Supplementary Material Available: Table II, containing complete NMR spectra, melting points, and observed molecular weights for the products prepared in this investigation (3 pages). Ordering information is given on any current masthead page.

Registry No.—*p*-Diisopropylbenzene, 100-18-5; Tris(2,5-diisopropylphenyl)phosphine, 63600-29-3.

References and Notes

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Palladium-Catalyzed Arylation of Unsaturated Acetals and Ketals

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Acetals of α,β-unsaturated aldehydes react readily with aryl bromides and iodides in the presence of triethylamine and a palladium catalyst at 100 °C. The reaction products are mixtures of 3-arylpropenal acetals and 3-arylpropanoate esters. The last products are believed to arise from palladium hydride elimination of the acetal hydrogen to form ketene acetals, which are converted into esters by reaction with the triethylammonium halide present. 3-Buten-2-one ethylene ketal reacts with bromobenzene under the same conditions to produce benzalacetone ethylene ketal in 92% yield.

The palladium-catalyzed olefin arylation reaction with organic halides has been shown to be a useful and practical synthetic method. While a variety of reactants have been used,[1-4] no reports of applications of the reaction to unsaturated aldehydes or ketones have appeared. We have now investigated this potentially useful variation and find that product yields are quite low, apparently because the unsaturated carbonyl compounds largely polymerize under the basic reaction conditions and elevated temperatures required. The reaction had previously been shown to take place in moderate yields under less practical conditions with diarylmercury compounds and $LiPdCl_3$ as the arylating combination.[5] In order to effect the reaction under the more practical, newer conditions, we have made the usual modification of carbonyl compounds and used the related acetals and ketals to avoid the polymerization problem. This paper reports the result of a brief study of this reaction.

Results and Discussion

Reactions carried out between bromobenzene and acrolein, crotonaldehyde, and 3-buten-2-one at 60 to 100 °C with triethylamine and a palladium acetate catalyst with various triarylphosphines gave dark viscous reaction mixtures. They never contained more than 5–10% of the 3-phenylcarbonyl product expected or any other volatile product as determined by gas chromatography. Acrolein dimethyl acetal, crotonaldehyde diethyl acetal, and 3-buten-2-one ethylene ketal, however, all reacted normally with bromobenzene at 100 °C under the above conditions in 15–24 h, giving yields of products above 80%. Tri-*o*-tolylphosphine was used in the catalyst in these reactions, since it generally gives somewhat higher yields than the triphenylphosphine used previously.[6] The results are summarized in Table I.

Mixtures of products were obtained from the two aldehyde acetals. Two major products were formed in each case. Isolation of the products from each reaction showed that the expected 3-phenylated acetal was one product and a 3-phenylated ester was the other.

$$PhBr + CH_2{=}CHCH(OCH_3)_2 + Et_3N \xrightarrow[100\ °C]{Pd(OAc)_2/Po\text{-}tol_3} PhCH{=}CHCH(OCH_3)_2 + PhCH_2CH_2CO_2CH_3 + Et_3NH^+Br^-$$

Examination of the intermediate proposed in the arylation reactions reveals the possibility of several isomeric products being formed in our reactions depending upon which of the possible hydrogen groups is eliminated with the palladium. Of the possible *E* and *Z* forms of the 3-phenylacrolein dimethyl acetal expected from acrolein dimethyl acetal the large coupling constant of the vinyl hydrogens (16 Hz) indicates only the *E* form was present. While the 3-phenylcrotonaldehyde diethyl acetal isolated from the crotonaldehyde diethyl acetal reaction was not as easily identified as to isomeric structure, it is probably also the *E* isomer judging by the stereochemistry observed in related reactions.[1]

Elimination of the hydrogen substituent from the acetal group would form a ketene acetal. We initially thought small amounts of water in our reaction mixtures were hydrolyzing the ketene acetals to esters; however, careful drying of all reactants did not alter the products formed, suggesting that amine hydrobromide was involved in the conversion of the ketene acetal into ester. The reactions are believed to occur according to the following equations, where R = H, CH_3 and R′ = CH_3, C_2H_5.

The corresponding reaction of bromobenzene with 3-buten-2-one ethylene ketal produces only one product, *E*-4-phenyl-3-buten-2-one ethylene ketal in over 90% yield.

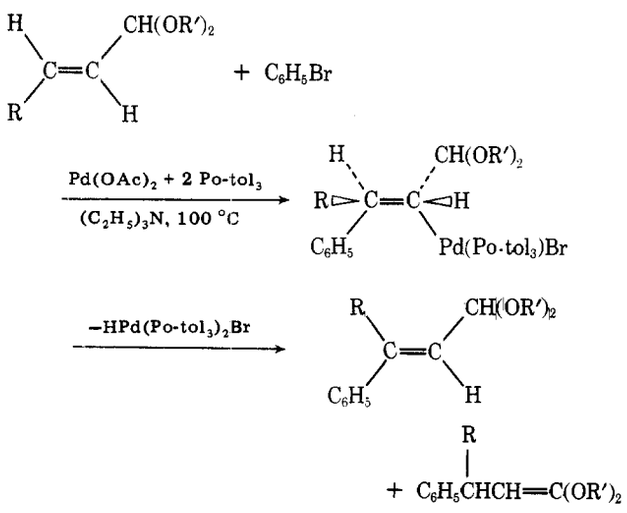
The usefulness of the last reaction is somewhat diminished by the relative difficulty in obtaining the α,β-unsaturated ketal. This ketal apparently cannot be formed directly from ethylene glycol and the unsaturated ketone. Our sample was prepared by dehydrohalogenation of 4-chloro-2-butanone ethylene ketal.

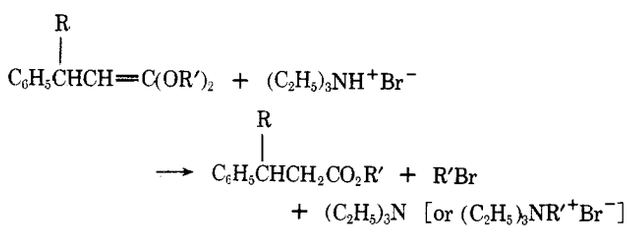
The usefulness of the acetal arylation is also limited because of the formation of mixtures of products. The direction of palladium hydride elimination in such reactions is believed

Table I. Arylation Reactions of Acetals and Ketals

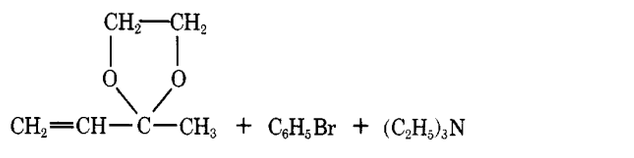
Aryl halide (moles)	Registry no.	Acetal or ketal (moles)	Registry no.	Moles of Et_3N	Catalyst (mmol)	Reaction times, h	Product (% yield)[a]	Registry no.
C_6H_5Br (0.020)	108-86-1	CH_2=CHCH$(OCH_3)_2$ (0.025)	6044-68-4	0.025	$Pd(OAc)_2$ (0.2) PPh_3 (0.4)	24	*E*-C_6H_5CH=CHCH$(OCH_3)_2$ (45) $C_6H_5CH_2CH_2CO_2CH_3$ (10)	63511-93-3 103-25-3
C_6H_5Br (0.020)		CH_2=CHCH$(OCH_3)_2$ (0.025)		0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (0.4)	24	*E*-C_6H_5CH=CHCH$(OCH_3)_2$ (47) $C_6H_5CH_2CH_2CO_2CH_3$ (34)	
C_6H_5Br (0.020)		CH_2=CHCH$(OCH_3)_2$ (0.025)		0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (0.8)	22	*E*-C_6H_5CH=CHCH$(OCH_3)_2$ (56) $C_6H_5CH_2CH_2CO_2CH_3$ (39)	
C_6H_5Br (0.020)		*E*-CH_3CH=CHCH$(OEt)_2$ (0.025)	63511-92-2	0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (0.8)	24	$C_6H_5C(CH_3)$=CHCH$(OEt)_2$ (50)[b] $C_6H_5CH(CH_3)CH_2CO_2Et$ (30)[b]	63511-94-4 62690-29-3
C_6H_5Br (0.020)		CH_2=CHC$(O_2C_2H_4)$-CH_3 (0.025)	26924-35-6	0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (0.8)	21	*E*-C_6H_5CH=CHC$(O_2C_2H_4)CH_3$ (92)[a] (58)[c]	63511-95-5
4-$NO_2C_6H_4Br$ (0.020)	586-78-1	CH_2=CHCH$(OCH_3)_2$ (0.025)		0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (0.4)	15	4-$NO_2C_6H_4CH_2CH_2CO_2$-CH_3 (42)	54405-42-4
4-$NO_2C_6H_4Br$ (0.020)		CH_2=CHCH$(OCH_3)_2$ (0.025)		0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (1.6)	18	4-$NO_2C_6H_4CH_2CH_2CO_2$-CH_3 (59)[a] (35)[c]	
C_6H_5I (0.020)	591-50-4	CH_2=CHCH$(OCH_3)_2$ (0.025)		0.025	$Pd(OAc)_2$ (0.2)	67	*E*-C_6H_5CH=CHCH$(OCH_3)_2$ (8)	
4-$(CH_3)_2NC_6H_4$ Br (0.020)	586-77-6	CH_2=$CHCO_2CH_3$ (0.025)	96-33-3	0.025	$Pd(OAc)_2$ (0.2) P(o-tolyl)$_3$ (1.6)	24	*E*-4-$(CH_3)_2NC_6H_4CH$=C-HCO_2CH_3 (80)	63511-96-6
$(C_6H_5)_2Hg$ (0.0015)	587-85-9	CH_3CH=CHCH$(OEt)_2$ (0.0020)	10602-34-3		$Pd(OAc)_2$ (0.0015)	24	*E*-$C_6H_3(CH_3)C$=CHCH$(OEt)_2$ (52)	

[a] GLC yield, unless otherwise noted. [b] Yield determined by NMR. [c] Yield of isolated product.

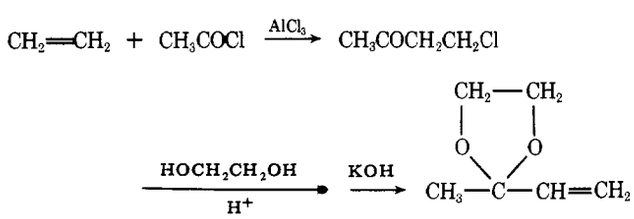




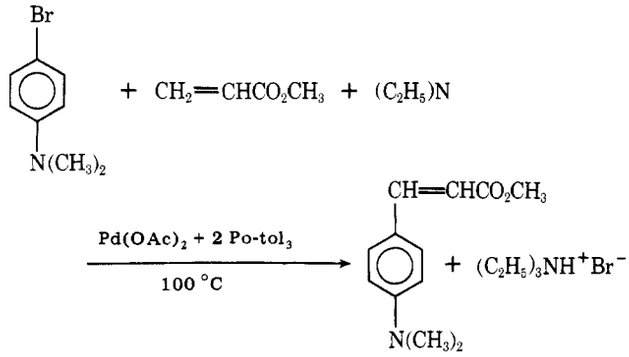
to be influenced by the hydridic character of the available β hydrogens[3] and by steric effects. Thus, it would be expected that varying the substituents on the acetal carbon or in the



aryl group would change the ratio of products formed. A brief look at 3,3-diacetoxy-1-propene was not encouraging, however, since no identifiable products were formed (π-allylic palla-



dium complexes are suspected to be the products) while acrolein ethylene acetal appeared to produce a mixture similar to that obtained with the dimethyl acetal. Changing the substituent in the aryl halide, however, did show some effect.



Acrolein dimethyl acetal with 4-nitrobromobenzene gave exclusively (59%) methyl 3-(4-nitrophenyl)propionate as would be predicted. However, 4-bromoanisole unexpectedly gave a mixture containing predominantly ester. Since the yields were rather low in these cases, the conclusions are uncertain.

We have attempted to react *p*-bromodimethylaniline with acrolein dimethyl acetal also, but the product apparently polymerized since a dark tar-like nonvolatile product was obtained. That *p*-bromodimethylaniline reacted normally with other alkenes was shown by its reaction with methyl acrylate which yielded the expected methyl *p*-dimethylaminocinnamate in 80% yield. In this reaction the use of the tri-*o*-tolylphosphine catalyst produced about twice the yield of product that triphenylphosphine did.

Experimental Section

Materials. Palladium acetate was prepared by the method of Wilkinson[7] and recrystallized from acetic acid. Triethylamine was dried over 4-Å molecular sieves and distilled before use. Acrolein dimethyl acetal was obtained from the Shell Oil Co. and the crotonaldehyde diethyl acetal was prepared by the method of Fischer and Baer.[8] The tri-*o*-tolylphosphine was prepared from *o*-tolylmagnesium bromide and phosphorus trichloride in THF solution, mp 125 °C. The NMR spectra and molecular weights of the products prepared are given in Table II which will appear only in the microfilm edition of this journal. (See note on supplementary material at the end of the paper.)

Reaction of Bromobenzene with Acrolein Dimethyl Acetal. A mixture of 25.5 g (0.25 mol) of acrolein dimethyl acetal, 32.8 g (0.25 mol) of bromobenzene (Aldrich), 0.45 g (0.002 mol) of palladium acetate, and 1.22 g (0.004 mol) of tri-*o*-tolylphosphine was prepared in a 160-mL heavy-walled Pyrex bottle. The air in the bottle was blown out with argon and the bottle was quickly capped with a rubber-lined cap. The mixture was warmed and shaken until it was homogeneous and then heated in a steam bath for 22 h. Gas chromatographic analysis of the reaction mixture at this time showed all of the bromobenzene had reacted. The cooled mixture was then diluted with ca. 100 mL of benzene and filtered. The solid amine salt remaining was rinsed several times with fresh benzene and the filtrate was concentrated under reduced pressure. The residue was fractionated through a 2-ft "spinning band" column to give 42% methyl 3-phenylpropionate, bp 109–110 °C (13 mm), and 37% 3-phenylacrolein dimethyl acetal, bp 125–127 °C (11 mm). There was no indication of the presence of the ketene acetal. The crude amine salt showed a weak methyl peak at δ 2.73 in D_2O by NMR which we believe came from methyl bromide produced in the conversion of the ketene acetal into ester by triethylamine hydrobromide. Authentic triethylmethylamine hydrobromide showed this methyl absorption also.

Reaction of Bromobenzene with Crotonaldehyde Diethyl Acetal. A reaction was carried out as described above employing the appropriate quantity of crotonaldehyde diethyl acetal[8] in place of acrolein dimethyl acetal. After 24 h at 100 °C the reaction was complete and products were separated from the concentrated benzene solution by distillation under reduced pressure, bp ~30 °C (35 mm). Analysis of the product mixture by NMR showed that 50% *E*-3-phenylcrotonaldehyde diethyl acetal and 30% ethyl 3-phenylbutanoate had been formed. The NMR spectra of the purified products were obtained by fractional distillation of the mixture through a 2-ft "spinning band" distillation column. The boiling point of the acetal was 96–98 °C (0.9 mm) and of the ester 85–87 °C (0.9 mm). The acetal product decomposed on attempted analyses by GLC at temperatures as low as 140 °C.

3-Buten-2-one Ethylene Ketal. 4-Chloro-2-butanone,[9] 73.5 g (0.7 mol), ethylene glycol, 36.7 g (0.7 mol), *p*-toluenesulfonic acid monohydrate, 0.44 g, and benzene, 1 L, were heated to boiling, and the water formed in the reaction was separated by means of a Dean–Stark trap. After about 7 h, no more water was collected and the benzene was distilled. The product was then distilled under reduced pressure. The acetal, bp 40–43 °C (1 mm), weighed 57 g (55% of theory). The NMR spectrum in $CDCl_3$ was as follows: δ 1.28 (s, 3 H), 2.12 (t, 2 H), 3.60 (t, 2 H), 3.90 (s, 4 H).

The above chloro acetal, 23 g (0.15 mol), was added dropwise to a stirred solution of 50 g of potassium hydroxide and 100 mL of ethylene glycol heated to 125 °C. The product distilled from the mixture. Redistillation gave 9.6 g (56%) of the unsaturated ketal, bp 110–112 °C. The NMR spectrum was as follows: δ 1.37 (s, 3 H), 3.73 (s, 4 H), 5.00–6.10 (m, 3 H).

(*E*)-4-Phenyl-2-butanone Ethylene Ketal. This product was prepared by the above procedure with the quantities of reagents shown in Table I. The product had the boiling point 115–117 °C (0.8 mm).

Methyl 3-*p*-Nitrophenylpropionate. Acrolein dimethyl acetal and *p*-nitrobromobenzene were reacted as above to give a 35% yield of product, bp 155 °C (0.4 mm). The distillate solidified on standing, mp 68–70 °C. The yield by GLC was 59%.

The Reaction of 4-Bromoanisole with Acrolein Dimethyl Acetal. A mixture of 2.55 g of acrolein dimethyl acetal (25 mmol), 3.74 g (20 mmol) of *p*-bromoanisole, 2.52 g (25 mmol) of triethylamine, 0.48 g (1.6 mmol) of tri-*p*-tolylphosphine, and 0.05 g (0.2 mmol) of palladium acetate was heated at 100 °C in a capped argon-filled tube at 100 °C for 60 h. Products were isolated as in the previous examples and separated by preparative GLC. Assuming a sensitivity coefficient of 1, there was formed 22% of methyl 3-*p*-anisylpropionate and 10% *p*-methoxycinnamaldehyde dimethyl acetal. No effort was made to optimize the yield in this case. Pure samples of the products were isolated by preparative GLC and identified by NMR.

Methyl 4-Dimethylaminocinnamate. A solution of 2.15 g (25 mmol) of methyl acrylate, 4.60 g (20 mmol) of *p*-bromo-*N*,*N*-dimethylaniline, 2.52 g (25 mmol) of triethylamine, 0.48 g (1.6 mmol) of tri-*o*-tolylphosphine, and 0.05 g (0.2 mmol) of palladium acetate was heated in a capped tube at 100 °C for 15 h. After cooling, the solid in the tube was stirred with water, and the insoluble product was separated by filtration, air dried, and recrystallized (Celite) from methanol. There was obtained an 80% yield of product, mp 135–137 °C.

Acknowledgments. The mass spectral data were kindly obtained by Dr. Barbara Jelus. This project was supported by a grant from the National Science Foundation.

Supplementary Material Available: Table II, containing complete NMR spectra and observed molecular weights for the products prepared in this investigation (1 page). Ordering information is given on any current masthead page.

Registry No.—4-Chloro-2-butanone, 6322-49-2; ethylene glycol, 107-21-1; 4-chloro-2-butanone ethylene ketal, 57398-28-4; 4-bromoanisole, 104-92-7; methyl 3-*p*-anisylpropionate, 15823-04-8; *p*-methoxycinnamaldehyde dimethyl acetal, 63511-97-7.

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