Further Evidence for Single Electron Transfer during the Alkylation of the Benzophenone Anil Dianion

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Abstract: Evidence for single electron transfer (SET) in the alkylation of the benzophenone anil dianion was obtained by effecting the alkylation with 5-hexenyl halides and cyclopropylmethyl halides. Alkyl radicals derived from these alkyl halides are known to undergo rapid intramolecular change so that the appearance of rearranged alkyl groups in the alkylation products provides evidence for SET during the alkylation. Such rearrangements were observed only in alkylations with cyclopropylmethyl bromide and iodide. This implied that radical anion–radical coupling was well in excess of 10^5 s^{-1}, the rate for cyclization of the 5-hexenyl radical to the cyclopentylmethyl radical. It also implied that alkylation with primary alkyl chlorides did not involve a SET process. Ring-alkylation products were observed in those instances when SET processes occurred and are thus felt to be characteristic of the radical process.

Earlier, evidence for the occurrence of single electron transfer (SET) in the alkylation of the benzophenone anil dianion (**1**) relied upon the observed[1] efficient alkylation of **1** by tertiary and bridgehead halides. We report here additional evidence which involves alkylation of **1** with alkyl halides whose alkyl group, should it be converted to a radical, will undergo rapid intramolecular change. The structure of the alkylation products will then reflect the intermediate formation of a radical and hence the presence of SET (see Scheme I). Similar studies have been reported for radical anions,[2] for phosphide anions,[3] for the dianion derived from tetraphenylethylene,[4] and for metalate anions.[5]

Since 5-hexenyl radicals are known[5] to undergo rapid cyclization to cyclopentylmethyl radicals, the dianion **1** (counterion Li^+, Na^+, or K^+) was treated with 5-hexenyl chloride, bromide, and iodide at 22 °C.[7] Authentic samples of the expected products **2** and **3** (also **4** and **5**) were prepared by alkylating **1** with the appropriate alkyl bromide at −78 °C. Gas chromatographic (GC) analysis of the reaction product showed the absence of any detectable **3** under all conditions studied. The *only* alkylation product observed was **2**.

The cyclopropylmethyl radical is known[8,9] to rearrange to the 3-butenyl radical at a rate 1000 times more rapidly than the 5-hexenyl radical cyclizes. Repeating the preceding experiment using cyclopropylmethyl halides gave, under certain conditions, reaction mixtures containing both cyclopropylmethyl and 3-butenyl groups. Table I summarizes the GC analyses of these mixtures.

Among the reaction products were two others in addition to the expected **4** and **5**. We were unable to separate these in a pure form but have identified them as **6** and **7** on the following evidence:

(1) A Fourier transform ^1H NMR spectrum of a chromatographic fraction rich in **7** showed the presence of vinyl protons and the absence of cyclopropyl protons.

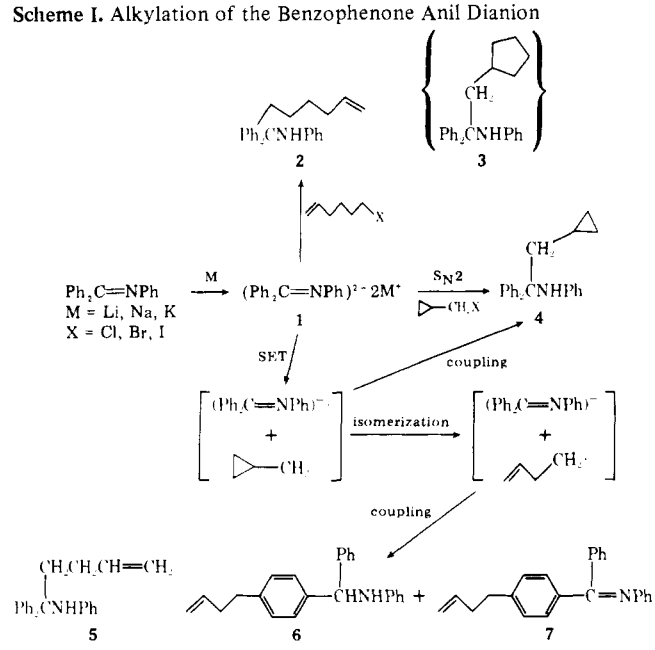
(2) After lithium aluminum hydride reduction of the alkylation mixture, GC analysis showed that **7** had disappeared and **6** had increased in quantity. The compounds were thus an anil–amine pair—such have been observed[1,11] before.

(3) Hydrogenation of the reaction mixture converted **6** and **7** to a product which must be an *N*-(butylbenzhydryl)aniline.

(4) Synthesis of both *N*-(*o*- and *p*-butylbenzhydryl)aniline[12] showed that the latter had a retention time identical with that of the hydrogenation product.

It is clear from the data obtained that the coupling of the radical anion–radical pair formed in the SET process is extremely rapid, well in excess of the rate of cyclization of the 5-hexenyl radical and competitive with the rate of ring opening of the cyclopropylmethyl radical.

Scheme I. Alkylation of the Benzophenone Anil Dianion



Since diffusion rate constants[13] are typically 10^{10} s^{-1}, the question arises[14] whether or not intramolecular rearrangement of the cyclopropylmethyl radical competes with geminate coupling. It has been noted[3] that evidence for such a competition has been reported.[15] However, some diffusion does occur since reduction products (RH) and dimers (RR) of the alkyl halide have been observed both in the case of the tetraphenylethylene dianion[4] and **1**.[1,16] Clearly, a decision on this point will require further experimentation.

Since rearranged alkyl groups are not found in the alkylation products formed from alkyl chlorides, it is unlikely that a SET process is involved here but it is in the cases of alkyl bromides and iodides. This would be anticipated from the known half-wave reduction potentials[17] of primary alkyl halides, which indicate that the dianion **1** is insufficiently strong a reducing agent[18] to react with primary alkyl chlorides but is capable of reducing bromides and iodides.

It is noteworthy that the ring-alkylated products are entirely the result of an SET process since *only* rearranged alkyl groups were encountered. This association of ring alkylation with SET has been noted by Ashby[19] in the reaction between Grignard reagents and benzophenone. On the basis of the evidence

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Table I. Product Distribution in Reactions of **1** with Cyclopropylmethyl Halides

alkali metal	halide	products,[a] % 4	5	6 + 7
Li	Cl	100	0	0
Li	Br	61	17	22
Li	I	38	37	25
Na	Cl	100	0	0
Na	Br	80	15	5
Na	I	52	42	6
K	Cl	100	0	0
K	Br	99	1	0
K	I	68	28	4

[a] Peak areas of alkylation products are normalized.

available, the possibility of some nucleophilic component in the alkylation of **1** by alkyl bromides or iodides to form **4** cannot be excluded.[20] Indeed, such a mixed mechanism has been suggested for alkylations of the anthracene[2c] and benzophenone[2b,d] radical anions.

In addition, it can be seen from the data in Table I that the occurrence of SET is dependent on the cation, the greatest amount (largest amount of 3-butenyl derivatives) being observed with lithium as the counterion and the least with potassium. This is in agreement with Garst's report[1b] that lithium benzophenone ketyl reacts chiefly by electron transfer but S_N2 processes may occur when other cations are present.

Experimental Section

All operations involving alkali-metal compounds were conducted in an atmosphere of purified, dry nitrogen. Tetrahydrofuran (THF) was dried by refluxing over lithium aluminum hydride and distilling into the reaction vessel on need.

Melting points are uncorrected and were determined in open capillaries with a Mel-Temp apparatus. NMR spectra were recorded on a Varian T-60 spectrometer in $CDCl_3$ using tetramethylsilane (Me_4Si) as the internal reference. Chemical shifts are reported in parts per million downfield from Me_4Si. Infrared spectra were recorded on a Beckman IR-10 spectrophotometer and high-resolution mass spectra on a VG 7070 Micromass spectrometer.

Column chromatography utilized silica gel 60 and aluminum oxide 90 from E. Merck AG. Elemental analyses were obtained from M-H-W Laboratories, Phoenix, Ariz.

Gas Chromatographic Analyses. Reaction mixtures were analyzed on a Varian 1420 gas chromatograph using a 5 ft by $\frac{1}{8}$ in. stainless steel column packed with 3% SE-30 on 100/120 mesh Chromosorb W. The temperature was programmed isothermally at 180 °C for 6 min, raised at 4 °C/min for 16 min, and then held isothermally at the higher temperature until elution was complete. Injection port temperature was maintained at 200 °C to avoid decomposition of some of the products. The alkylation products eluted with the following relative retention times; benzophenone anil (0.87), *N*-benzhydrylaniline (1.00), **5** (1.35), **4** (1.46), **7** (1.56), **6** (1.71).

Peak areas were measured with a DISC integrator and the area percents are reproducible on a run-to-run basis to ±5%. Benzophenone anil and *N*-benzhydrylaniline, which were present to the extent of 1-15% of the total products, are omitted from the analytical data in Table I.

Hydrogenation (5% Pd on carbon, ethyl acetate, 20 °C, 5 h) of the reaction mixture (M = Li; X = Br) converted the 3-butenyl groups to butyl groups and the anils to amines. Comparison of the retention times of the product with those of authentic samples of *N*-(*o*- and *p*-butylbenzhydryl)aniline showed that the ring-substituted product was para. This comparison was made using both the standard SE-30 column and a column containing 5% OV-17 on Gas Chrom Q (5 ft by $\frac{1}{8}$ in.).

The alkyl chlorides and bromides were either obtained commercially or prepared from the corresponding alcohols using the method of Wiley[21] et al. The alkyl iodides were prepared from the bromides by treatment with excess sodium iodide in dry acetone. The alkyl halides were distilled under nitrogen or vacuum immediately prior to use.

Reduction of Benzophenone Anil. Benzophenone anil (0.0025 mol) was reduced by stirring a solution in 100 mL of THF with excess alkali metal under nitrogen for 24 h in a specially designed flask.[22] After removal of the excess alkali metal, the 5-hexenyl or cyclopropylmethyl halide (0.0025 mol) was injected through a septum and the reaction allowed to proceed for 1 h. Water was then added and the alkylation products were isolated by a chloroform extraction.

Reference Compounds. These were prepared from the benzophenone anil dianion (**1**) and the appropriate alkyl bromide using the procedure described above except that the solution of the dianion was cooled to −78 °C before the alkyl halide was injected. The crude product was purified by chromatography on neutral alumina (silica gel caused decomposition) eluting with 30-60 °C petroleum ether graded to benzene followed by recrystallization from petroleum ether.

1-Anilino-2-cyclopropyl-1,1-diphenylethane (4): mp 69-70 °C; NMR 0.1 to −0.1 (m, 2 H), 0.2-0.7 (m, 3 H), 2.5 (d, 2 H, J = 6 Hz), 5.0 (s, 1 H, NH), 6.4-8.0 ppm (m, 15 H); IR ($CHCl_3$) 3500 (NH), 3100, 3050, 2890, 1620, 1515, 1330, 690, 630 cm^{-1}.

Anal. Calcd for $C_{23}H_{23}N$: C, 88.13; H, 7.40; N, 4.47. Found: C, 88.31; H, 7.32; N, 4.26.

1-Anilino-1,1-diphenyl-4-pentene (5): mp 55-56 °C; NMR 1.8-2.3 (m, 2 H), 2.5-3.0 (m, 2 H), 4.5-5.2 (m, 3 H), 5.5-6.0 (m, 1 H), 6.4-7.8 ppm (m, 15 H); IR ($CHCl_3$) 3480 (NH), 3100, 3050, 2990, 1620, 1505, 1460, 1440, 1320, 910 (C=C), 680, 660 cm^{-1}.

Anal. Calcd for $C_{23}H_{23}N$: C, 88.13; H, 7.40; N, 4.47. Found: C, 88.20; H, 7.67; N, 4.31.

1-Anilino-2-cyclopentyl-1,1-diphenylethane (3): mp 74-75 °C; NMR 0.8-2.0 (m, 9 H), 2.6 (d, 2 H, J = 6 Hz), 4.6 (s, 1 H, NH), 6.2-7.6 ppm (m, 15 H); IR ($CHCl_3$) 3420 (NH), 3060, 3005, 2950, 2870, 1605, 1500, 1450, 1315, 690 cm^{-1}.

Anal. Calcd for $C_{25}H_{27}N$: C, 87.98; H, 7.92; N, 4.11. Found: C, 87.84; H, 8.18; N, 3.83.

***o*- and *p*-butylbenzophenone anils** were prepared from the corresponding ketones by the method of Reddelien.[11,23] Both anils were oils and were purified by column chromatography on neutral alumina using benzene as eluant. *p*-Butylbenzophenone anil: NMR 0.6-1.6 (m, 7 H), 2.4 (distorted t, 2 H), 6.7-8.0 ppm (m, 14 H); IR ($CHCl_3$) 2980, 2950, 2880, 1590, 820, 740, 670 cm^{-1}.

Anal. Calcd for $C_{23}H_{23}N$: C, 88.14; H, 7.40; N, 4.46; *m/e* 313.1830. Found: C, 88.36; H, 7.56; N, 4.26; *m/e* 313.1831.

o-Butylbenzophenone anil: NMR 0.8-1.8 (m, 7 H), 2.7 (distorted t, 2 H), 6.8-8.0 ppm (m, 14 H); IR (neat) 2990, 2960, 2900, 1605, 750, 730, 680 cm^{-1}.

***N*-(*o*- and *p*-butylbenzhydryl)aniline** were prepared by lithium aluminum hydride reduction of the corresponding anils. Both amines were oils and purification was effected by column chromatography on neutral alumina using benzene as eluant.

N-(*p*-Butylbenzhydryl)aniline: NMR 0.6-1.8 (m, 7 H), 2.6 (distorted t, 2 H), 4.1 (s, 1 H), 5.7 (s, 1 H, NH), 6.5-7.6 ppm (m, 14 H); IR ($CHCl_3$) 3445 (NH), 2965, 2945, 2865, 1600, 1495, 1450, 825, 745, 670 cm^{-1}.

N-(*o*-Butylbenzhydryl)aniline: NMR 0.6-1.8 (m, 7 H), 2.6 (distorted t, 2 H), 4.0 (s, 1 H, NH), 5.67 (s, 1 H), 6.4-7.5 ppm (m, 14 H); IR (neat) 3435 (NH), 3060, 3045, 2960, 2940, 1600, 1495, 1305, 890, 730, 665 cm^{-1}.

Anal. Calcd for $C_{23}H_{25}N$: C, 87.57; H, 7.79; N, 4.44. Found: C, 87.76; H, 7.86; N, 4.18.

***p*-Butylbenzophenone** was prepared by a literature procedure.[24] ***o*-Butylbenzophenone** was prepared by treating *o*-butylbenzoic acid in benzene with 2 equiv of phenyllithium. Chromatography on silica gel using 30-60 °C petroleum ether graded to benzene as eluant provided a pure sample as a clear oil: NMR 0.6-1.9 (m, 7 H), 2.7 (t, 2 H, J = 8 Hz), 7.2-8.1 ppm (m, 14 H); IR ($CHCl_3$) 2960, 2930, 1660 (C=O), 1445, 1260, 915, 750, 695, 630 cm^{-1}.

Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.70; H, 7.78.

***o*-Butylbenzoic acid** was prepared in 67% yield by alkylating the dianion of *o*-toluic acid[25] with *n*-propyl bromide (4 equiv), mp 38-39 °C after recrystallization from 30-60 °C petroleum ether (reported[26] 40-41 °C).

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Effect of Solvation on β Values for Formyl, Acetyl, and Pivaloyl Transfer between Sulfur and Oxygen Nucleophiles

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Abstract: Second-order rate constants were measured in aqueous solution for the reaction of a series of oxy anions and thiol anions with the formate and pivalate esters of *p*-nitrophenol and *p*-nitrothiophenol. These data, along with literature data, provide a picture of the effect of alkyl substitution on the rates of uncatalyzed acyl transfer between sulfur and oxygen nucleophiles. Evidence is provided in support of the proposal that β values for oxy anions are altered by solvation, whereas those for thiol anions are not. The change of rate-determining step from formation to breakdown of tetrahedral intermediate occurs for formate and pivalate esters in the same manner that this occurs for acetate esters. The greater kinetic reactivity of formate esters compared to acetate esters is not a function of the entering or leaving nucleophile but is an inherent difference in the esters reflecting the relative ease of formation of the tetrahedral intermediates.

Introduction

Because the β value for the attack of a nucleophile on an electrophile must reflect the loss of charge upon reaching the transition state,[1] interpretation of these slopes in terms of transition-state bond order is reasonable. Other factors can influence β values, however, and make such an interpretation difficult. For example, nucleophilic attack by oxy anions on esters shows large values of β for phenoxides and small values of β for alkoxides.[1,2] Thus, β values suggest substantially different degrees of bond formation for these two classes of nucleophiles, whereas other indexes of transition-state structure (such as β values for leaving groups) suggest identical degrees of bond formation.

The Brønsted plot for proton abstraction from carbon by oxy anions shows substantial curvature.[3] We have proposed that this curvature is due to an effect of solvation stabilizing oxy anions in the transition state for attack on the proton. Since the curves for proton abstraction and nucleophilic attack on acetate esters are similar, it was proposed that the β values for both reactions were influenced similarly by solvation.[4] Consistent with this interpretation was the fact that the curvature was substantially diminished for pivalate esters, presumably because of the steric inhibition of this solvation effect. The literature data for oxy anion attack on acetate[1] and pivalate[4] esters are included in Figures 1 and 2.

We have recently shown that thiol anions are much poorer catalysts for proton abstraction from carbon than are comparably basic oxy anions.[5] Thus, even though the equilibrium constant for proton transfer from carbon to sulfur may be identical with that for transfer to oxygen, the latter may occur 50 times faster. These facts are also consistent with the solvation argument discussed above since thiol anions are less well solvated than oxy anions and thiols do not hydrogen bond readily. The rates of thiol anions are therefore not enhanced (and β values not altered) by solvation as are oxy anions. Ritchie has shown[6] that in Me_2SO, where this solvation difference should be absent, equally basic thiol anions and oxy anions have equal rates for proton transfer from carbon, as expected. A plot of rate constants for proton transfer from carbon to sulfur or oxygen bases vs. the equilibrium constants for the same process in the same medium was fit by a single correlation line.

The following general picture, therefore, begins to emerge. Oxy anions are assisted by solvation in the transition state for attack on an electrophile. This solvation effect results in a

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