available: Table III with physical properties and spectra of the products prepared (2 pages). Ordering information is given on any current masthead page.

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[Poly(styryl)bipyridine]palladium(0)-Catalyzed Isomerization of Quadricyclene[1]

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The isomerization of quadricyclene is catalyzed by [poly(styryl)bipyridine]palladium(0). The rate of isomerization increases with increased metal loading and with increased amounts of added catalyst, but decreases with increasing concentration of quadricyclene. Significantly decreased activity is observed on reuse of the catalyst, due in part to leaching of the metal. However, on a gram to gram basis, [poly(styryl)bipyridine]palladium(0) is ~30 times as active as 10% Pd/C. Even after two cycles, the recovered catalyst is as active as Pd/C.

The photochemical synthesis of quadricyclene from norbornadiene was first reported by Hammond, Turro, and Fischer in 1961.[2] In spite of a strain energy of ~80 kcal/mol[3] quadricyclene is thermally stable, the half life for rearrangement to norbornadiene being greater than 14 h at 140 °C.[2] However, this rearrangement is efficiently homogeneously catalyzed by a number of transition metal ions at or even below room temperature.[4]

For several reasons the interconversion of norbornadiene and quadricyclene has attracted attention as a model system for solar energy storage and utilization. Both isomerizations can be conducted efficiently under conditions where only very minor amounts of side products are produced. Quadricyclene has a high volumetric storage capacity[3b] and norbornadiene is readily available at relatively low cost.

One of the most reasonable designs for this type of solar energy utilization involves conducting the two isomerizations in separate chambers. This would require the development of heterogeneous catalysts, at least for the isomerization of quadricyclene to norbornadiene, but probably for the photochemical process as well. Some work in development of polymer bound catalysts for the photochemistry[9] and the isomerization of quadricyclene[10] has been reported. In the latter case, King has found that a polystyrene anchored phosphinepalladium(II) chloride catalyst was ca. 1000 times less active than the soluble $((C_6H_5)_3P)_2PdCl_2$. Moreover, extensive loss of catalytic activity was observed after several cycles of use.[10] King also reported the use of a polymer bound cobalt porphyin system which was more active than the palladium system, but which was subject to deactivation through oxidation.

We have recently reported the preparation of poly(styryl)-bipyridine.[11] This material holds promise as a polymer support for the preparation of a large number of heterogeneous transition metal catalysts.[1,12] We have examined the use of a variety of transition metal complexes of poly(styryl)bipyridine as catalysts for the quadricyclene to norbornadiene isomerization. We report the results of that work here.

Results and Discussion

Several transition metal complexes of poly(styryl)bipyridine were tested as catalysts for the isomerization of quadricyclene to norbornadiene. These included complexes of silver, nickel, cobalt, and palladium. The only complex of poly(styryl)bipyridine which was an effective catalyst involved Pd(0). Interestingly, [poly(styryl)bipyridine]palladium(II) acetate showed no catalytic activity.

The preparation of [poly(styryl)bipyridine]palladium(0),

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