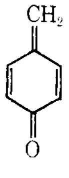
found that **4** gave good yields of *p*-hydroxybenzyl compounds when treated with nucleophiles.[5] Similar results were obtained with *o*-acetoxybenzyl acetate. The quinone methide (**6**) (or the ortho analogue) was postulated to be an intermediate in these reactions. Under the reduction conditions, **6** would be expected to be reduced to *p*-cresol. Since a quinone methide intermediate cannot be readily obtained from 3-acetoxybenzyl acetates, **2** would be expected to cleave without further reduction.

Monoacetate **3**, prepared by selective acetylation[6] of isovanillyl alcohol,[7] was converted into triester **7**.[8] Selective reduction of the triester with excess $NaBH_4$ produced the diphenol in 77% yield. Diacetate **9** was prepared from **3** by acylation with 3-(*p*-acetoxyphenyl)propionyl chloride.[9] Deacetylation of **9** afforded the diphenol **10** in 50% overall yield.



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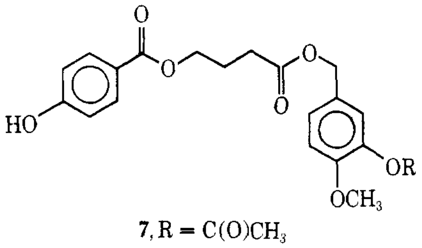
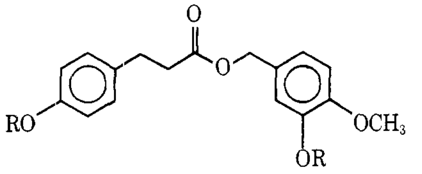


7, R = C(O)CH$_3$
8, R = H



9, R = C(O)CH$_3$
10, R = H

The procedure may be used to selectively cleave phenyl acetates in the presence of unsaturated esters. Thus, methyl *p*-acetoxycinnamate (**11**)[11] was converted to methyl *p*-hydroxycinnamate[11] in 90% yield.

These results indicate that a phenyl acetate may be reduced selectively in the presence of benzyl esters, benzoates, and cinnamates. Thus, $NaBH_4$ cleavage, in combination with selective acetylation, makes the acetyl group a very useful protecting group for phenols. Its utility in the hydroxybenzyl alcohol series is limited to those cases in which the hydroxyl group is in the 3 position.

Experimental Section

Representative examples of the acetate reduction and monoacetylation procedures are given here.

Reduction of Phenyl Acetates. 3-Hydroxy-4-methoxybenzyl Acetate (2). To a solution of 238 mg (1 mmol) of isovanillin alcohol diacetate (**1**)[4] in 5 mL of DME was added 200 mg (5.4 mmol) of sodium borohydride. The rapidly stirred suspension was heated at 45 °C for 18 h. After cooling in an ice-methanol bath, the reaction mixture was cautiously diluted with 5 mL of saturated aqueous NH_4Cl. The mixture was then diluted with 15 mL of ether and the organic layer was washed with saturated NH_4Cl (2 × 10 mL) and saturated NaCl (2 × 10 mL). After drying (Na_2SO_4) the organic layer was concentrated (in vacuo) to a pale yellow oil. Preparative TLC on silica gel (5% 2-propanol-benzene) afforded 171 mg (76% yield) of **2**: IR (film) 3420 (vb), 1750 (b), 1620 cm^{-1}; NMR ($CDCl_3$) δ 2.03 (s, 3 H, -C(O)-CH_3), 3.80 (s, 3 H, -OCH_3), 4.93 (s, 2 H, -CH_2Ar), 5.73 (brs, 1 H, -OH), 6.7–6.9 (m, 3 H, aryl).

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.41; H, 6.25.

Monoacetylation. 3-Acetoxy-4-methoxybenzyl Alcohol (3). Isovanillin alcohol (4.6 g, 30 mmol) was dissolved in aqueous potassium hydroxide (7 mL, 45 mmol). To this vigorously stirred solution was added 15 g of ice followed by 3.84 g (37 mmol) of acetic anhydride.[12] After the temperature had risen to 20 °C, an additional 250 mL of water was added and the mixture stirred for 0.5 h. The aqueous solution was then extracted with ether (3 × 30 mL). The combined extracts were washed with water (2 × 20 mL) and 20 ml of aqueous NaCl, dried (Na_2SO_4), and concentrated (in vacuo) to a pale yellow oil. Distillation of this oil [195–196 °C (0.25 Torr)] afforded 4.9 g (85% yield) of **3** along with a small amount of **1**. Separation of **3** from **1** could also be achieved in 37% yield by formation of the hexane-insoluble complex of **3** with $CaCl_2$.[13]

An analytical sample of **3** was obtained by preparative TLC (silica gel; 10% ether-benzene) followed by bulb-to-bulb distillation (Kugelrohr). **3**: IR (film) 3395, 1765, 1620 cm^{-1}; NMR ($CDCl_3$) δ 2.20 (s, 3 H, -C(O)CH_3), 3.40 (brs, 1 H, -OH), 3.70 (s, 3 H, -OCH_3), 4.36 (s, 2 H, -CH_2Ar), 6.8 (m, 3 H, aryl).

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.41; H, 6.01.

Acknowledgment. The authors gratefully acknowledge financial support of this research by a PHS Grant (NS 12007) from the National Institute of Neurological and Communicative Disorders and Stroke. We are grateful to Dr. Catherine Costello, Department of Chemistry, MIT, for high-resolution mass spectra obtained with the support of a PHS Grant (RR 00317) from the Biotechnology Resources Branch, Division of Research Resources.

Supplementary Material Available: Detailed procedures for the treatment of **4** with $NaBH_4$ and for the preparation of compounds **1**, **8**, and **10** (3 pages). Ordering information is given on any current masthead page.

Registry No.—**1**, 63866-99-9; **2**, 63867-04-9; **3**, 63867-05-0; **4**, 2937-64-6; **7**, 63867-01-6; **8**, 63867-02-7; **10**, 63876-03-8; isovanillin alcohol, 4383-06-6; acetic anhydride, 108-24-7; acetyl chloride, 75-36-5; 3-(*p*-acetoxyphenyl)propionyl chloride, 63867-00-5.

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Triphase Catalysis. C-Alkylation of Nitriles

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Received December 13, 1976

In two recent papers[1,2] Regen introduced the new concept of triphase catalysis to describe a process of phase-transfer catalysis in which the ammonium salt was supported on a polymer insoluble in the reaction medium (e.g., anion-exchange resins). Two reactions were tested: the cyanide displacement on 1-bromooctane and 1-chlorooctane and the generation of dichlorocarbene from chloroform. In both cases, the reaction proceeds normally (e.g., as expected in two-phase catalysis[3–6]), but at higher temperatures and with longer reaction time. Also, almost at the same period anion-exchange resins were used in the synthesis of esters,[7] tetrahydropyrimidines,[8] and other reactions.[9–11]

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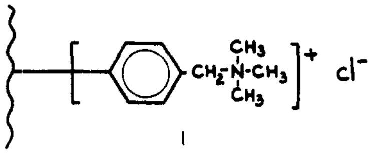
We wish to report in this note several results giving information on the reaction of C-alkylation catalyzed by anion-exchange resins (triphase catalysis). In this type of reaction it is important to point out the main differences in mechanism between the "true" phase-transfer catalysis and the "interfacial" catalysis, as both may be applied to triphase processes. In fact, in a reaction such as the alkylation of phenol or the cyanide displacement on 1-bromooctane using quaternary ammonium salt as catalyst, one of the reactants is transferred across the interface into the organic phase, where it exists in the form of an ion pair.

However, the situation seems to be rather different with substances containing labile hydrogens, for example, phenylacetonitrile (PAN). As Makosza[12,13] has shown, the alkylation of PAN can take place at the phase boundary. In such a reaction, carbanions seem to be formed at the interface upon the action of aqueous sodium hydroxide on PAN. These same carbanions then form organic phase soluble ion pairs (substrate$^-$$NR_4^+$) with cations supplied by the catalyst.

Now, in the case of triphase catalysis applied to the alkylation of PAN, the reaction mechanism will perhaps be more complicated, owing to the interference of carbanions coming from the phase boundary or from the hydrogen abstraction by hydroxide anion initially associated with the ammonium cations in the organic phase ($-NR_3^+OH^-$ belonging to the resin).

With a view to providing the best possible information we have determined the yield of the well-known reaction of PAN with *n*-butyl bromide using both classical phase-transfer catalysis (quaternary ammonium or phosphonium salts) and triphase catalysis. The resins used for this purpose were of the Dowex type: (a) Dowex 1-X8, 20–50 mesh ionic form Cl^-; (b) Dowex 2-X4, 20–50 mesh ionic form Cl^-; (c) Dowex 2-X8, 20–50 mesh ionic form Cl^-; (d) Dowex 11, 16–20 mesh ionic form Cl^-; (e) Dowex 21K, 20–50 mesh ionic form Cl^-; (f) Dowex 44, 20–50 mesh ionic form Cl^-/OH^-.

The structure of the resins of the types a, d, e, and f is indicated in I and that of the types b and c in II.[14]



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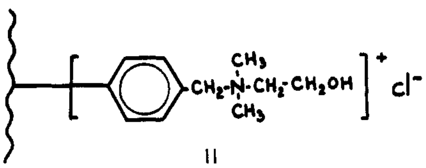

II

The results obtained are indicated in Tables I–V. In Table I we have summarized the results concerning the effect of various quaternary ammonium salts on the alkylation of phenylacetonitrile. Table II shows the effect of type and amount of resins, concentration of sodium hydroxide, temperature, and time on the reaction yield and selectivity (e.g., percent of dialkylated product). In Table III we have particularly examined the repeatability of the reaction using the same resins. Table IV indicates the result of the attempt made to protect the resin from contact with 50% sodium hydroxide by solvents of various type. Finally Table V shows the limit of the applicability of triphase catalysis. For this purpose we have alkylated different nitriles using this type of catalysis.

Discussion

Comparison of the different results obtained enables us to conclude that catalysis using resins (triphase catalysis) requires, in our case, more drastic conditions than biphase catalysis.

However, to make possible a better comparison we have determined by titration, and under our experimental conditions, the OH^- equivalent of 2 g of Dowex 1-X8 resin. We have found that 2 g of this resin is equivalent to a 0.0045 M aqueous solution of NaOH. Therefore, 4 g of Dowex 1-X8 used with 0.1 mol of substrate would be approximately equivalent to 10% of quaternary ammonium hydroxide per mole of substrate. This comparison shows again that for the resins to catalyze the reactions as efficiently as quaternary ammonium salts, the reaction conditions have to be more drastic.

Another remark is that whatever the catalyst (salt or resin) when the concentration of NaOH is low, the yield of hydrolysis of the nitrile and halide used is considerable.

To obtain information also on the behavior of alkyl iodide under our catalytic conditions, we have studied the alkylation of phenylacetonitrile with ethyl iodide. We have found that (see Experimental Section) the resins have no catalytic effect on this type of reaction: with or without a resin the overall yield of the alkylation was 30% after a reaction time of 2 h.

Table I. Alkylation of Phenylacetonitrile with Various Ammonium or Phosphonium Salts as Catalysts

Amount of catalysts[a]	Temp, °C	Reaction time, h	NaOH concn % by wt	% yield Monoalkylation	% yield Dialkylation
		Trimethylhexadecylammonium Bromide (CTAB)[b]			
1	70	5	50	60	1
10	35	10	10	32	1
		Triethylbenzylammonium Chloride (TEBA)[b]			
1	70	6	50	84	5
6	35	20	50	90	5
		Tetrabutylammonium Bromide (TBAB)[b]			
0.1	70	10	50	35	1
1	70	5	50	60	8–9
1	25	20	50	83	11
6	25	20	50	86	11
		Tributylhexadecylphosphonium Bromide (CTPB)[b]			
0.1	70	10	50	88	9
1	70	5	50	70	13
1	25	20	50	82	7
6	25	20	50	86	8

[a] In percent for 100% of substrate. [b] Registry no.: CTAB, 57-09-0; TEBA, 56-37-1; TBAB, 1643-19-2; CTPB, 14937-45-2.

Table II. Alkylation of Phenylacetonitrile

Amount of resin, g	Temp, °C	Reaction time, h	NaOH concn % by wt	Overall % yield	% dialkylation
			Dowex 1-X8[a]		
0.4	70	10	50	40	5
1	70	10	50	49	3
1	70	20	50	84	6
4	70	10	50	60	7
8	70	10	50	68	7
4	70	10	10	8.5	
4	70	5	50	20	
			Dowex 2-X4[a]		
1	70	10	50	72	4.5
4	70	10	50	69	7
			Dowex 2-X8[a]		
1	70	10	50	50	4
4	70	10	50	67	7
4	70	10	10	6	
			Dowex 11[a] 16–20 mesh		
1	70	10	50	58	1
4	70	10	50	55	5
			Dowex 21K[a]		
1	70	10	50	54	1
4	70	10	50	60	2
			Dowex 44[a]		
1	70	10	50	70	3
4	70	10	50	70	3
			Without Catalyst		
0	70	10	50	22	3

[a] Registry no.: Dowex 1-X8, 12627-85-9; Dowex 2-X4, 56996-51-1; Dowex 2-X8, 11138-20-8; Dowex 11, 9049-12-1; Dowex 21K, 9065-04-7; Dowex 44, 56996-52-2.

Table III. Repeatability of the Alkylation Reaction

Dowex 1-X8, 20–50 mesh		Dowex 2-X4, 20–50 mesh	
Run no.	Overall % yield	Run no.	Overall % yield
1	58	1	69
2	60	2	68
3	38	3	60
Dowex 2-X8, 20–50 mesh		Dowex 11, 16–20 mesh	
1	67	1	55
2	71	2	47
3	50	3	36
Dowex 21K, 20–50 mesh		Dowex 44, 20–50 mesh	
1	60	1	70
2	57	2	49
3	61	3	48

This result is different from those obtained with systems in which the ammonium groups are stoichiometric with respect to the anions.

The repeatability of the reaction is, however, not very good. This may be due to loss of catalytic activity by destruction of the resin backbone, or by dequaternization of the resin, which bears a benzyl group which behaves as good leaving group in such reaction.[15]

These overall results show that the use of resins in such reactions is possible but, with respect to the yields obtained with ammonium or phosphonium salts, the process is not the better one. New resins, which will lead to a better repeatability, will be necessary in such processes.

Experimental Section

(1) **Biphase Catalysis.** Phenylacetonitrile (0.1 mol), x mol % (see Table I) of catalyst per mole of substrate, 0.1 mol of n-butyl bromide, and 40 cm^3 of NaOH (50 or 10% by weight) are stirred magnetically at 70 °C (or other temperatures as stated). At the end of the reaction the crude products are washed with water and analyzed by GLC.

Table IV. Alkylation of Phenylacetonitrile Using Dowex 1-X8 Resin and Various Solvents

Amount of resin, g	Temp, °C	Reaction time, h	NaOH concn % by wt	Solvent	Overall % yield
4	80	10	50	Benzene	23
4	70	10	50	Cyclohexane	5
4	70	10	50	Dioxane (1) Cyclohexane (1)	10

Table V. Alkylation of other Nitriles

Registry no.	Nitriles[a]	% yield of monoalkylation
22364-68-7	*o*-methylphenylacetonitrile	60[b]
3215-64-3	2,6-Dichlorophenylacetonitrile	25[b]
124-12-9	*n*-Octylnitrile	0
766-05-9	Cyclohexylnitrile	0

[a] Using 4 g of Dowex 2-X4, 20–50 mesh, and a reaction time of 10 h for a reaction temperature of 70 °C. [b] The dialkylation yield found to be about 1%.

(2) **Triphase Catalysis.** Nitrile (0.1 mol), 0.1 mol of *n*-butyl bromide, 40 cm^3 of NaOH (50 or 10% by weight), and *x* g of resin (see Table II) were stirred vigorously at 70 °C for *x* h. At the end of the reaction the resin was removed by filtration, and the organic layer was separated and treated as usual.

(3) **Use of an Alkyl Iodide.** The same conditions as above were used, with 4 g of Dowex 1-X8, at a temperature of 70 °C for 10 h.

(4) **Determination of the Equivalence of the Catalytic Action of the Salts and Resin.** Dowex 1-X8 resin (2 g) was stirred for 30 min with 40 cm^3 of 50% (by weight) NaOH. After this time, the resin was removed by filtration and washed with distilled water (no reaction to phenolphthalein was observed). The resin was then titrated with dilute hydrochloric acid (helianthine used as indicator).

(5) **Structure of the Products.** The identification of the products has been carried out by GLC/MS (Varian MAT 111). Monoalkylated products: $C_{12}H_{15}N$ 173, 158, 144, 130, 129, 118, *117*, 116, 91, 90, 77, 57, 41; $C_{13}H_{17}N$ 187, 144, 143, 132, *131*, 130, 105, 104, 103, 91, 77, 65, 63, 57, 41; $C_{12}H_{13}NCl_2$ 245, 243, 241, 208, 206, 189, *185*, 182, 150, 114, 57, 41; $C_{10}H_{11}N$ 145 (45.8), 118 (8.3), 117 (100), 116 (87.5), 91 (41.6), 90 (29.1), 89 (20.8), 78 (4.1), 77 (4.1), 63 (8.3), 51 (8.3), 39 (6.2). Dialkylated product: $C_{16}H_{23}N$ 229, 187, *173*, 172, 158, 145, 130, 118, 117, 116, 91, 77, 58.

Registry No.—Butyl bromide, 109-65-9; ethyl iodide, 75-03-6; phenylacetonitrile, 140-29-4; α-butylphenylacetonitrile, 3508-98-3; α-butyl-*o*-methylphenylacetonitrile, 63866-33-1; α-butyl-2,6-dichlorophenylacetonitrile, 58830-65-2; α-ethylphenylacetonitrile, 769-68-6; α,α-dibutylphenylacetonitrile, 3508-99-4.

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(14) According to the manufacturer of the resins used, the complete name for each resin will include: (1) type, i.e., Dowex 1, 2, 21K, Dowex 50. (2) "X number" or percent divinylbenzene, i.e., X8. The Dowex resins used are based on styrene divinylbenzene copolymer. Sulfonation of these copolymers with sulfuric acid yields strong cation resin, while "amination" with amines yields anion resins. (3) Mesh size, i.e., 20–50 mesh (based on U.S. standard screen). (4) Ionic form, i.e., Cl$^-$. Dowex 1, Dowex 2, Dowex 11 and Dowex 21K resins are strong-base anion-exchange resins. All incorporate a quaternary ammonium functionality. Dowex 1, Dowex 11, and Dowex 21K resins are type 1 resins. In type 1 resins the four substituents on the nitrogen atom are a polymeric benzyl and three methyl groups. Dowex 2 resin is a type 2 resin in which one of the methyl groups is replaced by an ethanol group. Type 1 and type 2 resins differ primarily in their affinities for the hydroxide ion relative to other anions, and in chemical stability. Type 2 resins are more efficiently converted to the hydroxide form than type 1 resins, but the type 1 resins are inherently more stable chemically especially in the hydroxide form.
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Improved Syntheses of Bis(pentafluorophenyl)acetylene, (Pentafluorophenyl)phenylacetylene, and Hexakis(pentafluorophenyl)benzene

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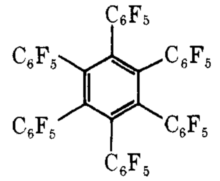
During the course of some recent investigations concerning the reactions of organometallic complexes with partially and completely halogenated diarylacetylenes,[1] we have been required to synthesize various quantities of bis(pentafluorophenyl)acetylene (1) and (pentafluorophenyl)phenylacetylene (2). As a result, we have developed reliable experimental procedures based on the commercially available reagent bromopentafluorobenzene, from which reasonable quantities of these acetylenes can be obtained. Moreover, a new synthesis of hexakis(pentafluorophenyl)benzene (3) is also presented.

$C_6F_5C{\equiv}CC_6F_5$

1

$C_6F_5C{\equiv}CC_6H_5$

2



3

Several synthetic routes to 1 have been reported.[2–8] Many of these, however, are not convenient for the production of practical amounts of this acetylene. Birchall et al.[2] have described a useful but potentially hazardous preparation of 1 in 56% yield by the cobalt-catalyzed reaction of pentafluorophenylmagnesium bromide with diiodoacetylene. A major drawback of this method involves the use of diiodoacetylene, a compound well known for its thermal and mechanical instability.[9]

Perhaps the most useful preparation of bis(polyhaloaryl)acetylenes such as 1 has been suggested by Gilman and coworkers.[6] Their method utilizes the reaction of polyhaloarylcopper reagents or their complexes with polyhaloethylenes or polyhaloethanes. The use of this method for the synthesis of 1 has been alluded to several times in the literature, but unfortunately no detailed experimental procedures have ever been reported.[7,8] The preparation of 1 presented here is therefore based upon the original communication of Gilman et al.[6] and consists of the reaction of pentafluorophenylcopper, formed from pentafluorophenylmagnesium bromide and cuprous iodide, with tetrabromoethylene.

$$C_6F_5Br \xrightarrow[\text{(2) CuI}]{\text{(1) Mg, THF}} C_6F_5Cu \xrightarrow[\Delta]{C_2Br_4} \mathbf{1}$$

Of the several reported procedures for the synthesis of 2,[3,10–13] the most useful involves the reaction of iodopentafluorobenzene with phenylethynylcopper. A wide range of conditions, i.e., solvent, reaction temperature, and time, has been employed, and the yields vary from 20 to 74%.[3,11,12] Under similar conditions the reaction of bromopentafluorobenzene and phenylethynylcopper gave both lower yields of 2 as well as a more difficult purification. In the present synthesis of 2, we have found that by reversing the functionality of the aforementioned reagents, i.e., using pentafluorophenylcopper and phenyliodoacetylene, good yields of 2 can be conveniently obtained. This method thus eliminates the purchase or tedious preparation[11] of iodopentafluorobenzene.

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