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Unusual Alkylations of the 1,1-Diphenyl-2-Propanone Dianion

Ruth E. TenBrink

UNUSUAL ALKYLATIONS OF THE 1,1-DIPHENYL -2-PROPANONE DIANION

by

Ruth E. TenBrink

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Ruth E. TenBrink

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INTRODUCTION

The carbonyl moiety has long been one of the most versatile functional groups of organic chemistry. Not only does the carbonyl itself serve as a reaction site, but it is also used to influence reactions at adjacent carbons. Frequent use is made of the electron-withdrawing capability of the carbonyl to influence the acidity of adjacent carbon-hydrogen bonds. Due to the acidity enhancing character of the carbonyl, carbanions can be prepared at the alpha carbons. These carbanions may be reacted with other electron deficient species.

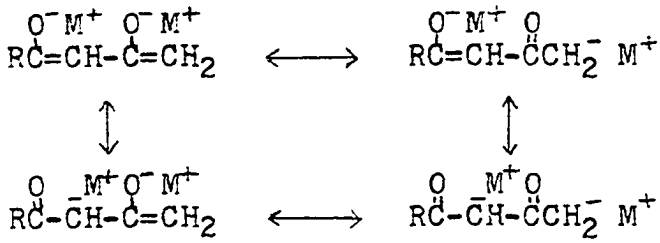
We wish to present here the results of our investigation of the reactions of the 1,1-diphenyl-2-propanone dianion with various alkyl halides and to discuss the somewhat subtle factors which determine the unexpected alkylation products.

HISTORICAL BACKGROUND

When β-diketones(1) are treated with a base such as a metal amide, the most acidic proton, the methylene proton, is removed and subsequent alkylation affords compounds of general structure 2. The addition of two equivalents of base gives the dianion 3. Addition

1 2

of one equivalent of an alkylating agent such as an alkyl halide, followed by an aqueous work-up, gives



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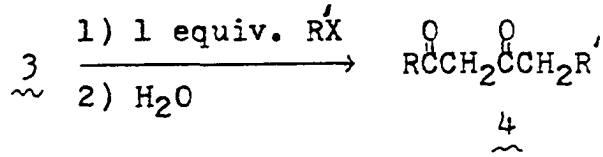
a terminally alkylated product(4) as the only product.[1]



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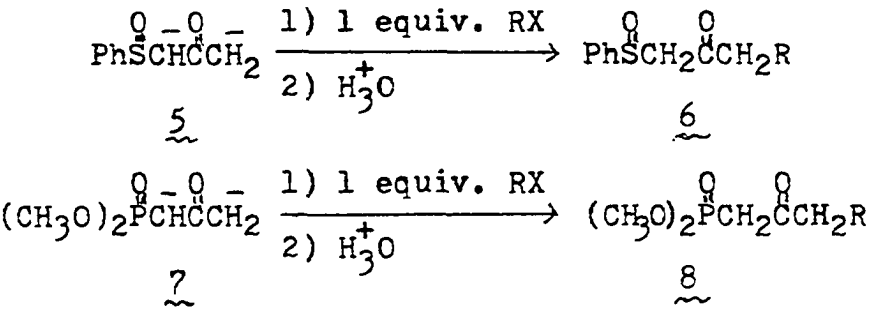
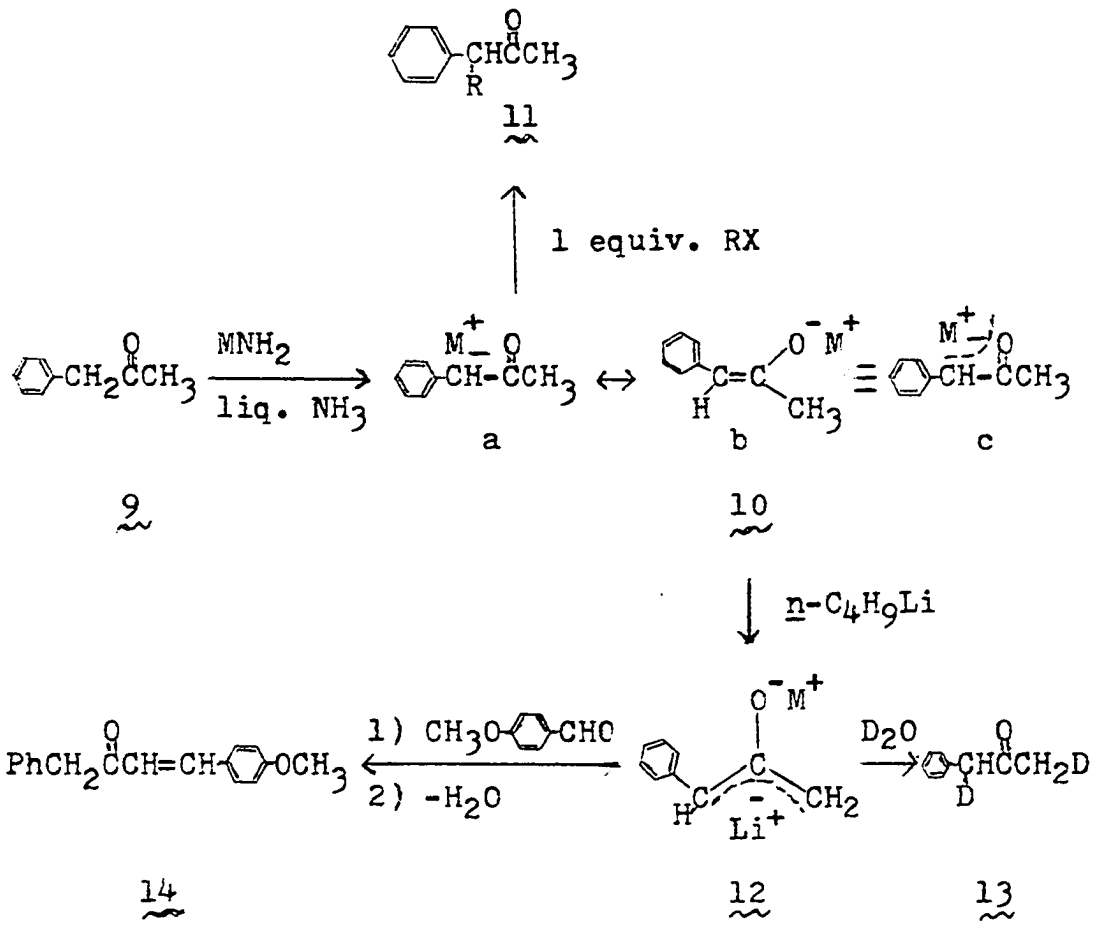
Harris and Harris theorize that under the conditions of the reaction (liquid ammonia), the nucleophilicity of the monocarbanion is too low to produce an observable reaction in the methylene position of the dianion as opposed to the terminal position.

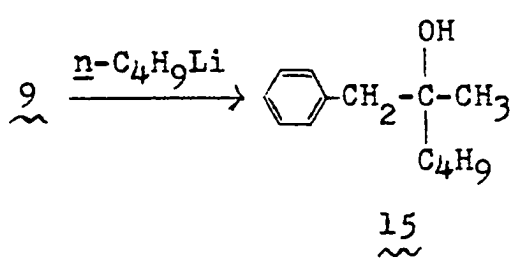
Groups other than the β-keto group can be used to activate the carbon-hydrogen bond towards anion formation. Both β-keto sulfoxides[2,3] and β-keto phosphonates[4,5] have been successfully converted to their dianions 5 and 6, respectively, with sodium hydride and n-butyllithium. Treatment with alkyl halides affords the terminally alkylated products 7 and 8, respectively.



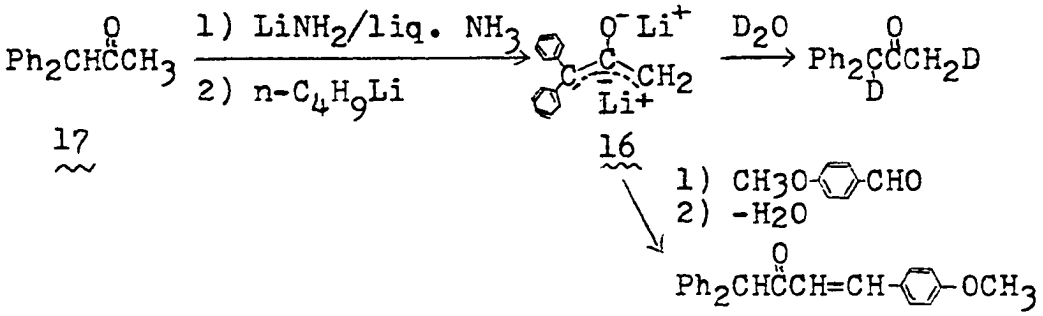
Hauser first successfully converted a monoketone (other than dibenzyl ketone) to its dianion.[6] The addition of one equivalent of base such as a metal amide to 1-phenyl-2-propanone (9) gives the mono-anion 10, which upon addition of an alkylating agent gives the C-1 alkylated product 11, as expected. The addition of two equivalents of metal amide to 9 gives no dianion. n-Butyllithium, a stronger base, would be expected to be capable of removing the second proton to give the dianion. However, Hauser found that the carbonyl was the site of attack



to give 15. To circumvent this problem, he used a metal amide to form the monoanion 10, thus effectively removing the carbonyl as the site of attack. Addition of n-butyllithium to 10 then gave the dianion 12, which after treatment with D_2O gave the dideuterated product 13. Treatment of the dianion 12 with p-anisaldehyde then gave the terminal (or C-3)



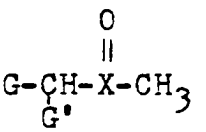
condensation product 14. In a similar manner, the 1,1-diphenyl-2-propanone dianion 16 also gave the dideuterated product after treatment with D_2O and the terminal condensation product after treatment with p-anisaldehyde. Hauser states that "the condensation of [12] with anisaldehyde was indicated initially to give the corresponding carbonyl addition product, but it was not isolated,"[6] but does not elaborate on this statement.



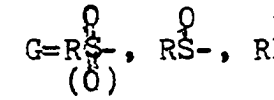
Nothing has yet appeared in the literature on the alkylation of monoketone dianions with alkyl halides. It has been shown by work done by Hinkley[7] in this laboratory that the alkylation of 12 affords mixtures of the C-1 and C-3 alkylated products, and in many cases the C-1 alkylated product alone. See Table I. This unexpected preference for C-1 alkylation (in view of the site of β-diketone alkylation and the much greater basicity of the C-3 anion) has led us to investigate the alkylation of the dianion of another phenyl-2-propanone, namely the dianion of 1,1-diphenyl-2-propanone.

STATEMENT OF PROBLEM

When the subject of ketone dianion alkylation is raised, one immediately thinks of β-diketone dianions and terminal alkylation. This word association response is due to the simple fact that the literature deals almost exclusively with β-diketone and β-diketone-like substrates of Type I.[1-5] Group G in Type I compounds always features a carbon, sulfur, or phosphorous π or $d\pi$ bonded to oxygen. This in fact represents only one type of functional group. G can be a number of other functional groups, as illustrated by Type II compounds.



X=C,S,P

Type I G'=H; G= 

Type II G'=H; G=Ar, CN, NO_2, RS, RO, C≡CR, etc.

Type IIIa G'=H; G=Ph

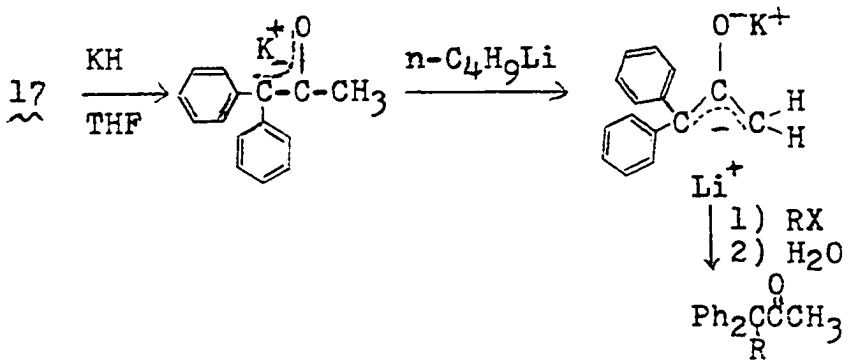
Type IIIb G'=G=Ph

Although hundreds of β-diketone (Type I) dianion alkylations have been published, alkylations of dianions of Type II compounds have either been ignored or have been assumed by analogy to follow the course of β-diketone dianion alkylations. Hinkley[7] has investigated the alkylation of the 1,3-dianion of 1-phenyl-2-propanone (Type IIIa) and found that alkylation occurs predominantly at the C-1 position--just the opposite of what would be expected from analogy with a β-diketone Type I system.

The purpose of this investigation is to examine the effect of a second phenyl group (Type IIIb) on the site of alkylation of the phenyl-2-propanone system.

RESULTS

As mentioned in the Statement of Problem section, the purpose of this work was to determine the site of alkylation of the 1,1-diphenyl-2-propanone dianion. The reaction sequence is summarized below.

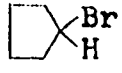


Approximately 1.5 equivalents of KH were added to 17, followed by 1.5 equivalents of n-butyllithium. Various alkyl halides were then added to the dark red dianion, followed by the addition of water. For a more detailed discussion, see the Experimental section.

The results of the reaction of the dianion of 1,1-diphenyl-2-propanone with various alkyl halides are summarized in Table II. For comparison, see the results of the alkylation of 1-phenyl-2-propanone in Table I.

Table I

Alkylation of the 1-Phenyl-2-propanone Dianion (12) with Alkyl Halides[7]

Alkyl Halide	Overall Yield[a] (%)	C-1 Alkylation : C-3 Alkylation
$(CH_3)_2CHBr$	63	Only C-1 alkylation
$(CH_3)_2CHCH_2Br$	57	Only C-1 alkylation
	61	Only C-1 alkylation
	65	Only C-1 alkylation
$n\text{-}C_4H_9Br$	72	19 : 1
$n\text{-}C_4H_9I$	57	9 : 1
CH_3CH_2Br	55	>99% C-1 alkylation
CH_3CH_2I	65	5 : 1
CH_3I	62	5.5 : 4.5

(a) Isolated by vacuum distillation.

Table II

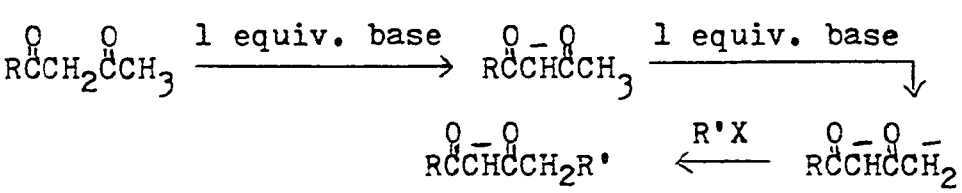
Alkylation of the 1,1-Diphenyl-2-propanone Dianion with Alkyl Halides

Alkyl Halide	Equivalents of RX	Overall Yield (%)	Product Distribution[a] (Relative %)		
			$Ph_2\overset{R}{C}COCH_2R$	$Ph_2CHCOCH_2R$	$Ph_2\overset{R}{C}COCH_3$
$(CH_3)_2CHCl$	1.5	60		19	81
$(CH_3)_2CHBr$	1.5	54		36	64
$CH_3CH_2CH_2Cl$	1.5	87		52	48
CH_3CH_2Br	1.5	87		61	39
CH_3CH_2I	1.5	76	25	68	7
CH_3I	1.0	77		48	52
CH_3I	3.0	86	100[b]		
CH_3CH_2I	1.0	40		71[c]	29[c]
CH_3CH_2I	3.0		36[c]	64[c]	

(a) Calculated from isolated yields. (b) An inseparable mixture of $Ph_2CRCOCH_2R$ and $Ph_2CRCOCHRR$ was obtained. (c) Calculated from the NMR spectrum.

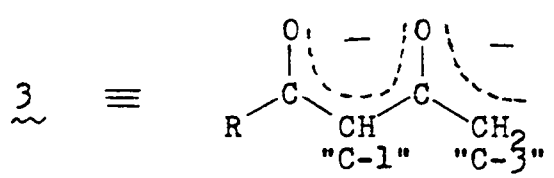
DISCUSSION

Traditionally β-diketone dianions have been the most extensively studied dianions. In β-diketone dianions it is found that the order of addition of an electrophile parallels the basicity, that is, the more basic site is the site of the first alkylation,[1,8] as shown below. Naturally, when the



1-phenyl-2-propanone dianion was first considered, it was assumed that the same pattern would be followed.

This is in fact not the case. This dissimilarity in mode of alkylation can best be explained by examining the electron distribution of the dianion of a β-diketone and a phenylpropanone. The β-diketone dianion 3 is more realistically depicted as a species in which the charge does not rest on a discrete atom at any instant, but is instead delocalized as shown in 18. As can be seen from 18, the charge in the



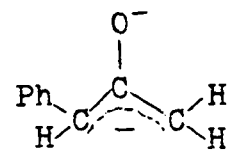
18

dianion is more localized on C-3 than on C-1, thus C-3 is the site of higher electron density and therefore the site of the addition of an electrophile.

The phenylpropanone dianion 12, on the other hand, shows a different pattern of delocalization.

$$PhCHCCH_2 \leftrightarrow PhCH{=}CCH_2 \leftrightarrow PhCHC{=}CH_2$$

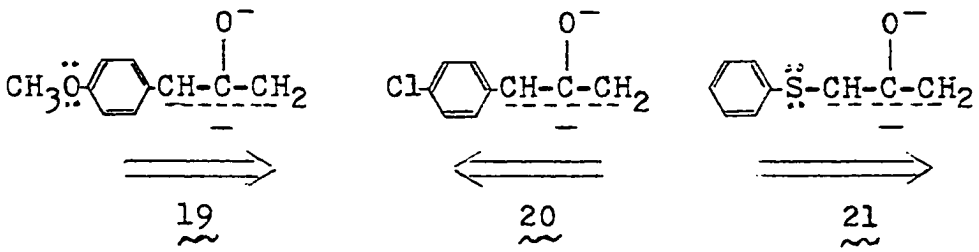
$$\equiv$$



12

The oxygen atom, the most electronegative atom in the molecule, effectively localizes one of the negative charges. Unlike the "doubly trapped" electron pairs in 18, the other pair of electrons in 12 is free to travel the length of the phenylpropanone molecule. This second electron pair will come to rest near the inductive phenyl group and thus C-1, rather than C-3, will be the site of highest electron density and thus the site of electrophilic addition.

Recent experiments in this laboratory[9] suggest that the presence of electron-donating and electron withdrawing groups on the phenyl substituent changes the ratio of C-1 to C-3 alkylation in the manner expected for species 12. The electron donating p-methoxy group in 19 would be predicted to shift the electron density away from C-1 toward C-3

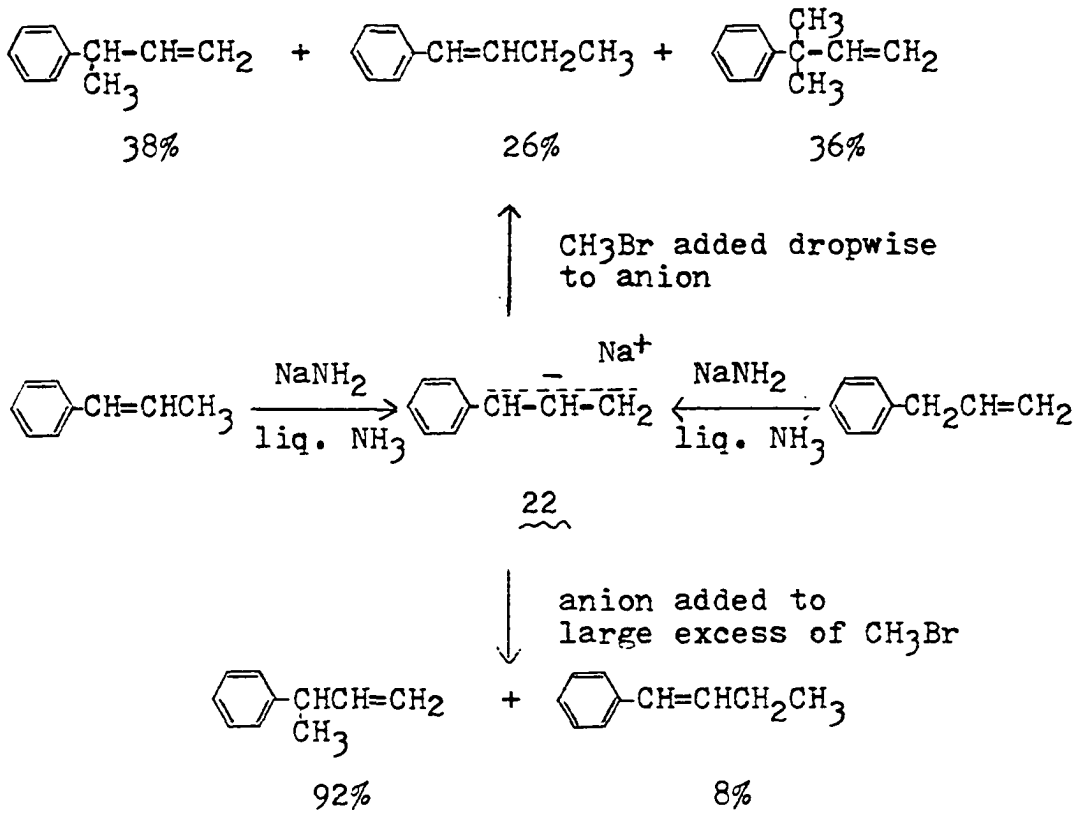


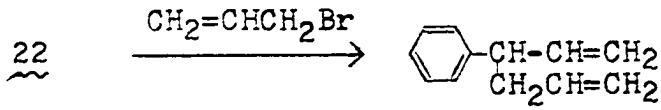
19 20 21

relative to phenylpropanone itself. This is borne out experimentally. The presence of a lone pair of electrons alpha to C-1 as in 21 has a similar effect.[10] A p-chloro-substituted phenyl group as in 20 would be even more inductively withdrawing than a simple phenyl group and would increase the incidence of C-1 alkylation of 20 relative to phenylpropanone itself.

In fact, the phenylpropanone dianion resembles an allyl benzene monoanion much more closely than a β-diketone dianion. The NMR spectrum of the allyl benzene monoanion[11] and the phenylpropanone dianion[7] are very similar. The manner of addition of alkyl halides to the phenylpropanone dianion is also very similar to that of the allyl benzene monoanion.

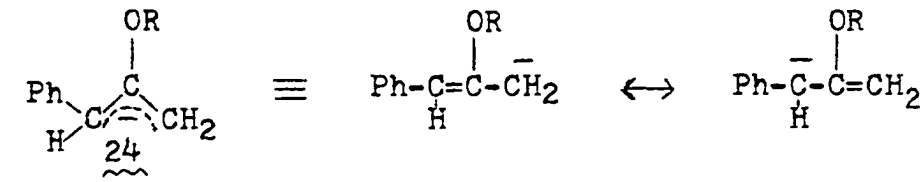
The addition of the monoanion 22 to an excess of methyl bromide gives the internally alkylated product in 92% yield, while addition of methyl bromide to the anion gives 38% of the internally mono-alkylated product and 26% of the externally mono-alkylated product.[12] Similarly, 22 was indicated to give 23 upon treatment with allyl

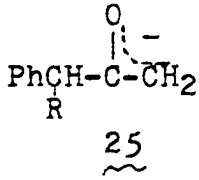




bromide. No other products are mentioned although the yield of 23 was about 50%.[13]

The possibility of initial alkylation at oxygen in 12 to give 24 exists (and some O-alkylation





does occur; see the Experimental section), but this does not change the pattern of electron distribution shown in 12. Vinyl ether anions (24) are known to be unstable and will rearrange to species such as 25. However, O-alkylation probably plays a minor role as further discussed later in this section.

It must be emphasized that simple relative basicity cannot be used as a criteria for predicting the site of alkylation of a dianion. Basicity is a kinetic phenomenon and as such is reversible. Alkylation is a thermodynamic phenomenon and is irreversible. Traditionally many authors have used the term basicity in the discussion of alkylations when in fact they mean electron density. This tendency is due to hundreds upon hundreds of β-diketone alkylations in the literature in which the first alkylation occurs at the more basic site, and although β-diketones are the most studied dianions, they are but one rather unique class of dianions. A more detailed discussion of the nucleophilicity of dianions toward electrophiles is in order.

It is apparent from Tables I and II that the simple basicities of the C-1 and C-3 anions does not account for their behavior toward alkyl halides.

The reactions do not follow the "last off, first on" order normally seen in carbon-hydrogen acid-base type reactions. We must conclude that, while acidity determines which of the protons is first removed and by what bases, it is the relative nucleophilicity of the C-1 and C-3 anions toward electrophiles which determines the alkylation products. We must, then, examine the factors which determine nucleophilicity.

Opinion is divided as to which factors are most relevant to nucleophilicity. Hendrickson, Cram, and Hammond state that, "Comparisons of nucleophiles having the same attacking atom does show that within such a restricted series increased basicity results in increased nucleophilic reactivity."[8] They also state that polarizability and solvation play an important role and that quantitative relationships among these three factors have not been devised.

Streitwieser[14] lists the solvation energy of the base, the strength of its bond with a carbon 2p orbital, its steric effect, electronegativity, and polarizability as the main factors determining nucleophilicity. Hudson[16] considers electrostatic attraction of the reactants as the most important factor in nucleophilicity. Edwards and Pearson[15] list basicity, polarizability, and the presence

of unshared electron pairs on neighboring atoms (the alpha effect) as the main factors affecting nucleophilicity. It is from Edward and Pearson's paper on factors determining nucleophilic reactivities that the following discussion is drawn.

Substitution reactions can be written as generalized acid-base reactions such as equation (1)

$$N + SX \longrightarrow NS + X \qquad (1)$$

where N is the nucleophile, S is the electrophilic substrate (S = H in acid-base reactions), and X is the leaving group. We must look at the relationship between the charge on S in the transition state and the basicity of N toward S.

> "A high positive charge on S in the transition state can lead to a strong interaction with the high negative potential of a basic reagent N. This will lower the energy of the activated complex and cause a high rate of reaction. Thus basicity will be an increasingly important factor in rate of substitution as the positive charge on the electrophilic atom in the substrate increases."[15]

From the above we would predict that CH_3CH_2+ would prefer the more basic anion in the dianion (the C-3 anion) as compared to $(CH_3)_2CH+$ due to high positive charge localized on the primary carbonium ion in CH_3CH_2+. In the isopropyl cation the methyl groups are electron donating so that less positive charge is localized on the secondary carbonium ion.

The 1,1-diphenyl-2-propanone case follows that of 1-phenyl-2-propanone but has a steric factor overlapping the relative nucleophilicity factor. Thus the additional phenyl group on C-1 will interfere with the approach of the C-1 anion to the electrophile and, by default, more C-3 alkylation will be observed compared to the 1-phenyl-2-propanone case. (The additional phenyl group would be expected to confer additional inductively-withdrawing characteristics upon the molecule and this may oppose the steric effects. However, even if the electron density at C-1 is increased, the electrophile may be prevented from approaching closely enough to form a bond by the two phenyl groups.)

Table I shows that for the 1-phenyl-2-propanone case ethyl iodide gave C-1 to C-3 alkylation in the ratio of 5 to 1. When more alkyl groups are added to the alkyl halide as in n-butyl iodide, the ratio of C-1 to C-3 alkylation increases to 9 to 1. The same trend is seen in the 1,1-diphenyl-2-propanone case. Table II shows that ethyl bromide alkylates the C-1 and C-3 positions in the ratio of 39 to 61. i-Propyl bromide, on the other hand, alkylates in the ratio of 64 to 36, C-1 to C-3, even though the increased steric hindrance of i-propyl bromide would favor C-3.

Thus the more concentrated the positive charge is on the electrophile, the more important basicity is in determining relative nucleophilicities. Indeed, the more the electrophile resembles a proton (high positive charge, no outer electrons), the more we should expect alkylation at the more basic site. This is most dramatically illustrated in the alkylations with methyl iodide. In the 1-phenyl-2-propanone case, methyl iodide gave a 55 to 45 mixture of C-1 to C-3 methylated products; in the 1,1-diphenyl-2-propanone case a 48 to 52 mixture of products was obtained. Again, the increased steric bulk of the diphenyl moiety shifts the ratio slightly in the direction of C-3 alkylation. Thus we see that the characteristics of the electrophile are very important in determining the contribution of basicity to the overall nucleophilicity of the nucleophile.

The second factor contributing to nucleophilicity which Edwards and Pearson discuss is polarizability. Two things can happen (simultaneously) in polarizable moieties which increase nucleophilicity. First, the bonding electrons are polarized toward the electrophile. Second, the non-bonding electrons will try to get as far away from the bonding electrons as possible, so they will be polarized away from the electrophile. The net

result is that the bonding electrons "reach out" to grab the electrophile while the non-bonding electrons step back out of the way and allow the electrophile to approach more closely than it otherwise would. That the orbitals must project well out from the reacting atoms is seen from the bonding distances in the transition state. The carbon-hydrogen bonding distance is about 1.0 Å whereas the bonding distance between the carbons of the nucleophile and the electrophile in the transition state is about 1.5 to 2.0 Å.[15]

Thus we would predict that in our phenylpropanone--alkyl halide reactions, a large transition state bond distance would favor the more polarizable site over the more basic site. The phenylpropanone dianion, with one charge localized on oxygen and the other charge free to travel the carbon backbone, has the highest electron density at C-1, as discussed earlier in this section. This high electron density at C-1 is then available for (or polarized toward) the electrophile. Tables I and II show that as the bulk of the alkyl halide increases (and consequently the transition state bond distance), the incidence of C-1 alkylation increases.

In β-diketone, β-ketosulfoxide, and β-ketophosphonate dianions polarizability would have a negligible contribution to nucleophilicity. The

negative charges are "trapped" and no pool of high electron density is available to reach out and bond with the electrophile. In allyl benzene monoanions one would expect a rather large contribution to nucleophilicity from polarizability due to the ability of the negative charge to travel the length of the molecule and "collect" at the alpha ("C-1") carbon.

The final factor affecting nucleophilicity is the presence of an unshared pair of electrons on the atom adjacent to the nucleophilic atom (the alpha effect). The importance of the alpha effect is rationalized by Edwards and Pearson as follows: One can imagine in the limiting case a nucleophile completely donating its pair of electrons to the electrophile. The nucleophile has, then, relative to its previous negative, electron-rich state, become more positive or carbonium ion-like. One might then expect factors which stabilize carbonium ions--such as an unshared pair of electrons on the alpha atom--to also stabilize the nucleophile in

$$\ddot{a}\text{-}b\text{-}c \longrightarrow \ddot{a}\text{-}b^{+} \longleftrightarrow \overset{+}{a}\text{=}b + c^{-}$$

the transition state.

In the phenylpropanone case the C-1 atom does not have an unshared pair of electrons alpha to it, but the relatively electron-rich phenyl group(s)

will help stabilize the nucleophile[15] as it donates its electrons.

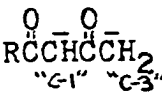
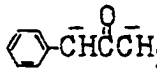
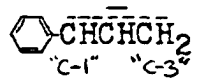
On the other hand, the presence of an unshared pair of electrons on the atom alpha to the nucleophilic atom will tend to discourage the buildup of negative charge on the nucleophilic atom due to repulsion. Whether the alpha effect helps or hinders is probably determined by other steric and electronic factors in the molecule. Indeed, one suspects that the alpha effect is greatly overshadowed by other effects. In the phenylpropanone and allyl benzene cases, the inductive withdrawing effect of the phenyl group(s), which increases the negative charge density on the C-1 carbon, would outweigh the alpha effect. In the case of the thiophenoxypropanone dianion 21 the free flowing negative charge would be repulsed by the lone pairs on sulfur and thus would tend to shift the electron density back towards C-3. (If one of the negative charges of the dianion were not localized on the oxygen atom, the other negative charge would not be so free to move around and a more "rigid" system would result.) The alpha effect would not be applicable to β-diketone, β-ketosulfoxide, or β-ketophosphonate dianions.

In summary (see Table III), we have discussed the contribution of basicity, polarizability, and the alpha effect to the nucleophilicity of the C-1

and C-3 anions of phenylpropanone. We have seen that in β-diketone dianions both the alpha effect and polarizability are negligible factors in bestowing

TABLE III

Contribution to Nucleophilicity

Nucleophile	Basicity	Polarizability	Alpha Effect
	C-1, C-3	-	-
	C-3	C-1	C-1
	-	C-1	C-1

nucleophilicity upon the anions. By default this leaves basicity as the most important factor. In the allyl benzene monoanion, we have rationalized that the alpha effect and polarizability are important factors and favor the C-1 position over the C-3 position. Basicity does not strictly apply in the sense that we are removing only one proton as opposed to dianion formation (and cannot say from which carbon it came since delocalization occurs immediately), so we cannot compare the relative basicities of the C-1 and C-3 carbons. Basicity will apply in the sense of re-protonation of the anion, in which case the C-3 position is favored.[18] When an alkyl

halide becomes the electrophile, the C-1 position becomes more favored the less the electrophile resembles a proton.

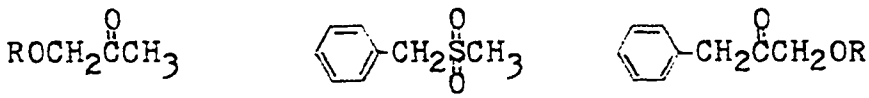
In the phenylpropanone case we see a composite of the β-diketone and allyl benzene cases. Polarizability and the alpha effect (if it is important at all) favor C-1 as the more nucleophilic carbanion, while basicity favors C-3. It is polarizability (along with the inductive effect of the phenyl group) which dominates using alkyl halides as the electrophile.

The influence of the group being attacked by the nucleophile is illustrated when the electrophile is changed from an alkyl group to a carbonyl, in which case basicity becomes the dominant factor. This is reflected in the reaction of the 1-phenyl-2-propanone dianion with p-anisaldehyde to give the C-3 condensation product. Reaction of the 1,1-diphenyl-2-propanone dianion with benzophenone gave only unreacted starting material. It might be expected that the steric bulk of both the 1,1-diphenyl-2-propanone dianion and benzophenone would disfavor the reaction. Free radical formation in benzophenone can also reasonably be suspected as a facile alternative reaction.

What we have operating, then, is a "power play" among the various factors affecting nucleophilicity.

We have seen that we can manipulate which factors are dominant by changing the character of the electrophile. The problem--and considerable challenge--confronting chemists is to make measurements of these factors such that numbers can be "plugged into" equations and numbers representing nucleophilicity will come out.

Many questions remain and several speculations can be made. What if the phenyl moiety of the phenylpropanone system is replaced with an ether moiety as in 26? Will the alpha effect at C-1 be large enough to offset the loss of the phenyl group



26 27 28

such that alkylation will still occur at C-1? (This problem has been addressed earlier in this paper. See page 13.) If the carbonyl is replaced with a sulfone as in 27, will polarizability become an important factor in the nucleophilicity of the C-3 anion due to the available d orbitals on the sulfur? What if the molecule is set up as in 28 such that the electrophile is confronted with a "stacked deck"? Here one would predict that the lone pairs on the oxygen would "push" the negative charge toward C-1, while the phenyl group would "pull" the electrons toward the C-1 position.

The net result would be a very large preference for C-1 alkylation.

Three factors remain to be discussed. These are the effects of solvent, the effects of the counter-ion, and C- versus O-alkylation.. Often these factors are interdependent.

As with any reaction in organic chemistry, the solvent plays an important role in determining the final outcome of the reaction (except in gas phase studies). Solvents are generally classified according to their polarity (as measured by their dielectric constant or ability to separate charges) and the availability of protons. Thus we have dipolar, protic solvents such as water and the alcohols; dipolar, aprotic solvents such as dimethylformamide and dimethyl sulfoxide; and non-polar, aprotic solvents such as tetrahydrofuran and hexane. THF was the solvent of choice in the phenylpropanone reactions because (1) it is compatible with the strong bases used in generating the dianion, (2) as a non-polar, aprotic solvent it favors the S_N2 reaction with alkyl halides, and (3) it is easily obtained in the anhydrous form.

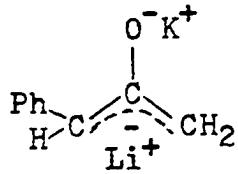
For reasons discussed in the Historical Background section, potassium hydride and n-butyllithium were chosen as the bases. The potassium cation is

a large species which tends to form contact ion pairs. The lithium cation, on the other hand,

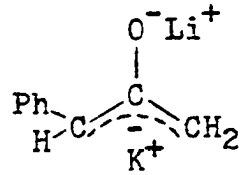
$$MX \rightleftharpoons \underset{\substack{\text{contact}\\\text{ion}\\\text{pair}}}{M^+X^-} \rightleftharpoons \underset{\substack{\text{solvent}\\\text{separated}\\\text{ion pair}}}{M^+\|X^-} \rightleftharpoons \underset{\substack{\text{free}\\\text{ion}}}{M^+ + X^-}$$

is small and tends to form solvent-separated ion pairs.[19]

The cation-anion species can be either of the species shown below, or a mixture of the two. From



29



30

the order of addition, we would expect 29 rather than 30 as the more logical species. Metathesis cannot, however, be ruled out.

The possibility of O-alkylation also exists in the ambident phenylpropanone dianion. The presence of some O-alkylation is indicated by the presence of a signal in the NMR spectrum of several of the crude reaction mixtures at about 3.8 ppm, typical of enol ethers. These O-alkylated products are minor products and are also known to be unstable. They can be isolated in some cases (see Experimental) under the relatively mild conditions of high pressure liquid chromatography, but would be expected to fall apart at the higher temperatures of distillation or GC.

Kornblum proposes that the incidence of O- and C-alkylation is determined by the amount of S_N1 and S_N2 character of the reaction.[17] When S_N1 character dominates, alkylation occurs predominantly on the atom with the highest electronegativity. When S_N2 character predominates, alkylation occurs on the atom with the lower electronegativity (and higher polarizability). Using this principle, we would predict C-alkylation using an S_N2 favoring solvent such as THF. We might also predict that if a more polar solvent such as DMF were used the incidence of O-alkylation would increase.

Hogen-Esch and Smid have shown that at -30° in THF fluorenyllithium exists entirely as the solvent-separated ion pair.[19] Fluorenylpotassium, however, exhibits little if any solvent separation of ions. From this and a variety of other pieces of experimental evidence they conclude that the solvent-separated ion pair is much more reactive than the contact ion pair. This comes about because as the cation and anion approach each other the solvation shell each one has must be removed. This will require an input of energy. Once the solvation shell is removed, however, strong electrostatic forces come into play and a great deal of energy is required to overcome these forces--

more than is needed to remove the solvation shell. (See Figure 1.) The smaller cations such as lithium

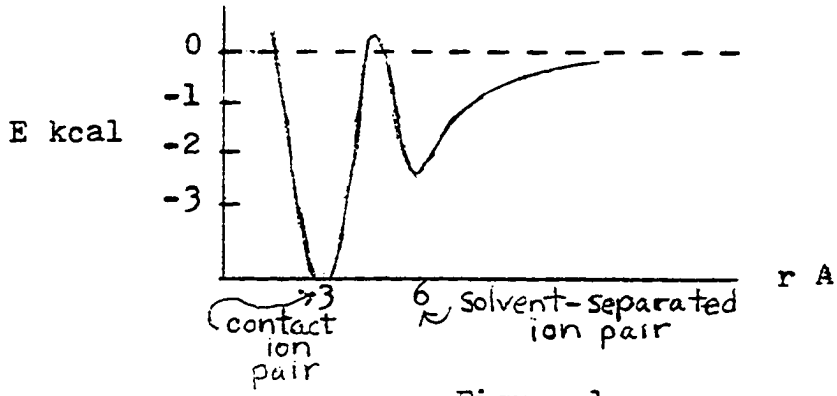


Figure 1.

are much more effectively (tightly) solvated than the larger cations such as potassiom and cesium due to the higher charge density on the compact lithium cation.

Neglecting for the moment the fact that we are comparing the ion pairs of two different anions (C^-M^+ and O^-M^+) and looking only at the effects of the cation and solvent, we would predict that if we do indeed have species 29, then we would expect the carbon-lithium solvent-separated ion pair to be more reactive toward alkylation than the oxygen-potassium contact ion pair.

The C- versus O-alkylation product ratios of the phenylpropanone dianions would be expected to shift as we moved to solvents which promoted solvent-separated ion pairs. More polar solvents or solvents capable of chelating the cations would increase the

proportion of solvent-separated ions as compared to a solvent which does not promote ion separation Thus a switch from THF to the more polar DMF or DMSO would increase the proportion of oxygen-potassium solvent-separated ion pairs and thus the amount of O-alkylation. A switch to dimethoxyethane or dioxane, solvents of comparable polarity, would be expected to increase the proportion of solvent-separated ion pairs due to their ability to solvate the cation via bidentate-type coordination.[19] The addition of crown ethers which could chelate cations according to size would also be expected to have a dramatic effect on C- versus O-alkylation ratios. As we move from KH to NaH as the first base we might also expect more O-alkylation due to the greater proportion of solvent-separated ion pairs on going to the smaller sodium cation.

In conclusion, we have seen that many factors may be responsible for the site of alkylation on the phenylpropanone dianion. The presence of functional groups such as a phenyl group beta to the carbonyl has a profound effect on the nucleophilicity of the dianion toward alkyl halides, making analogy with the β-diketone dianion reaction unwarranted. The electrophilic properties of the alkyl halide, in conjunction with the group beta

to the carbonyl, also influence the alkylation products.

EXPERIMENTAL

General

Materials

All glassware was dried by heating at 80-100° for several hours. Tetrahydrofuran (THF) from Burdick and Jackson Laboratories was distilled from sodium and benzophenone immediately prior to use. Potassium hydride (Alpha) was purchased as a 24.3% KH-mineral oil suspension. The mineral oil was removed prior to use by washing three times with Skelly Solve B or cyclohexane. n-Butyllithium (Foote) was used as a 1.6 M solution in hexane. 1,1-Diphenyl-2-propanone was purchased from Aldrich and was purified by chromatography to remove a small, highly fluorescent impurity. All reactions were run under an argon atmosphere.

Instruments

The compounds were isolated via high pressure liquid chromatography on Merck 60 silica gel using a 1" by 4' column. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. NMR's were taken on a Varian A-60D using tetramethylsilane as an internal standard.

The high resolution mass spectrum of 9 was taken on a CEC 21-110B mass spectrometer. Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer.

General procedure

A 250 ml three-necked, round bottomed flask and a magnetic stir bar were heated for several hours at 80-100° in a drying oven. About 10 ml of cyclohexane or Skelly Solve B was added to the flask, two of the openings were covered with rubber septa, and the flask and contents were tared. Potassium hydride in mineral oil was then added, the remaining opening was covered with a rubber septum, and the apparatus was then connected to an argon source.

The cyclohexane or Skelly Solve B was removed with a syringe having a flat-tipped needle. More cyclohexane or Skelly Solve B was added, the mixture was stirred briefly and then allowed to settle for several minutes, and the cyclohexane or Skelly Solve B was again removed with the syringe. This washing procedure was repeated a third time and then freshly distilled, dry THF was added to the remaining KH. The apparatus was then connected to a mineral oil bubbler.

1,1-Diphenyl-2-propanone was dissolved in a minimum amount of freshly distilled, dry THF in a dry round bottomed flask. The argon source was removed and the 1,1-diphenyl-2-propanone solution was added dropwise from a syringe to the KH suspension. When hydrogen evolution ceased the bubbler was removed and the argon source was reattached. The yellow-orange monoanion solution was stirred for 30 minutes and then cooled in a Dry Ice-acetone bath. n-Butyllithium in hexane was added dropwise from a syringe to the monoanion solution. After the addition of n-butyllithium was complete, the Dry Ice-acetone bath was removed and the deep rose red reaction mixture was stirred for an additional thirty minutes. In every instance a precipitate formed five to ten minutes after the Dry Ice-acetone bath was removed and the reaction mixture became a quite easily stirred slurry.

For very reactive or low boiling alkyl halides the reaction mixture was cooled again in an ice bath and the alkyl halide was then added rapidly from a syringe to the dianion. In the more reactive cases the loss of the red dianion color was almost immediate. The red (or slightly pink-yellow) color was still visible twenty-four hours later for the more unreactive alkyl halides.

When the twenty-four hour reaction period was over the reaction mixture was cooled in an ice bath and water was carefully added. The mixture was transferred to a separatory funnel and, after shaking, the aqueous layer was transferred to a second separatory funnel, where it was extracted twice with methylene chloride. The THF and methylene chloride layers were combined, filtered through anhydrous sodium sulfate, and taken to dryness on a rotary evaporator. At this point a small aliquot was removed for NMR analysis.

Separation of products was accomplished via high pressure liquid chromatography on Merck 60 silica gel using either methylene chloride or methylene chloride: Skelly Solve B as eluent. A 1" x 10" scrubber column followed by a 1" x 4' column was used and fractions were collected in 10, 20, or 50 ml aliquots. The compounds have very poor uv absorption and turn color very slowly with potassium permanganate spray. The separations were best monitored by TLC elution with a 40:60 methylene chloride: Skelly Solve B solvent system, followed by spraying with a 5% phosphomolybdic acid: 95% ethanol solution and warming on a hot plate to effect visualization of the plate. A vanillin-H_3PO_4 spray also works

nicely (the C-1 and C-3 alkylated products have different colors with the spray) but the spray tends to decompose rather rapidly.

The products were identified by their distinctive NMR spectra and by semicarbazone or 2,4-dinitrophenylhydrazone derivatives, which were made by textbook procedures.[25] The C-3 alkylated products were usually slightly yellow in color, usually very foul smelling, and tended to decompose upon standing for several days or weeks. The C-1 alkylated products were clear, stable, and very viscous--even crystalline in the isopropyl case.

Reactions

1,1-Diphenyl-2-hexanone (1) and 3,3-Diphenyl-2-hexanone (2)

To 4.95 g (0.03 moles) of 24.3% KH in 25 ml of dry THF was added dropwise 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of dry THF. After 35 minutes, the orange-yellow reaction mixture was cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added dropwise. The Dry Ice-acetone bath was then removed and the deep red mixture was stirred for an additional 35 minutes (a precipitate formed after several minutes), after which 2.64 ml (0.03

moles) of n-propyl chloride was then added and the reaction mixture was stirred for 44 hours at room temperature. The flask was then cooled in an ice-water bath and water was slowly added. The organic layer was removed and washed with water. The aqueous layers were combined and washed twice with methylene chloride. The organic layers were filtered through sodium sulfate and taken to dryness. The residue was chromatographed twice via high pressure liquid chromatography (hplc) using methylene chloride as eluent, to afford 2.26 g of 1,1-diphenyl-2-hexanone (1) and 2.11 g of 3,3-diphenyl-2-hexanone (2).

1 NMR ($CDCl_3$): δ 0.85, 3 H, multiplet; δ 1.41, 4 H, multiplet; δ 2.55, 2 H, triplet; δ 5.14, 1 H, singlet; δ 7.28, 10 H, singlet. 2,4-DNP: m.p. 158-159° (lit.[20] 159°).

2 NMR ($CDCl_3$): δ 0.90, 5 H, multiplet; δ 2.02, 3 H, singlet; δ 2.29, 2 H, triplet; δ 7.30, 10 H, singlet. 2,4-DNP: m.p. 170.5-171.5° (lit.[21] 174-175°).

1,1-Diphenyl-2-pentanone (3) and 3,3-Diphenyl-2-pentanone (4)

To 4.95 g (0.03 moles) of 24.3% KH in 25 ml of dry THF was added dropwise 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone. The yellow-orange mixture was stirred for 25 minutes. After cooling

in a Dry Ice-acetone bath, 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added and a deep red solution was obtained. The Dry Ice-acetone bath was removed and the mixture was stirred for an additional 20 minutes. The dropwise addition of 2.24 ml (0.03 moles) of bromoethane led to rapid disappearance of the red color. After stirring for an additional 3 hours at room temperature, the flask was cooled in an ice-water bath and water was carefully added.

The organic layer was separated and washed once with water. The water layers were combined and washed twice with methylene chloride. The organic layers were then combined, filtered through sodium sulfate, and taken to dryness in vacuo.

The residue was chromatographed twice via hplc using methylene chloride as the eluent to give 2.53 g of 1,1-diphenyl-2-pentanone (3) and 1.63 g of 3,3-diphenyl-2-pentanone (4).

3 NMR ($CDCl_3$): δ 0.86, 3 H, triplet; δ 1.61, 2 H, sextuplet; δ 5.12, 1 H, singlet; δ 7.27, 10 H, singlet. Semicarbazone: m.p. 190-191° (lit.[20] 191-192°).

4 NMR ($CDCl_3$): δ 0.69, 3 H, triplet; δ 2.02, 3 H, singlet; δ 2.38, 2 H, quadruplet; δ 7.31, 10 H, singlet. Semicarbazone: m.p. 197-199° (lit.[21] 199-200°).

1,1-Diphenyl-4-methyl-2-pentanone (5) and 3,3-Diphenyl-4-methyl-2-pentanone (6)

To 4.95 g (0.03 moles) of 24.3% KH in 30 ml of dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of THF. The yellow-orange mixture was stirred at room temperature for 30 minutes. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red solution was stirred for 30 minutes (a precipitate formed after several minutes), after which the flask was placed in an ice-water bath and 2.74 ml (0.03 moles) of isopropyl chloride was added. After about 24 hours the flask was cooled again in an ice bath and water was carefully added to the still red-brown reaction mixture.

The organic layer was separated and washed once with water. The aqueous layers were combined and extracted twice with methylene chloride. The organic phases were then combined, filtered through sodium sulfate, and taken to dryness in vacuo.

The resulting residue was chromatographed twice via hplc on silica gel with methylene chloride as eluent to give 0.57 g of 1,1-diphenyl-4-methyl-2-pentanone (5) and 2.45 g of 3,3-diphenyl-4-methyl-2-pentanone (6).

5 NMR ($CDCl_3$): δ 0.87, 6 H, doublet, J = 6.5 Hz; δ2.12, 1 H, broad multiplet; δ2.38, 2 H, multiplet; δ5.10, 1 H, singlet; δ7.28, 10 H, singlet. Ir (Nujol mull): C=O, 1710 cm^{-1}. Lit.[22] NMR: δ 0.86, 6 H, doublet, J = 5.10 Hz; δ2.37, 2 H, doublet; δ 5.08, 1 H, singlet; δ7.26, 10 H, singlet. Ir (KBr): C=O, 1708 cm^{-1}.

6 NMR ($CDCl_3$): δ0.74, 6 H, doublet, J = 6.8 Hz; δ1.97, 3 H, singlet (sharp); δ3.31, 1 H, quintuplet; δ7.31, 10 H, singlet. Ir (Nujol mull): C=O, 1700 cm^{-1}. M.p. 92.5-94.0° from methylene chloride: cyclohexane.

1,1-Diphenyl-4-methyl-2-pentanone (7) and 3,3-Diphenyl-4-methyl-2-pentanone (8)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of dry THF. The yellow-orange mixture was stirred at room temperature for 40 minutes. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red mixture was stirred for 30 minutes (a precipitate formed after 5-10 minutes), after which the flask was placed in an ice-water bath and 2.82 ml (0.03 moles) of isopropyl bromide was added. After 24 hours the

flask was cooled again in an ice bath and water was carefully added to the yellow-pink mixture.

The organic layer was separated and washed once with water. The aqueous layers were combined and extracted twice with methylene chloride. The organic layers were combined, filtered through sodium sulfate, and taken to dryness in vacuo. The residue was chromatographed via hplc on a silica gel column using methylene chloride as eluent to give 0.98 g of 1,1-diphenyl-4-methyl-2-pentanone (7) and 1.75 g of 3,3-diphenyl-4-methyl-2-pentanone (8).

7 NMR ($CDCl_3$): δ 0.87, 6 H, doublet, J = 6.5 Hz; δ2.12, 1 H, multiplet; δ2.38, 2 H, multiplet; δ5.10, 1 H, singlet; δ7.26, 10 H, singlet. Ir (neat): C=O, 1710 cm^{-1}. Lit.[22] NMR ($CDCl_3$): δ 0.86, 6 H, doublet, J = 5.5 Hz; δ2.37, 2 H, doublet; δ7.26, 10 H, singlet. Ir (KBr): C=O, 1708 cm^{-1}.

8 NMR ($CDCl_3$): δ 0.74, 6 H, doublet, J = 6.8 Hz; δ1.97, 3 H, singlet; δ3.31, 1 H, quintuplet; δ7.31, 10 H, singlet. Ir (Nujol mull): C=O, 1700 cm^{-1}. M.p. 92.5-94.0° from EtOH: water. Calculated for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.54; H, 8.14.

1,1-Diphenyl-2-pentanone (9), 3,3-Diphenyl-2-pentanone (10), and 3,3-Diphenyl-4-heptanone (11)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of dry THF. The yellow-orange mixture was stirred at room temperature for 40 minutes. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red mixture was stirred for 40 minutes (a precipitate formed after 5-10 minutes), after which the flask was cooled in an ice-water bath and 2.40 ml (0.03 moles) of ethyl iodide was added. After 18 hours the flask was cooled again in an ice-water bath and water was carefully added.

The organic layer was separated and washed once with water. The aqueous phases were combined and extracted twice with methylene chloride. The organic phases were combined, filtered through sodium sulfate, and taken to dryness in vacuo.

The residue was chromatographed twice via hplc on a silica gel column using methylene chloride as eluent to give 0.92 g of 3,3-diphenyl-4-heptanone (9), 2.46 g of 1,1-diphenyl-2-pentanone (10), and 0.25 g of 3,3-diphenyl-2-pentanone (11).

9 NMR ($CDCl_3$): δ 0.68, 6 H, broad triplet; δ 1.28, 2 H, multiplet; δ 2.35, 4 H, multiplet; δ 7.28, 10 H, singlet. High resolution mass spectrum: Calculated for $C_{19}H_{22}O$, m^+/e 266.1671. Found, m^+/e 266.1651. Semicarbazone: m.p. 82° from ethanol: water.

10 NMR ($CDCl_3$): δ 0.86, 3 H, triplet; δ 1.61, 2 H, quintuplet; δ 2.52, 2 H, triplet; δ 5.12, 1 H, singlet; δ 7.25, 10 H, singlet. This spectrum is superimposable with that of 3.

11 NMR ($CDCl_3$): δ 0.69, 3 H, triplet; δ 2.00, 3 H, sharp singlet; δ 2.36, 2 H, quadruplet; δ 7.28, 10 H, singlet. This NMR spectrum is superimposable with that of 4.

1,1-Diphenyl-2-butanone (12) and 3,3-Diphenyl-2-butanone (13)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of dry THF. The yellow-orange solution was stirred for 30 minutes at room temperature. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red mixture was stirred for 50 minutes (after 5-10 minutes a precipitate formed), after which the flask was cooled in an ice-water bath

and 1.25 ml (0.02 moles) of methyl iodide was added. After 24 hours water was carefully added and the organic layer was separated and washed once with water. The aqueous layers were combined and extracted twice with methylene chloride. The organic layers were combined, filtered through sodium sulfate, and taken to dryness in vacuo.

The residue was chromatographed twice via hplc on a silica gel column using methylene chloride as eluent to give 1.61 g of 1,1-diphenyl-2-butanone (12) and 1.82 g of 3,3-diphenyl-2-butanone (13).

12 NMR ($CDCl_3$): δ 1.05, 3 H, triplet; δ 2.56, 2 H, quadruplet; δ 5.12, 1 H, singlet; δ 7.27, 10 H, singlet. Semicarbazone: m.p. 193-194° from ethanol: water (lit.[23] 194-195°).

13 NMR ($CDCl_3$): δ 1.87, 3 H, sharp singlet; δ 2.10, 3 H, sharp singlet; δ 7.27, 10 H, singlet. Semicarbazone: m.p. 180-182° from ethanol: water (lit.[24] 182°).

2,2-Diphenyl-3-pentanone and 2,2-Diphenyl-4-methyl-3-pentanone (14)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of dry THF. The yellow-orange solution was stirred for 20 minutes at room tempera-

ture. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M of n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red mixture was stirred for 50 minutes (after about 10 minutes a precipitate formed), after which the flask was cooled in an ice-water bath and 3.74 ml (0.06 moles) of methyl iodide was added. After 24 hours water was carefully added and the organic layer was separated and washed once with water. The aqueous phases were combined and extracted twice with methylene chloride, filtered through sodium sulfate, and taken to dryness in vacuo.

Hplc twice on silica gel with 70:30 methylene chloride: Skelly Solve B gave a single fraction which mass spec and NMR showed to be a mixture (3.87 g) of 1,1-diphenyl-3-pentanone and 2,2-diphenyl-4-methyl-3-pentanone. The mass spectrum showed two peaks, m^+/e 238 and 252, in a ratio of approximately 5 to 1.

1,1-Diphenyl-2-pentanone (15) and 3,3-Diphenyl-2-pentanone (16)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in dry THF. The yellow-orange solution was stirred at room temperature for 25 minutes. The flask was then cooled in a Dry Ice-acetone

bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red mixture was stirred for 20 minutes (after about 5-10 minutes a precipitate formed), after which the flask was placed in an ice-water bath and 1.60 ml (0.02 moles) of ethyl iodide was added. After 24 hours water was carefully added and the organic layer was washed twice with methylene chloride. The organic layers were combined, filtered through sodium sulfate, and taken to dryness in vacuo.

The residue was chromatographed via hplc on a silica gel column using methylene chloride as eluent to give 1.88 g of a mixture of 1,1-diphenyl-2-propanone and 3,3-diphenyl-2-pentanone in a ratio (NMR) of 2.4 to 1.

3,3-Diphenyl-4-heptanone (17) and 1,1-Diphenyl-2-pentanone (18)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in dry THF. The yellow-orange mixture was stirred at room temperature for 20 minutes, after which it was cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red mixture was stirred for 20 minutes (after 5-10 minutes a precipitate formed).

The flask was then cooled in an ice bath and 4.80 ml (0.06 moles) of ethyl iodide was added. After stirring for 24 hours water was carefully added and the organic layer was separated and washed once with water. The aqueous layers were combined and washed twice with methylene chloride. The organic layers were combined, filtered through sodium sulfate, and taken to dryness *in vacuo*.

The residue was chromatographed via hplc on a silica gel column using methylene chloride as eluent to give 5.20 g of a mixture of 3,3-diphenyl-4-heptanone and 1,1-diphenyl-2-pentanone in a ratio (NMR) of 1 to 1.75.

1,1-Diphenyl-4-methyl-2-pentanone (19) and 3,3-Diphenyl-4-methyl-2-pentanone (20)

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in 20 ml of dry THF. The yellow-orange solution was stirred at room temperature for 20 minutes. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 *M* *n*-butyllithium in hexane was added. The Dry Ice-acetone bath was removed and the deep red solution was stirred for 20 minutes (after 5-10 minutes a precipitate formed), after which the flask was placed in an ice-water bath and 2.74 ml (0.03 moles)

of isopropyl chloride was added.

After 24 hours the flask was cooled in an ice-water bath and water was added. The red-orange color of the reaction mixture was immediately dissipated. The organic layer was removed and washed once with water. The aqueous layers were combined and extracted twice with methylene chloride. The organic layers were combined, filtered through sodium sulfate, and taken to dryness *in vacuo*.

The residue was chromatographed via hplc on silica gel with methylene chloride as eluent. The mixed fractions were rechromatographed using 50:50 methylene chloride: Skelly Solve B to give 0.40 g of 1,1-diphenyl-4-methyl-2-pentanone (19) and 1.90 g of 3,3-diphenyl-4-methyl-2-pentanone (20). Note that the product ratio is the same as that of 5 and 6.

19 NMR ($CDCl_3$): δ 0.87, 6 H, doublet; δ 2.12, 1 H, broad multiplet; δ 2.38, 2 H, multiplet; δ 5.11, 1 H, singlet; δ 7.28, 10 H, singlet.

20 NMR ($CDCl_3$): δ 0.72, 6 H, doublet; δ 1.95, 3 H sharp singlet; δ 3.30, 1 H, quintuplet; δ 7.30, 10 H, singlet.

Addition of Benzophenone to the 1,1-Diphenyl-2-propanone Dianion

To 4.95 g (0.03 moles) of 24.3% KH in dry THF was added 4.21 g (0.02 moles) of 1,1-diphenyl-2-propanone in dry THF. The yellow-orange solution was stirred at room temperature for 45 minutes. The flask was then cooled in a Dry Ice-acetone bath and 18.7 ml (0.03 moles) of 1.6 M n-butyllithium in hexane was added. The Dry Ice-acetone bath was then removed and the deep red mixture was stirred for 45 minutes, after which 5.47 g (0.03 moles) of benzophenone was added. The deep red color changed to dark brown and then to dark green as soon as the benzophenone addition was completed (within about 30 seconds).

The reaction mixture was stirred for 16 hours, after which it was cooled in an ice-water bath and water was carefully added. The organic layer was removed and washed once with water. The organic layers were combined and extracted twice with methylene chloride. The organic layers were combined, filtered through sodium sulfate, and taken to dryness *in vacuo*.

TLC of the crude reaction mixture exhibited two spots with the same R_f's as the starting materials. NMR ($CDCl_3$) of the mixture: δ 2.20, sharp singlet;

δ5.11, singlet; δ7.28, singlet; δ7.1-7.9, complex multiplet.

3,3-Diphenyl-2-heptanone (21)

To 1.65 g (9.2 mmoles) of 24.3% KH in 20 ml of dry THF was added 1.94 g (9.2 mmoles) of 1,1-diphenyl-2-propanone in dry THF. After stirring for 20 minutes, 1.37 g (10 mmoles) of n-butylbromide was added. The reaction mixture was stirred for 17 hours, after which water and methylene chloride were added, the mixture shaken in a separatory funnel, and the organic layer filtered through sodium sulfate.

The mixture was chromatographed via hplc using methylene chloride as the eluent to give 1.18 g of 3,3-diphenyl-2-heptanone (21), 0.34 g of recovered starting material, and a small amount of the O-alkylated product.

21 NMR ($CDCl_3$): δ0.6-1.4, 7 H, broad multiplet; δ2.0, 3 H, sharp singlet; δ2.15-2.45, 2 H, multiplet; δ7.32, 10 H, singlet.

Benzyl Methyl Sulfoxide and Benzyl Methyl Sulfone

To 7.57 g (0.0548 moles) of benzyl methyl sulfide in about 150 ml of methylene chloride was added dropwise 11.12 g (0.0548 moles) of 85% m-chloroperoxybenzoic

acid in a minimum amount of methylene chloride. An exotherm resulted (cooling would be in order here in future runs).

The reaction mixture was stirred for about 2 hours or until TLC shows no unreacted starting material remaining. After extraction with saturated aqueous sodium bicarbonate solution, the organic layer was filtered through sodium sulfate, taken to dryness, and chromatographed via hplc on silica gel using 5% methanol: 95% methylene chloride as eluent to give 7.50 g (89%) of benzyl methyl sulfoxide and 0.47 g of benzyl methyl sulfone. Benzyl methyl sulfone can be made to be the exclusive product if two equivalents of m-chloroperoxybenzoic acid are used.

Benzyl methyl sulfoxide NMR ($CDCl_3$): δ 2.42, sharp singlet; δ 3.97, singlet; δ 7.33, singlet.

Benzyl methyl sulfone NMR ($CDCl_3$): δ 2.04, 3 H, sharp singlet; δ5.10, 2 H, sharp singlet; δ 7.35, 5 H, singlet.

Attempt to Alkylate the Benzyl Methyl Sulfoxide Dianion

To 8.03 g (0.0486 moles) of 24.3% KH in 40 ml of dry THF was added 5.00 g (0.0324 moles) of benzyl methyl sulfoxide in dyr THF. The orange-brown reaction mixture was stirred for 30 minutes, after which it was

cooled in a Dry Ice-acetone bath and 30.4 ml (0.0486 moles) of 1.6 M n-butyllithium in hexane was added.

The Dry Ice-acetone bath was removed and the mixture was stirred for 30 minutes, after which 5.22 g (0.0486 moles) of n-butyl bromide was added. (After about 1 ml of n-butyl bromide was added an exotherm began, so the Dry Ice-acetone bath was added during the addition of the remaining n-butyl bromide.)

After stirring for 3 hours at room temperature, the reaction mixture was cooled in an ice bath and water was carefully added. The organic layer was removed and washed once with water. The aqueous phases were combined and washed twice with methylene chloride. The organic phases were then combined, filtered through sodium sulfate, and taken to dryness in vacuo.

TLC of the reaction mixture showed a plethora of spots (but no starting material) and the reaction was not further pursued.

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