[Chem. Pharm. Bull. 23(11)2620—2628(1975)]

UDC 547.572.057 : 547.539.04 : 547.284.04

On the Synthesis of Arylacetones by the *SRN* 1 Arylation of Acetone Enolate Ion[*,1]

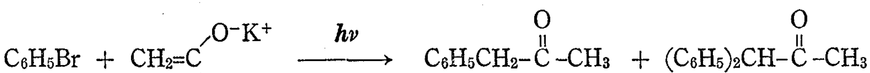
JOSEPH F. BUNNETT and JOHN E. SUNDBERG

University of California, Santa Cruz[2]

(Received May 28, 1975)

Numerous aryl bromides and iodides react with acetone enolate ion in liquid ammonia under irradiation to form arylacetones in high yield. This synthesis is successful with bromo- or iodobenzene derivatives carrying alkoxy, alkyl, phenyl, halogen, and carboxylate substituents, and with halogen derivatives of polynuclear aromatic hydrocarbons. The method is remarkably insensitive to steric hindrance; for example, 2,4,6-triethylbromobenzene reacts quite well. With greater steric hindrance, as in 2,4,6-triisopropyliodobenzene, reactivity falls and a side reaction of dehalogenation becomes appreciable, for reasons which are suggested. The synthesis was unsuccessful with the diethylamino, nitro and ionized hydroxy ($-O^-$) substituents. Potassium metal-stimulated reactions of a few aryl diethyl phosphates with acetone enolate ion give generally lower yields of arylation and larger yields of dephosphation (hydrocarbon) products, compared even to potassium-stimulated reactions with aryl bromides. It is postulated that the lesser formation of hydrocarbon products from the aryl bromides is related to transport effects and solution inhomogeneity.

Unactivated aryl halides were long considered to be unreactive with nucleophiles. However, it was recently shown[3] that bromobenzene reacts readily with acetone enolate ion, under irradiation in liquid ammonia, to afford phenylacetone (I) in high yield, together with some 1,1-diphenyl-2-propanone (II).



$$C_6H_5Br + CH_2{=}C\begin{matrix}\diagup O^-K^+\\ \diagdown CH_3\end{matrix} \xrightarrow[NH_3]{h\nu} \underset{I}{C_6H_5CH_2-\overset{O}{\overset{\|}{C}}-CH_3} + \underset{II}{(C_6H_5)_2CH-\overset{O}{\overset{\|}{C}}-CH_3}$$

Under similar conditions halobenzenes, as well as certain other aryl halides, also effect the arylation of other types of carbanions.[4,5] Furthermore, aryl iodides and bromides undergo facile photostimulated reaction with thiophenoxide ion[6,7] or with dialkyl phosphite ions[8] to give, respectively, diaryl sulfides or dialkyl arylphosphonate esters.

Apparently closely related in mechanism are the potassium metal-stimulated condensations of aryl halides and aryl diethyl phosphate esters with enolate ions; for example, phenyl diethyl phosphate (III) reacts with acetone enolate ion and potassium metal in ammonia to form some phenylacetone (I), but mainly the related alcohol, 1-phenyl-2-propanol (IV), as well as some benzene.[9]

---

[*] Dedicated to the memory of Prof. Eiji Ochiai.

1) Based in part on the Dissertation of J.E. Sundberg, University of California, Santa Cruz, 1975. Presented in part at the national meeting of the American Chemical Society, Philadelphia, April, 1975. Research supported in part by the U.S. National Science Foundation.

2) Location: *Santa Cruz, California, U.S.A. 95064.*

3) R.A. Rossi and J.F. Bunnett, *J. Org. Chem.*, **38**, 1407 (1973).

4) R.A. Rossi and J.F. Bunnett, *J. Org. Chem.*, **38**, 3020 (1973).

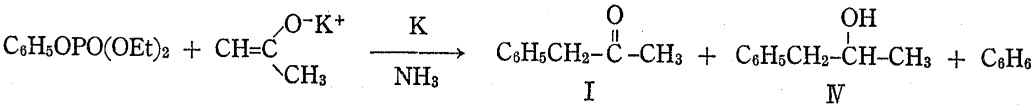
5) J.F. Bunnett and B.F. Gloor, *J. Org. Chem.*, **39**, 382 (1974).

6) J.F. Bunnett and X. Creary, *J. Org. Chem.*, **39**, 3173 (1974).

7) J.F. Bunnett and X. Creary, *J. Org. Chem.*, **39**, 3611 (1974).

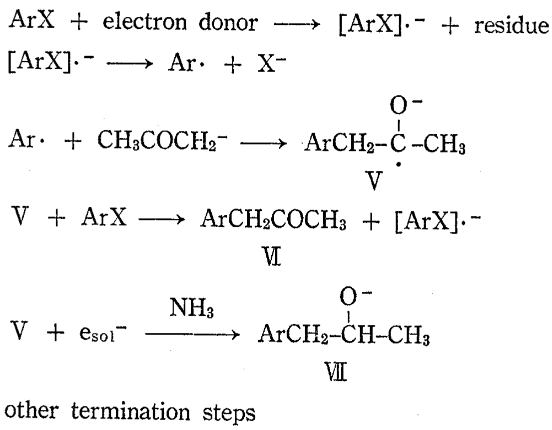
8) J.F. Bunnett and X. Creary, *J. Org. Chem.*, **39**, 3612 (1974).

9) R.A. Rossi and J.F. Bunnett, *J. Am. Chem. Soc.*, **94**, 683 (1972).



$$C_6H_5OPO(OEt)_2 + CH{=}C\begin{matrix}O^-K^+\\CH_3\end{matrix} \xrightarrow[NH_3]{K} \underset{\text{I}}{C_6H_5CH_2\overset{O}{\overset{\|}{C}}CH_3} + \underset{\text{IV}}{C_6H_5CH_2\overset{OH}{\overset{|}{C}H}CH_3} + C_6H_6$$

These reactions are all believed to occur by the $S_{RN}1$ mechanism.[10,11,12] That mechanism, for the arylation of acetone enolate ion, is sketched in Chart 1. It is a chain mechanism, with steps 2, 3, and 4 constituting a cycle of propagation steps. Although the cycle involves radical and radical anion intermediates and an electron transfer step, its overall consequence is *nucleophilic substitution*.



$$ArX + \text{electron donor} \longrightarrow [ArX]\cdot^- + \text{residue} \quad (1)$$

$$[ArX]\cdot^- \longrightarrow Ar\cdot + X^- \quad (2)$$

$$Ar\cdot + CH_3COCH_2^- \longrightarrow \underset{\text{V}}{ArCH_2\overset{O^-}{\overset{|}{\underset{\bullet}{C}}}CH_3} \quad (3)$$

$$\text{V} + ArX \longrightarrow \underset{\text{VI}}{ArCH_2COCH_3} + [ArX]\cdot^- \quad (4)$$

$$\text{V} + e_{sol}^- \xrightarrow{NH_3} \underset{\text{VII}}{ArCH_2\overset{O^-}{\overset{|}{C}H}CH_3} \quad (5)$$

other termination steps (6)

Chart 1

Initiation of the radical chain occurs in step 1. Sometimes the electron donor is the nucleophile itself, electron transfer being stimulated photochemically or (rarely) thermally. Alternatively, the electron donor may be the solvated electron. Stimulation of $S_{RN}1$ reactions by solvated electrons is convenient in liquid ammonia solution, inasmuch as solutions of alkali metals in ammonia contain solvated electrons and alkali metal cations.

A radical chain mechanism necessarily has termination steps. Reaction of radical anion V, a ketyl, with a solvated electron in step 5 terminates a chain as it leads to the anion of an 1-aryl-2-propanol product. Thus solvated electrons, if present, can serve both to initiate and to terminate the chain. Other chain termination steps may involve acquisition of solvated electrons, if present, by aryl radicals, and also the combination of pairs of radicals.

We now report a study of the scope and limitations of the $S_{RN}1$ arylation of acetone enolate ion.

Results

We studied the reactions of a number of substituted bromo- and iodobenzenes with excess acetone enolate ion under photochemical stimulation. Results are summarized in Table I. All reactions were performed in liquid ammonia, with the substrate about 0.01 M and the enolate reagent about 0.04 M. Reactions were performed in Pyrex flasks in a Rayonet photochemical reactor equipped with lamps emitting maximally at 350 nm.

Rossi and Bunnett[3] reported that bromobenzene and acetone enolate ion react under photostimulation to form, as well as phenylacetone (I), appreciable amounts of the by-product, 1,1-diphenyl-2-propanone (II). However, we did not seek or find diarylacetones in the experiments summarized in the Tables.

---

10) N. Kornblum, R.E. Michel, and R.C. Kerber, *J. Am. Chem. Soc.*, **88**, 5662 (1966).
11) G.A. Russell and W.C. Danen, *J. Am. Chem. Soc.*, **88**, 5663 (1966); **90**, 347 (1968).
12) J.K. Kim and J.F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463, 7464 (1970).

Most of the entries in the Tables represent single experiments. No systematic efforts to optimize yields were made.

Experiments 1, 2, and 3, Table I. demonstrate that methoxy substituents do not impede the synthesis under consideration, either electronically or sterically. Alkoxy substituents appear to be equally innocuous whether *ortho*, *meta*, or *para* to the site of substitution.

TABLE I. Photostimulated Reactions of Substituted Phenyl Halides with Acetone Enolate Ion in Liquid Ammonia

Expt. No.	Nucleofugic halogen	Other Substituent (s)	Irradiation Time, Min	Yields,[a] %			
				Substrate	Arylacetone	ArH[b]	X$^-$
1	Br	2,4-(OMe)$_2$	120[c]		76	5	
2	I	3,5-(OMe)$_2$	60		68		
3	I	2,4,6-(OMe)$_3$	90		92	tr.	
4	Br	2-COO$^-$	90		85[d]	10[d]	100
5	Br	3-COO$^-$	140		80[d]	8[d]	100
6	Br	4-COO$^-$	90		70[e]		97
7	I	2,5-(iso-Pr)$_2$	130		78[f]	5[g]	93
8	I	2,5-(*t*-Bu)$_2$	130	65	26[g]	6[g]	34
9	I	2,4,6-Me$_3$[h]	32		82	10	
10	Br	2,4,6-Et$_3$	120		70	22	
11	Br	2,4,6-(iso-Pr)$_3$	150	92[g]	2[g]	7[g]	
12	I	2,4,6-(iso-Pr)$_3$	180	45[g]	16[g]	37[g]	
13	Br	4-C$_6$H$_5$	150	tr	69	tr	
14	I	3-F	70		56[i]		
15	I	3-CF$_3$	90	34[g]	35[g]	14[g]	
16	Br	4-COCH$_2^-$[j]	100	84[g]	tr	tr	16
17	Br	4-NEt$_2$	90	21[g]	0	8[g]	
18	Br	4-O$^-$[k]	85	72[g]	0	22[g]	29
19	Cl	3-NO$_2$	dark[l]	46[g]	0	0	0
20	Cl	3-NO$_2$	150	48[g]	0	0	6
21	Br	3-NO$_2$	150	58[g]	0	0	

[a] Yields by isolation and weighing unless otherwise noted; "tr" means trace ($<$1%), determined by gas-liquid partition chromatography (glpc).
[b] dehalogenation product
[c] *t*-BuOK prepared *in situ* from *t*-BuOH and K
[d] As methyl ester, prepared by treatment with CH$_2$N$_2$.
[e] 4-acetonylbenzoic acid
[f] yield 89% by glpc
[g] by glpc
[h] experiment by X. Creary
[i] *m*-fluorophenylacetone
[j] enolate ion of 4-bromoacetophenone
[k] 4-bromophenoxide ion
[l] 180 min

An ionized carboxy group is shown by Expts. 4, 5, and 6 to have no deleterious effect on the synthesis.

Experiments 7—12, inclusive, concern the effects of alkyl substituents. It is remarkable that the synthesis provides good yields of arylacetones when one isopropyl group (Expt. 7), two methyl groups (Expt. 9), or even two ethyl groups (Expt. 10) are *ortho* to the site of substitution. These results show that alkyl groups do not have an adverse electronic effect on the reaction. Also, the synthesis is spectacularly insensitive to the steric effects of *ortho* alkyl groups.

Steric hindrance does become evident when one *t*-butyl group (Exp. 8) or two isopropyl groups (Expts. 11 and 12) are *ortho* to the nucleofugic halogen. It manifests itself principally in low overall reactivity: substantial amounts of aryl halide remain unreacted even after comparatively long periods of irradiation. There is also a tendency of the more hindered systems to form larger amounts of the hydrocarbon by-product that represents replacement of the original halogen with hydrogen. Compare especially Expts. 9, 10, 12.

Comparison of Expts. 11 and 12 reaffirms⁶⁾ that aryl iodides are more reactive than the corresponding aryl bromides. The results indicate that in a marginal case there is a significant advantage in using an aryl iodide rather than bromide as an arylating agent, although in most systems either the iodide or the bromide seems to be equally satisfactory for synthetic purposes.

The reaction occurs in reasonable yield when a phenyl group is *para* to nucleofugic bromine (Expt. 13).

3-Fluoroiodobenzene (Expt. 14) reacts to form 3-fluorophenylacetone in 56% yield. Retention of the fluorine substituent finds precedent in the photostimulated reactions of the same substrate with thiophenoxide ion and diethylphosphite ion to form, respectively, 3-fluorophenyl phenyl sulfide[7)] and diethyl 3-fluorophenylphosphonate.[8)]

When a trifluoromethyl group is *meta* to nucleofugic iodine (Expt. 15), the synthesis is less satisfactory than in most cases. The yield of 3-(trifluoromethyl)phenylacetone was only 35%, a good deal (14%) of deiodination occurred, and a significant amount of the substrate remained unreacted.

Three substrates with electron-donating substituents, namely, 4-bromodiethylaniline (Expt. 17), the 4-bromophenoxide ion (Expt. 18), and the enolate ion of 4-bromoacetophenone (Expt. 16) behave very poorly in the arylacetone synthesis.

TABLE II. Photostimulated Reactions of Halogen Derivatives of Naphthalene, Anthracene and Phenanthrene with Acetone Enolate Ion in Liquid Ammonia

Expt. No.	System	Halogen	Irradiation time, min	Arylacetone, %[a)]
22	naphthalene	1-I	60	76
23	naphthalene	2-I	90	75
24	anthracene	9-Br	dark[b)]	0
25	anthracene	9-Br	60	84[c)]
26	phenanthrene	9-Br	80	62

a) yields by isolation and weighing
b) 120 min
c) yield 98% by glpc

A *mete* nitro substituent is also unfavorable, as shown by Expts. 19—21. No 3-nitrophenylacetone was obtained, although there was some reaction as evidenced by the formation of dark colors and consumption of about half the substrate. The formation of dark colors preceded irradiation, and the results of a dark reaction (Expt. 19) were similar to those with irradiation.

The results listed in Table II indicate that halogen derivatives of polynuclear aromatic hydrocarbons react satisfactorily with acetone enolate ion to form arylacetones. We note that other workers[13)] have recently observed the photostimulated reaction of 1-chloronaphthalene with acetone enolate ion in ammonia to form 1-naphthylacetone, analogous to Expt. 22.

The experiments summarized in Table III concern the arylation of acetone enolate ion by aryl diethyl phosphates, stimulated by potassium metal. The reaction of unsubstituted phenyl diethyl phosphate (Expt. 27) was studied previously,[9)] but the present experiment is improved in two respects. First, a preparation of the enolate ion free of contamination by

---

13) R.A. Rossi, R.H. de Rossi and A.F. López, Abstracts, International Symposium on Nucleophilic Substitution, Pocono Manor, Pennsylvania, April, 1975, No. 50.

TABLE III. Potassium Metal-Stimulated Reactions of Substituted Phenyl Diethyl Phosphates with Acetone Enolate Ion in Liquid Ammonia

Expt. No.	Substituent	Yields, %[a]		
		Arylacetone	1-Aryl-2-propanol	ArH
27	H	5	56	27
28	2-$CHMe_2$	6	24	54
29	2-CMe_3	1.0	3.6	73

a) by glpc

isopropoxide ion³⁾ has been used. Also, the yield of benzene (27%) has been determined. We now find yields of both phenylacetone (I) and 1-phenyl-2-propanol (IV) somewhat higher than previously reported,⁹⁾ with IV by far the major product. Phenol was sought as a product,¹⁴⁾ but only a trace of it was found.

When an isopropyl group is *ortho* to the phosphate ester moiety (Expt. 28), the yield of arylation products is only about half as great as in its absence, and the yield of hydrocarbon is correspondingly increased. An *ortho* *t*-butyl group (Expt. 29) interferes even more seriously, for only meager amounts of arylation products are obtained. However, the yield of *t*-butylbenzene is 73%. Thus, despite the presence of the enolate ion, the procedure of Expt. 29 served rather well for the purpose of dephosphation or, with attention to the *o*-*t*-butylphenol from which the phosphate ester was made, dehydroxylation.¹⁵⁾

TABLE IV. Photostimulated Reactions of Bromobenzene with Acetone Enolate Ion in Various Solvents

Expt. No.	Solvent	Irradiation time, min	Yields, %[a]				
			PhBr	I	II	C_6H_5	Br^-
30	ammonia	10	0	93	6	tr	
31	50% NH_3: 50% $(C_2H_5)_2O$	30	44	41		13	55
32	HMPA[b]	65	98	0			
33	Me_2SO	60	31	61	6	0	71

a) by glpc
b) hexamethylphosphorotriamide

Comparison of Expts. 8 and 29 shows that *o*-*t*-butylarylation is effected far better in photostimulated condensation with the aryl iodide than in potassium metal-stimulated reaction with the aryl diethyl phosphate ester.

A few experiments exploring the suitability of other solvents are summarized in Table IV. The high yields of I and II obtained in neat liquid ammonia in a short reaction time (Expt. 30) are similar to those reported previously.³⁾ The efficacy of 50% ammonia: 50% diethyl ether was investigated because some substrates that are not very soluble in neat ammonia dissolve well in ether/ammonia. The results of Expt. 31 show, however, that reactivity is low and that there is substantial formation of benzene as a by-product when diethyl ether is a major solvent component. Hexamethylphosphorotriamide (Expt. 32) is wholly unsuitable as a reaction solvent. Dimethyl sulfoxide (Expt. 33) is better, but not nearly as good as ammonia.

Further advantages of ammonia as a solvent are that it is cheap and that the isolation and purification of reaction products are simple and efficient.

---

14) S.J. Shafer and W.D. Closson, Abstracts, American Chemical Society Meeting, Atlantic City, New Jersey, Sept., 1974, ORGN 20.
15) R.A. Rossi and J.F. Bunnett, *J. Org. Chem.*, 38, 2314 (1973).

In an experiment not tabulated, acetone enolate ion (0.01 M) was allowed to react photochemically with excess bromobenzene (0.03 M) in ammonia, the period of irradiation being 120 min. The yields of I (by glpc) and of II (isolated and weighed) were 32% and 58%, respectively. Benzene and 1,1,1-triphenyl-2-propanone were found in trace amounts.

TABLE V. NMR[a)] and Melting Point[b)] Data on 1-Aryl-2-propanones

Expt. No.	Compound	mp (°C)	$-CH_2\overset{\mathrm{O}}{\overset{\|}{C}}-$[c)]	$-\overset{\mathrm{O}}{\overset{\|}{C}}CH_3$[d)]	Aromatic protons[e)]	Other[e)]
1	1-(2,4-dimethoxyphenyl)-2-propanone		3.42	1.97	6.91(m, 1) 6.38(m, 2)	$-OCH_3$ 3.73(d, 6)
2	1-(3,5-dimethoxyphenyl)-2-propanone		3.50	2.04	6·32(s, 3)	$-OCH_3$ 3.76(s, 6)
3	1-(2,4,6-trimethoxyphenyl)-2-propanone	87 — 88	3.48	1.92	6.09(s, 2)	$-OCH_3$ 3.73(s, 9)
4	2-acetonylbenzoic acid	119 —122	3.68	2.12	7.88(m, 2) 7.23(m, 2)	$-COOH$ 9.15(s, 1)
5	methyl 3-acetonylbenzoate		3.79	2.08	7.20(m, 4)	$COOCH_3$ 3.69(s, 3)
6	4-acetonylbenzoic acid	146 —148	3.86	2.24	8.26(d, 2) 7.46(d, 2)	$-COOH$ 9.10(s, 1)
7	1-(2,5-diisopropylphenyl)-2-propanone		3.56	1.98	6.92(d, 3)	$-CH(CH_3)_2$ 2.89(m, 2) 1.19(m, 12)
8	1-(2,5-di-*t*-butylphenyl)-2-propanone	32.5— 34	3.72	1.90	6.90(d, 3)	$-C(CH_3)_3$ 1.21(d, 18)
10	1-(2,4,6-triethylphenyl)-2-propanone		3.81	2.25	7.00(s, 2)	$-CH_2CH_3$ 2.60(m, 6) 1.22(m, 9)
12	1-(2,4,6-triisopropylphenyl)-2-propanone	72.5— 73	3.72	1.86	6.70(s, 2)	$-CH(CH_3)_2$ 2.73(m, 3) 1.08(m, 18)
13	1-(4-biphenylyl)-2-propanone	48 — 50	3.64	2.10	7.50(m, 9)	
14	1-(3-fluorophenyl)-2-propanone		3.47	2.08	7.08(m, 4)	
15	1-(3-trifluoromethylphenyl)-2-propanone		3.48	2.09	7.66(m, 4)	
16	1-(4-acetophenyl)-2-propanone		3.59	2.06	7.60(m, 4)	$-COCH_3$ 2.47(s, 3)
22	1-(1-naphthyl)-2-propanone		4.03	1.98	8.10—7.40 (m, 7)	
23	1-(2-naphthyl)-2-propanone		4.63	2.97	8.90—8.18 (m, 7)	
25	1-(9-anthryl)-2-propanone	98 —102	4.63	1.92	8.57—7.47 (m, 9)	
26	1-(9-phenanthryl)-2-propanone	96 — 98	4.18	2.14	8.85(m, 1) 7.80(m, 8)	
27	1-phenyl-2-propanone		3.50	1.96	7.09(s, 5)	
28	1-(2-isopropylphenyl)-2-propanone		3.33	1.66	6.77(m, 4)	$-CH(CH_3)_2$ 2.73(m, 1) 0.90(d, 6)
29	1-(2-*t*-butylphenyl)-2-propanone		3.50	1.92	7.03(m, 4)	$-C(CH_3)_3$ 1.27(s, 9)

a) In parts per million downfield relative to Me_4Si. All spectra were made using a 60 MHz spectrometer with CCl_4 as solvent.
b) uncorrected
c) all singlets of relative area 2
d) all singlets of relative area 3
e) multiplicity and relative area appear in parentheses.

Experimental

Materials——Liquid ammonia was the solvent for all reactions except those mentioned in Table IV. Diethyl ether (Expt. 31) was distilled from lithium aluminum hydride directly into the reaction flask. HMPA (Expt. 32) was dried over KOH pellets for 24 hours, vacuum-distilled, and stored over molecular sieves.

Dimethyl sulfoxide (DMSO) (Expt. 33) was dried over NaOH for 3 hr, vacuum-distilled, and stored in a refrigerator.

Ventron 98% pure commercial potassium *t*-butoxide was stored in 25-g bottles under argon in a desiccator and used without further purification. See also experimental procedure, variation 1.

All aryl halide substrates were reagent grade commercial chemicals or were synthesized by known procedures; details appear elsewhere.[16] Commercial chemicals of 99% purity were not further purified. All prepared substrates were recrystallized or fractionally distilled and melting points of solids were verified. Analytical glpc analyses were made of all liquids and the more volatile solids. Commercial samples of 3-bromo- and 3-chloronitrobenzenes were purified by recrystallization and of bromobenzene and 1-bromo-2,4,6-triethylbenzene by fractional distillation.

General Procedure for Arylation of Acetone Enolate Ion——In a typical run (Expt. 10, Table I), done entirely under nitrogen atmosphere, a solution of potassium acetone enolate ion was prepared by the reaction of 4.88 g (0.0435 mole) of commercial potassium *t*-butoxide with 2.324 g (0.0400 mole) of spectral grade acetone in 250 ml of liquid ammonia distilled from sodium. This was done in a three-neck flask provided with a cold finger condenser cooled by solid CO_2 in 2-propanol. The flask was cooled to $-70°$ by a solid CO_2 in 2-propanol bath before addition of the acetone. Distilled 1-bromo-2,4,6-triethylbenzene (2.250 g, 0.00933 mole) was added, and the reaction was stirred and placed in a Rayonet photochemical reactor[17] equipped with 350 nm ultraviolet lamps. The reaction was irradiated for 120 min. Frost was wiped from the outside of the flask every 20 min. The reaction was treated with NH_4NO_3; 100 ml of diethyl ether was added and the ammonia was allowed to evaporate through the cold finger condenser cooled with solid CO_2 in 2-propanol to $-20°$ to assure the complete entrapment of hydrocarbon product. Water was added and the solution was extracted with diethyl ether. The ether layer was dried over $MgSO_4$ and analyzed by glpc. If only the expected product was found to be present, the ether solution was concentrated by evaporation and the residue was distilled at reduced pressure. If a mixture of products was present, yields were determined by glpc, the ether was removed by evaporation and pure samples of the products were isolated from the residue by preparative glpc. In many cases the aqueous layer remaining after extraction with ether was analyzed to determine the percentage of released halide ion. The aqueous layer was first acidified using 6M aqueous HNO_3 and then titrated potentiometrically with a standard solution of $AgNO_3$.

This general procedure was used for all the reactions listed in the tables with the following variations:

1) Sometimes the potassium *t*-butoxide was prepared in the ammonia solvent by the reaction of potassium metal with *t*-butyl alcohol and a trace of $Fe(NO_3)_3$.

2) When the aryl halide was a solid, it was weighed in a separate flask purged with nitrogen, and the potassium ketone enolate ion in the liquid ammonia solvent was transferred to this flask *via* a glass tube under nitrogen pressure.

3) When the aryl halide contained an acidic proton, an extra equivalent of potassium *t*-butoxide was used in order to generate the anion of the substrate.

Reactions stimulated by potassium metal (Table III) were conducted according to the procedure of Rossi and Bunnett.[4]

Identification of Products——Unreacted substrate, hydrocarbon products, and dehalogenated products were in most cases identified by glpc comparisons with authentic samples. In cases where doubt existed, spectroscopic comparisons with authentic samples were also made. The aldol-type condensation product 4-hydroxy-4-methyl-2-pentanone was found in some cases; it was identified by mass spectral, infrared, and nuclear magnetic resonance (NMR) analyses and comparison of spectra with those of an authentic sample.

Table V presents NMR and melting point data on all the 1-aryl-2-propanones prepared in the present study. Other physical parameters used for identification of products are presented in detail elsewhere,[16] as are elemental analyses for carbon and hydrogen which were obtained for all new compounds and which support the structures assigned.

Discussion

Our results show that the photostimulated arylation of acetone enolate ion by aryl bromides and iodides is a synthetic method of wide generality. (Our study dealt with scarcely any aryl chlorides, but other work[3,13] indicates that they may also be used.)

Certain limitations are however revealed. The synthesis is unsuccessful when strongly electron-releasing groups such as $-NEt_2$ and $-O^-$ are *para* to the nucleofugic group. It also fails with *m*-nitrohalobenzenes and is only marginal with *m*-iodobenzotrifluoride.

The synthesis is remarkably insensitive to steric hindrance by *ortho* substituents, but the accumulation of massive bulk at *ortho* positions eventually interferes.

---

[16] J.E. Sundberg, Dissertation, University of California, Santa Cruz, June, 1975.

The fact that low overall reactivity in the arylation reaction is associated with the formation of dehalogenation products in substantial amounts is of mechanistic interest. See for instance Expts. 8, 12, and 15, Table I. When the aryl radical is encumbered with large *ortho* substituents it is plausible that a second mode of reaction with acetone enolate ion, besides covalent bond formation as in equation 3, may come into play. The second mode is electron transfer, as in equation 7, generating an aryl anion and acetonyl radical. The aryl anion would

$$\text{Ar}\cdot + \text{CH}_3\text{COCH}_2^- \longrightarrow \text{Ar}:^- + \text{CH}_3\text{COCH}_2\cdot \qquad (7)$$

quickly take a proton from the solvent to form the observed dehalogenation product. If the acetonyl radical then took part in one or more steps leading to termination products, the association of low reactivity with dehalogenation would find explanation.

Conceivably an aryl radical would have a tendency to react in the manner of equation 7 not only if it were sterically hindered about its reactive site, but also if it carried an electron-attracting substituent that would stabilize a phenyl anion. If so, the results of Expt. 15, Table I, find interpretation.

That carboxylate substituents (Expts. 4—6, Table I) do not interfere with the arylacetone synthesis is noteworthy inasmuch as sodium benzoate has a pronounced affinity for solvated electrons in ammonia.15,18,19) Presumably any special electron affinity due to the carboxylate group is enjoyed both by bromobenzoate dianions and by the radical dianions of type V that result from combination of $\cdot C_6H_4COO^-$ radicals with acetone enolate ion. Therefore electron transfer in step 4 (Chart 1) of the mechanism is not impeded by the presence of the carboxylate groups.

We now face the question: why does the potassium metal-stimulated reaction of phenyl diethyl phosphate with acetone enolate ion (Expt. 27, Table III) form so much benzene (27%) as a by-product? That reaction was conducted by adding bits of potassium metal to a solution of the ester and the enolate ion until a blue color persisted. In contrast, reaction of bromobenzene with acetone enolate ion under similar conditions gives only 5% of benzene by-product.20)

We hypothesize that the bromobenzene reaction may be so fast as to occur in large part before mixing of reactants has formed an homogeneous solution. We visualize two zones in the reacting mixture: a zone with excess solvated electrons, for the most part in the vicinity of a bit of potassium metal, and a zone with few or no solvated electrons. If should be noted that mechanical action may separate provinces of the electron-rich zone from the vicinity of a bit of potassium and send them out into the general medium. There is evidence that bromobenzene reacts with solvated electrons at encounter-controlled rate;21) therefore, the electron-rich zone is free of bromobenzene. Bromobenzene does however exist in the electron-poor zone, with the enolate ion, until it has been wholly consumed.

There are reasons to believe that the propagation steps of the $S_{RN}1$ mechanism (Chart 1) are, in the case of bromobenzene reacting with acetone enolate ion, extremely fast. Accordingly, initiation step 1 occurs at the interface between the zones on encounter, and is quickly followed by step 2. The resulting phenyl radical may migrate by diffusion into either the electronrich or the electron-poor zone. If into the former, it may react either with enolate ion (step 3) or with a solvated electron to form phenyl anion and thence benzene, and there is a substantial probability of reaction with the solvated electron in the electron-rich zone. Ketyl V, to the extent that it is formed in the electron-rich zone, may either be reduced to alkoxide

---

17) Product of the Southern New England Ultraviolet Co., Middletown, Connecticut.
18) A.P. Krapcho and A.A. Bothner-By, *J. Am. Chem. Soc.*, **81**, 3658 (1959).
19) S.S. Hall, S.D. Lipsky, J.F. McEnroe, and A.P. Bartels, *J. Org. Chem.*, **36**, 2588 (1971).
20) R.A. Rossi and J.F. Bunnett, *J. Am. Chem. Soc.*, **96**, 112 (1974).
21) J.F. Bunnett and X. Creary, unpublished observations.

ion (step 5) in a termination step or migrate back to the interface and perhaps across into the electron-poor zone.

If phenyl radical generated at the interface migrates into the electron-poor zone, it finds conditions conducive not only for combination with enolate ion (step 3) but also for the whole propagation sequence. Moreover, as the chain propagates the place "where the action is" may move deeper into the electron-poor zone through migration of intermediates. Thus a substantial amount of reaction may occur within the electron-poor zone, a region where very little reduction of phenyl radical to phenyl anion occurs.

When the substrate is phenyl diethyl phosphate, however, the propagation cycle of steps 2, 3, and 4 is less efficient, because step 2 and/or step 4 is slow relative to the bromobenzene case. Therefore the advancing front of solvated electrons, diffusing from the electron-rich zone, overtakes and engulfs the reacting intermediates of the propagating cycle before there has been much time for reaction to occur. Consequently phenyl radicals are nearly always generated in a region more or less well supplied with electrons, and relatively large amounts of benzene are formed.

As a solvent for arylacetone synthesis, 50% ammonia: 50% diethyl ether is clearly less suitable than neat ammonia; see Expts. 30 and 31, Table IV. The reason presumably is that phenyl radicals may in part abstract hydrogen atoms from the α-positions of diethyl ether, forming benzene (an observed product) and the α-ethoxyethyl radical. The latter is apparently unreactive with the enolate ion and waits about until it can combine with some other radical in a termination step.

The unsuitability of HMPA as a reaction solvent (Expt. 32) is probably of similar origin. With phenyl radical, the reactivity in hydrogen atom abstraction, per hydrogen atom relative to ethane, is 33 for diethyl ether and 13 for the methyl hydrogens of N,N-dimethylbenzamide.22) If the latter may also be attributed to HMPA, the reactivity per molecule is 132 for diethyl ether and 234 for HMPA. The suggested interpretation is thus plausible. If pathways leading to termination predominate overwhelmingly, very little overall reaction by a radical chain mechanism will occur.

Dimethyl sulfoxide (Expt. 33) is marginally suitable as a reaction solvent. Hydrogen atom capture from the solvent is apparently not a big problem. It is unclear why DMSO is less suitable than ammonia.

---

22) G.A. Russell, in J.K. Kochi, "Free Radicals," Vol. I, John Wiley and Sons, Inc., New York, 1973, pp. 299—300.