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## The Effects of Electron-Donating and Electron-Withdrawing Groups on the Alkylation Sites of Para-Substituted Phenylacetones

Abraham L. Faburada

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THE EFFECTS OF ELECTRON-DONATING AND  
ELECTRON-WITHDRAWING GROUPS ON THE ALKYLATION  
SITES OF PARA-SUBSTITUTED PHENYLACETONES

by

Abraham L. Faburada

A Thesis  
Submitted to the  
Faculty of The Graduate College  
in partial fulfillment  
of the  
Degree of Master of Arts

Western Michigan University  
Kalamazoo, Michigan  
August 1978

THE EFFECTS OF ELECTRON-DONATING AND  
ELECTRON-WITHDRAWING GROUPS ON THE ALKYLATION  
SITES OF PARA-SUBSTITUTED PHENYLACETONES

Abraham L. Faburada, M. A.

Western Michigan University, 1978

The dianions of phenylacetone and its para-substituted derivatives were generated using potassium hydride and n-butyl lithium in tetrahydrofuran. Methyl, ethyl, and n-butyl iodides were used to alkylate the dianions. The results of alkylation indicate that C<sub>1</sub> is preferentially attacked by the less active ethyl and n-butyl iodides. The results further show that terminal alkylation is enhanced by electron-donating groups at the para-position of the phenyl ring. The results are rationalized in terms of the difference in electron density at C<sub>1</sub> and at C<sub>3</sub> in the dianion, on the basis of resonance theory. The regioselectivity of alkylation as a function of the alkylating agent's activity, and the factors which appear to dictate the fate of alkylation between carbon and oxygen in the ambident dianion are discussed.

## ACKNOWLEDGEMENTS

To Dr. George B. Trimitsis, my research adviser, for providing me the much needed help, guidance, understanding, and encouragement during the course of this project; to the members of my research committee, Dr. Donald C. Berndt and Dr. Jochanan Stenesh, for their kind attention in the evaluation on the amount of work done and in reviewing the written material; to the Chemistry Department for the teaching assistantships it provided me through; and to the people who, in one way or another, have extended a hand or two in the completion of this project; I wish to express my profound thanks of gratitude and appreciation.

Abraham L. Faburada

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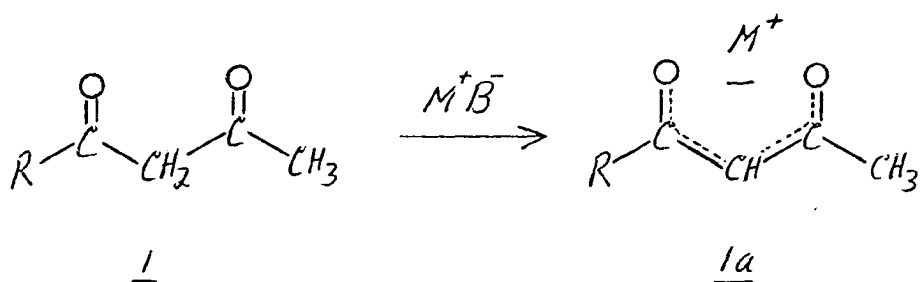
## I. INTRODUCTION

Past work involving the dianions of  $\beta$ -diketo and similar compounds, including phenylacetone, has established the fact that alkylation of such intermediates with various alkylating agents occurs at the carbon atom which, for many years, has always been thought of as being the most basic site in the dianion (terminal position of compounds having an  $\alpha$ -methyl group).

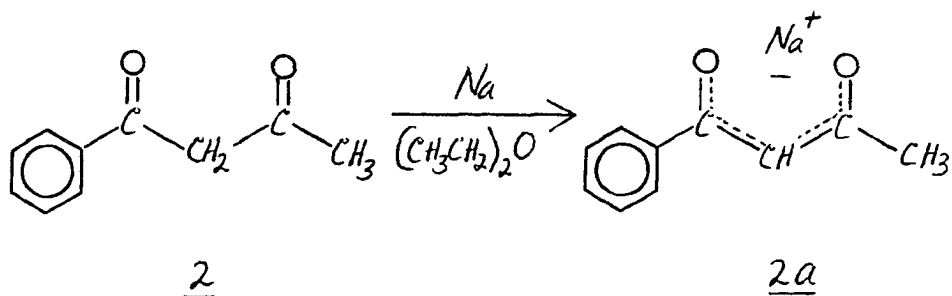
In a more recent study of the dianion of phenylacetone however, the results of alkylation with a number of alkyl halides indicate that the  $C_1$  position is preferentially attacked by electrophiles. As an extension of this work, we wish to report the results of our examination on the effects of electron-donating and electron-withdrawing groups on the alkylation sites of para-substituted phenylacetones.

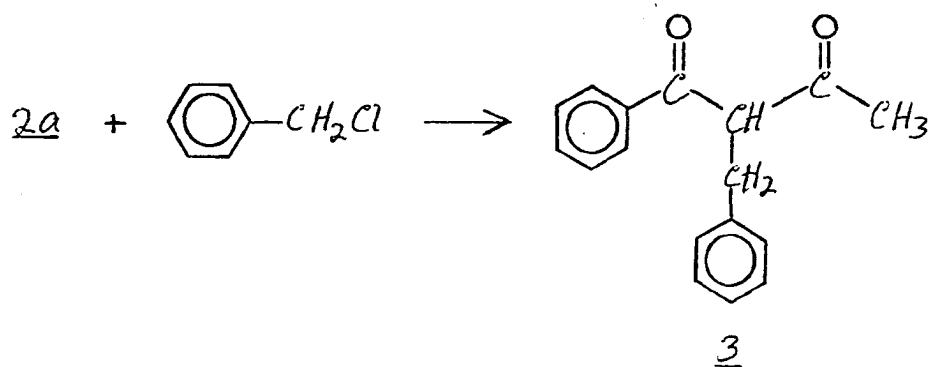
## II. HISTORICAL

It is well known that a compound like 1, when treated with a strong base, can be converted to a monoanion, 1a, in which the negative charge is delocalized throughout the carbonyl groups. Since oxygen has a higher electronegativity than carbon<sup>1</sup>, much of the charge therefore, is

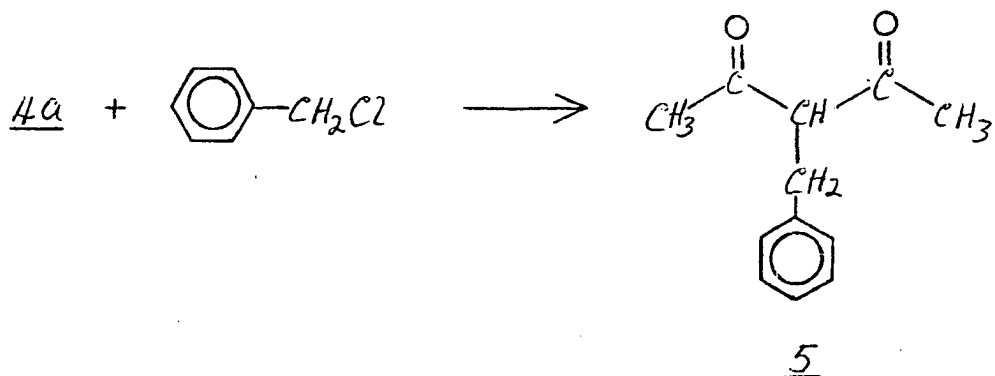
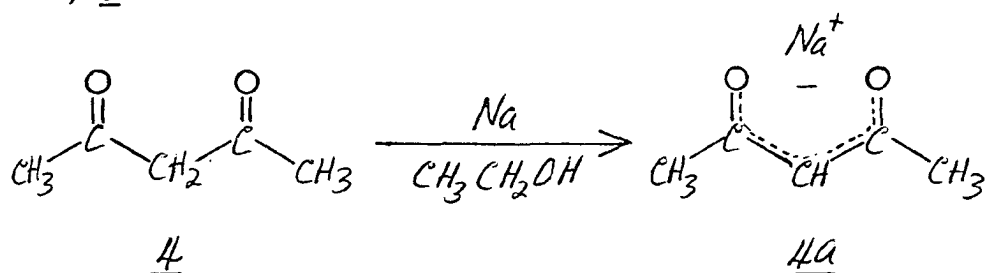


expected to reside on the atoms of the former, thereby making these oxygen ends also potential sites of alkylation. However, early studies by E. R. Trotman involving the enolate, 2a, of benzoylacetone, 2, generated by treatment of the latter with sodium metal in ether, showed that alkylation of the anion with benzyl chloride occurred exclusively at the methylene position<sup>3</sup>.



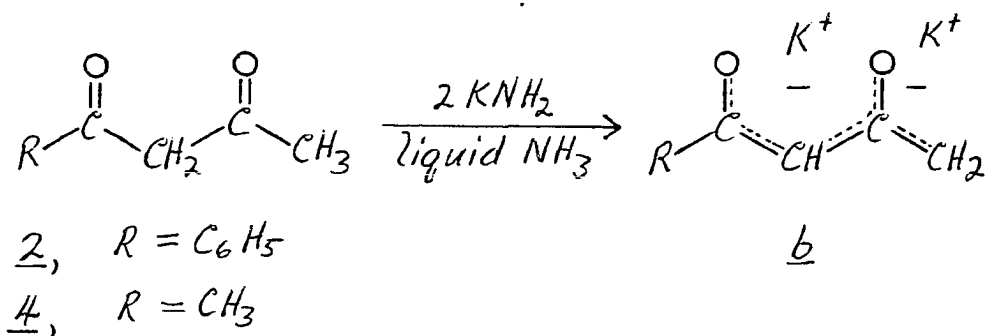


In a similar experiment, G. T. Morgan and C. J. A Taylor alkylated the monoanion, 4a, of acetylacetone, 4, with benzyl chloride and obtained the C-alkylation product, 5<sup>4</sup>.

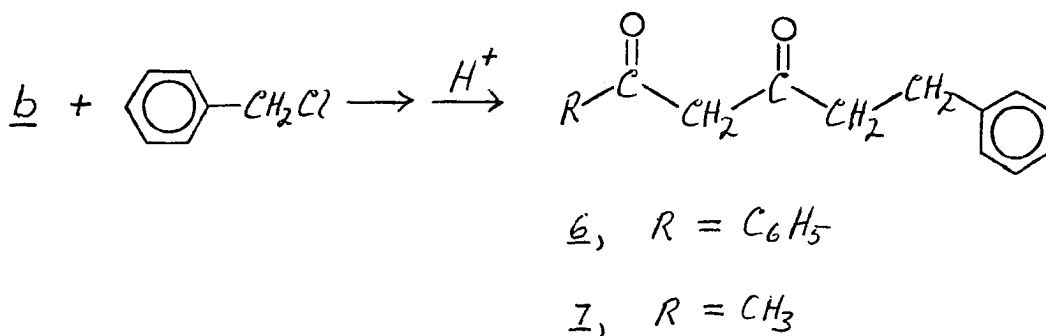


Using stronger bases, such as alkali metal amides, it has been possible to generate a second negative charge on the existing monoanion<sup>5, 6</sup>. For example, C. R. Hauser

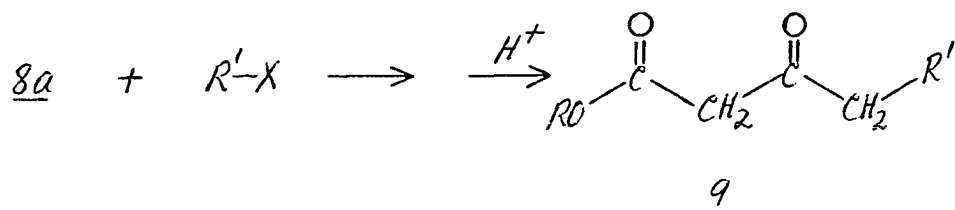
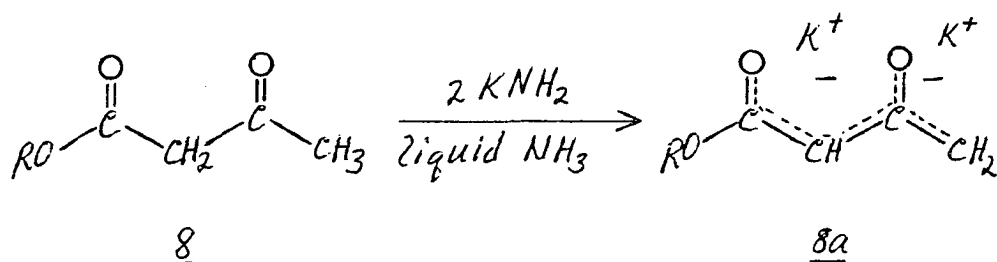
and T. M. Harris have reported that dianions of benzoyl- and acetylacetones were formed when two equivalents of potassium amide in liquid ammonia were used. In theory, these intermediate dianions should have their most basic



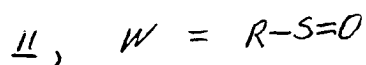
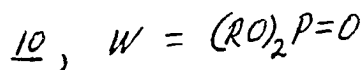
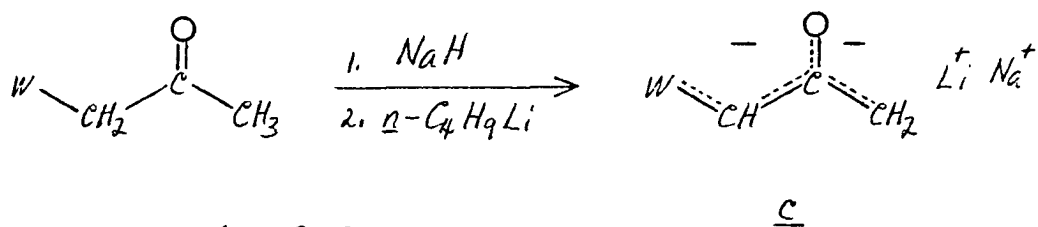
site at the terminal carbon of b, since that atom has only one adjacent electron-withdrawing carbonyl group. This carbon atom is therefore, expected to show greater reactivity towards electrophiles. This has been observed to be the case since the alkylation of these dianions with benzyl chloride resulted in an exclusive condensation at the terminal site.

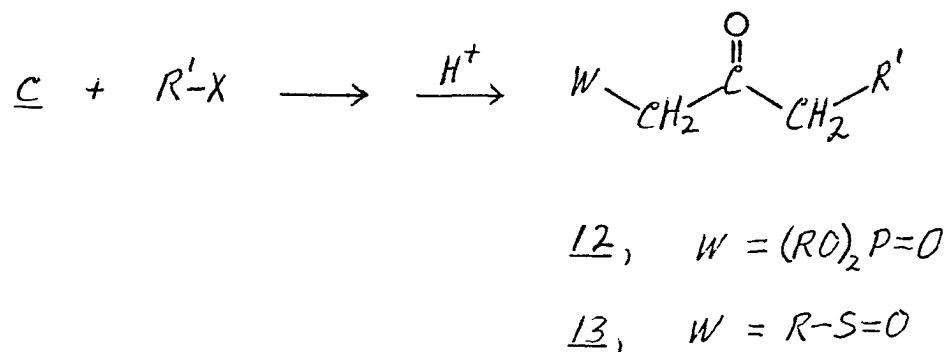


Dianions of some  $\beta$ -keto esters, 8, have also been generated in a similar manner and found to undergo alkylation with various alkyl halides only at the terminal

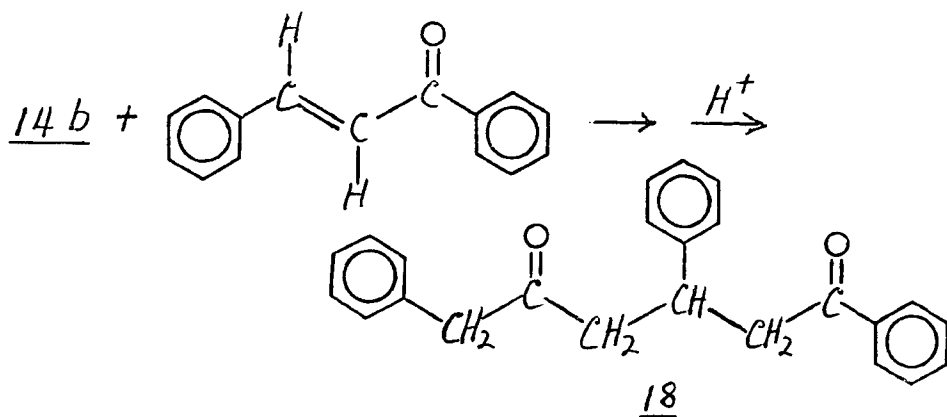
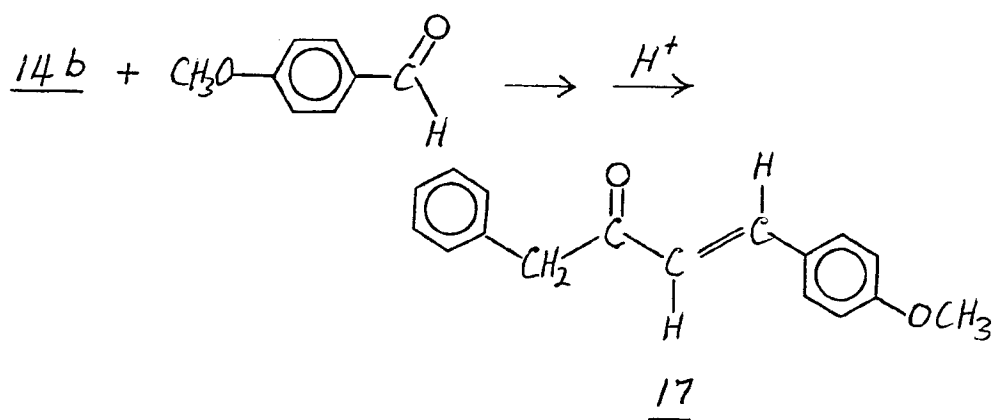
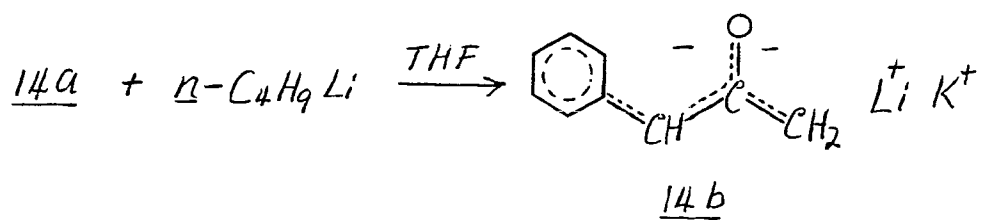
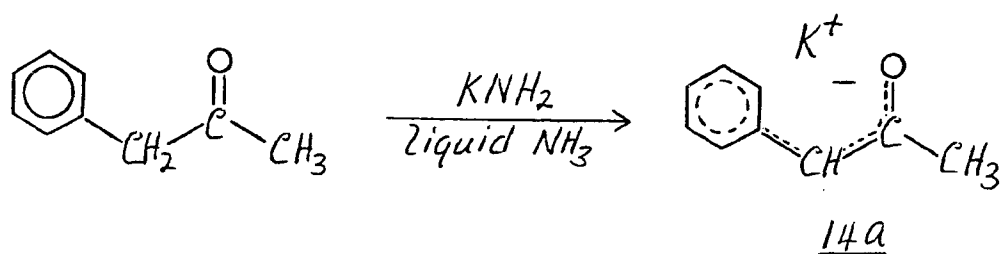
carbon<sup>6, 7</sup>.

Compounds of  $\beta$ -keto phosphonates, 10, and  $\beta$ -keto sulfoxides, 11, have also been converted to their respective dianions by treating each precursor first with sodium hydride, followed by treatment with n-butyl lithium. These dianions likewise, showed an exclusive terminal alkylation when treated with a number of alkyl halides<sup>8, 9</sup>.

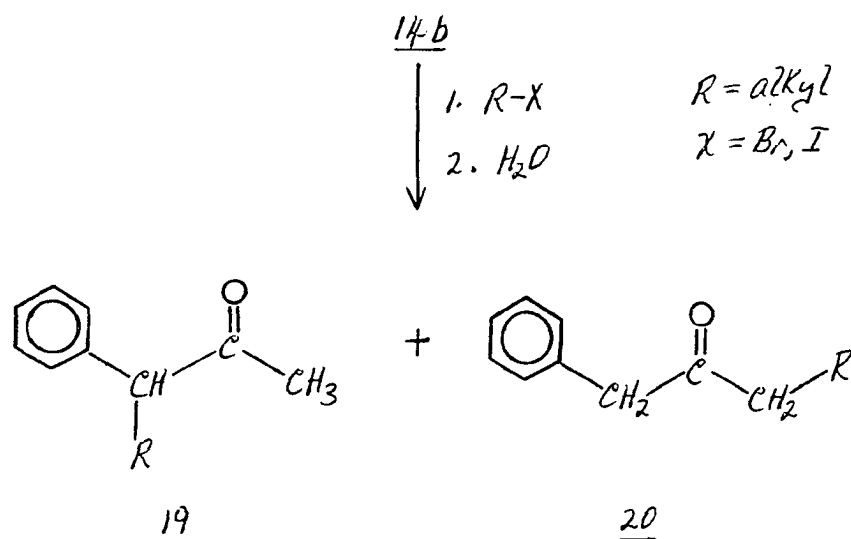




In an earlier report, C. Mao and C. R. Hauser made an attempt to generate a dianion from a monoketone, phenylacetone, 14, using two equivalents of potassium amide in liquid ammonia. The experiment however, proved to be a failure. The reagent appeared not to be a strong enough base to abstract the second proton from the monoanion. In order to overcome this difficulty, phenylacetone was directly treated with a much stronger reagent, n-butyl lithium. This reagent however, was observed to attack the carbonyl group preferentially forming the carbinol derivative. The authors then reacted the original ketone first with one equivalent of the alkali amide and then with n-butyl lithium. The amide led to the formation of the monoanion, 14a, and the n-butyl lithium to the formation of the dianion, 14b. The intermediate dianion underwent terminal condensation with para-anisaldehyde, 15, and chalcone, 16, forming the  $\alpha,\beta$ -unsaturated ketone, 17, and the conjugate addition product, 18, respectively<sup>10</sup>.



In a more recent work<sup>11</sup>, the dianion of phenylacetone was generated by first treating the ketone with potassium hydride in tetrahydrofuran (THF), followed by treatment with n-butyl lithium. Results of alkylation with various alkyl halides showed that the dianion reacted regioselectively with the more active alkylating agents, and even regiospecifically with the less active ones, at the C<sub>1</sub> position.





### III. STATEMENT OF PROBLEM

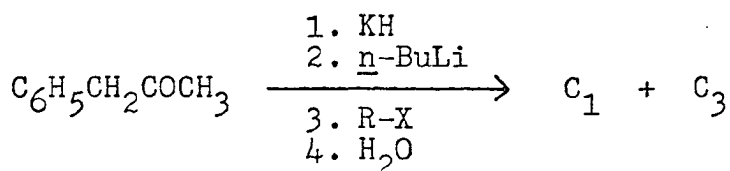
In contrast to the earlier reports on the alkylation of  $\beta$ -diketo and similar compounds, including phenylacetone, the results obtained by Trimitsis and his co-workers appear to indicate that the  $C_1$  position in the dianion of phenylacetone is more nucleophilic than that of  $C_3$ , and hence, the more basic site.

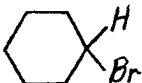

The purpose of the present study is to determine the effects of electron-donating and electron-withdrawing groups on the alkylation sites of para-substituted phenylacetones.

#### IV. RESULTS

Based on the Hammett substituent constants<sup>12</sup>, methyl and methoxy were chosen as electron-donating groups, and Cl as an electron-withdrawing group. Based on the distribution of alkylation products in Table 1<sup>11</sup>, methyl, ethyl, and n-butyl iodides were chosen as alkylating agents for the present study.

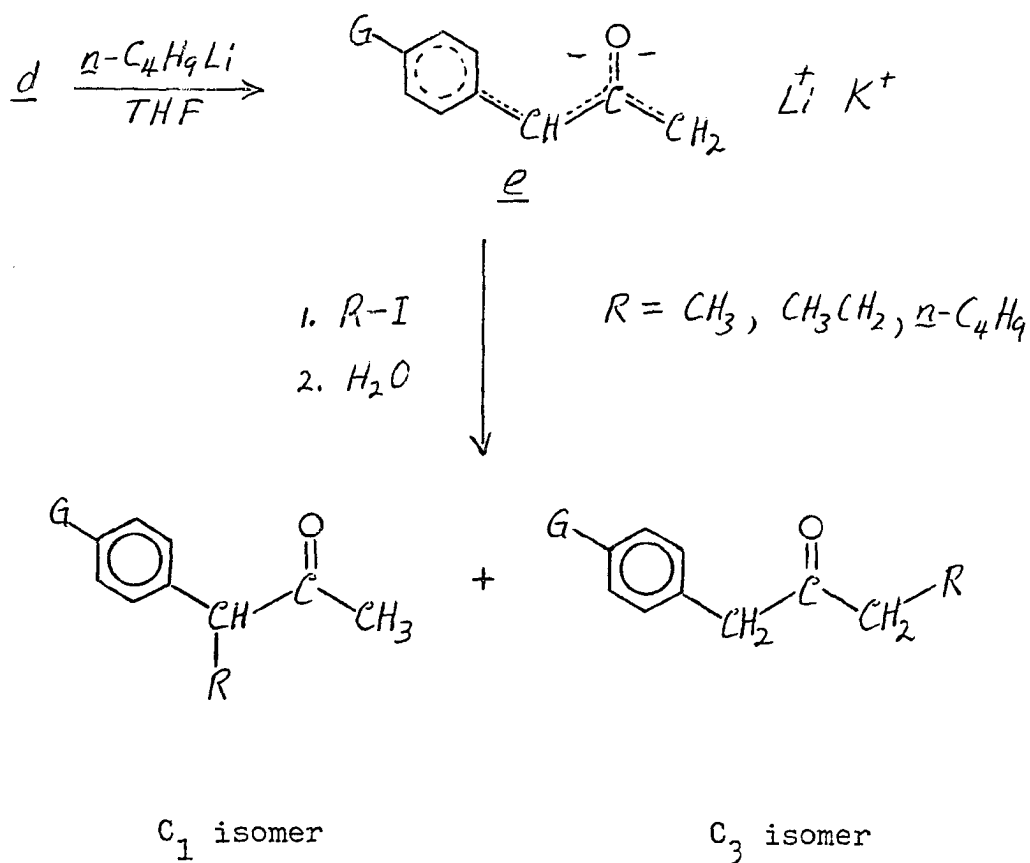
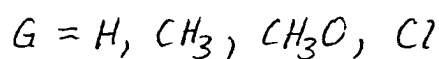
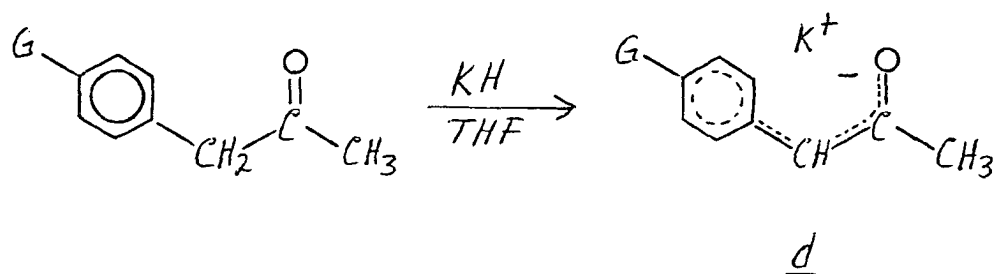
Table 1  
Distribution of Alkylation Products  
of 1-Phenyl-2-propanone



R-X	C <sub>1</sub> : C <sub>3</sub>
(CH <sub>3</sub> ) <sub>2</sub> CHBr	only C <sub>1</sub> alkylation
(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub> Br	only C <sub>1</sub> alkylation
	only C <sub>1</sub> alkylation
	only C <sub>1</sub> alkylation
<u>n</u> -C <sub>4</sub> H <sub>9</sub> Br	19 : 1
<u>n</u> -C <sub>4</sub> H <sub>9</sub> I	9 : 1
CH <sub>3</sub> CH <sub>2</sub> Br	99 % C <sub>1</sub> alkylation
CH <sub>3</sub> CH <sub>2</sub> I	5 : 1
CH <sub>3</sub> I	5.5 : 4.5

The alkylation of each phenylacetone was accomplished in a way as illustrated in Scheme 1. Thus, the

Scheme 1

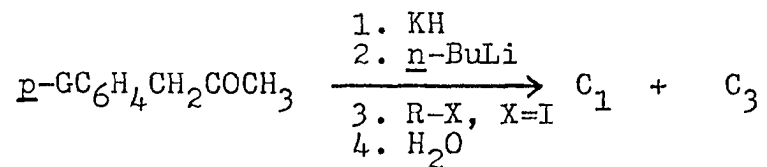


monoanion, d, was generated from equivalent amounts of the initial ketone and potassium hydride in tetrahydrofuran (THF), which gave a yellow orange color to the mixture. The para-chloro compound appeared to be more reactive than the other ketones, and a darker solution resulted in that system. The monoanion was then converted to the dianion, e, with a small excess of n-butyl lithium, and a further change in color of the mixture to a deep red occurred. It may be noted that the para-chloro system had a more vigorous reaction with the n-butyl lithium resulting in a much darker solution. Alkylation of the dianion with one equivalent of an alkyl iodide transformed the mixture into a yellow slurry. Finally, the process was completed by hydrolyzing the salt mixture with water.

Gas chromatographic analyses of the alkylation mixtures showed in each case, except for the para-chloro compound, essentially only two components which were later identified by nmr, mass spectrometry, and elemental analyses to be the isomeric C<sub>1</sub> and C<sub>3</sub> alkylation products. The relative ratios of products for the p-methyl, p-methoxy, and the unsubstituted phenylacetones were determined from their respective gas chromatograms, and are listed in Table 2.

In the case of the para-chloro derivative, gas chromatography indicated the presence of at least two other products in the alkylation mixture with methyl

Table 2  
Distribution of Alkylation Products of 1-Phenyl-2-propanone  
and its para-Substituted Derivatives



G	R								
	CH <sub>3</sub>			CH <sub>3</sub> CH <sub>2</sub>			CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub>		
	C <sub>1</sub>	C <sub>3</sub>	% Yield <sup>a</sup>	C <sub>1</sub>	C <sub>3</sub>	% Yield <sup>a</sup>	C <sub>1</sub>	C <sub>3</sub>	% Yield <sup>a</sup>
H	44	56	73	69	31	66	77	23	82
CH <sub>3</sub>	40	60	67	66	34	65	73	27	64
CH <sub>3</sub> O	38	62	72	61	39	79	66	34	73
Cl	--	--	--	--	--	--	--	--	--

(a) Total yield of both C<sub>1</sub> and C<sub>3</sub> alkylation products.

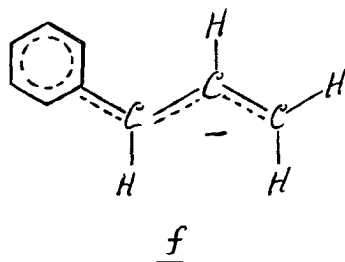
iodide. These appeared as shoulders on both sides of the  $C_3$  peak, making it impossible to take a reliable measurement of the latter. The ethylated mixture also resulted in a third gas chromatographic peak which occurred so close to the  $C_3$  component that measurement of the latter would entail a considerable error. On the other hand, the alkylation mixture with n-butyl iodide resulted in well-separated peaks so that quantitative measurement could be done accurately. Unlike the corresponding alkylations of the other phenylacetones however, the reaction of the para-chloro compound with n-butyl iodide appeared to be incomplete by the fact that the gas chromatogram indicated 30 to 40 % of the original ketone. It was felt the results of alkylation of para-chlorophenylacetone did not provide any significance to the present study. Hence, no data is included in the table.

It is important to note that the use of excess potassium hydride or alkyl iodide, or both, led to the formation of other products, possibly having higher boiling points than the monoalkylated ketones on the basis of their gas chromatographic behaviour. No attempt was made to isolate these components. The use of a small or a large excess of n-butyl lithium did not alter the results of alkylation.

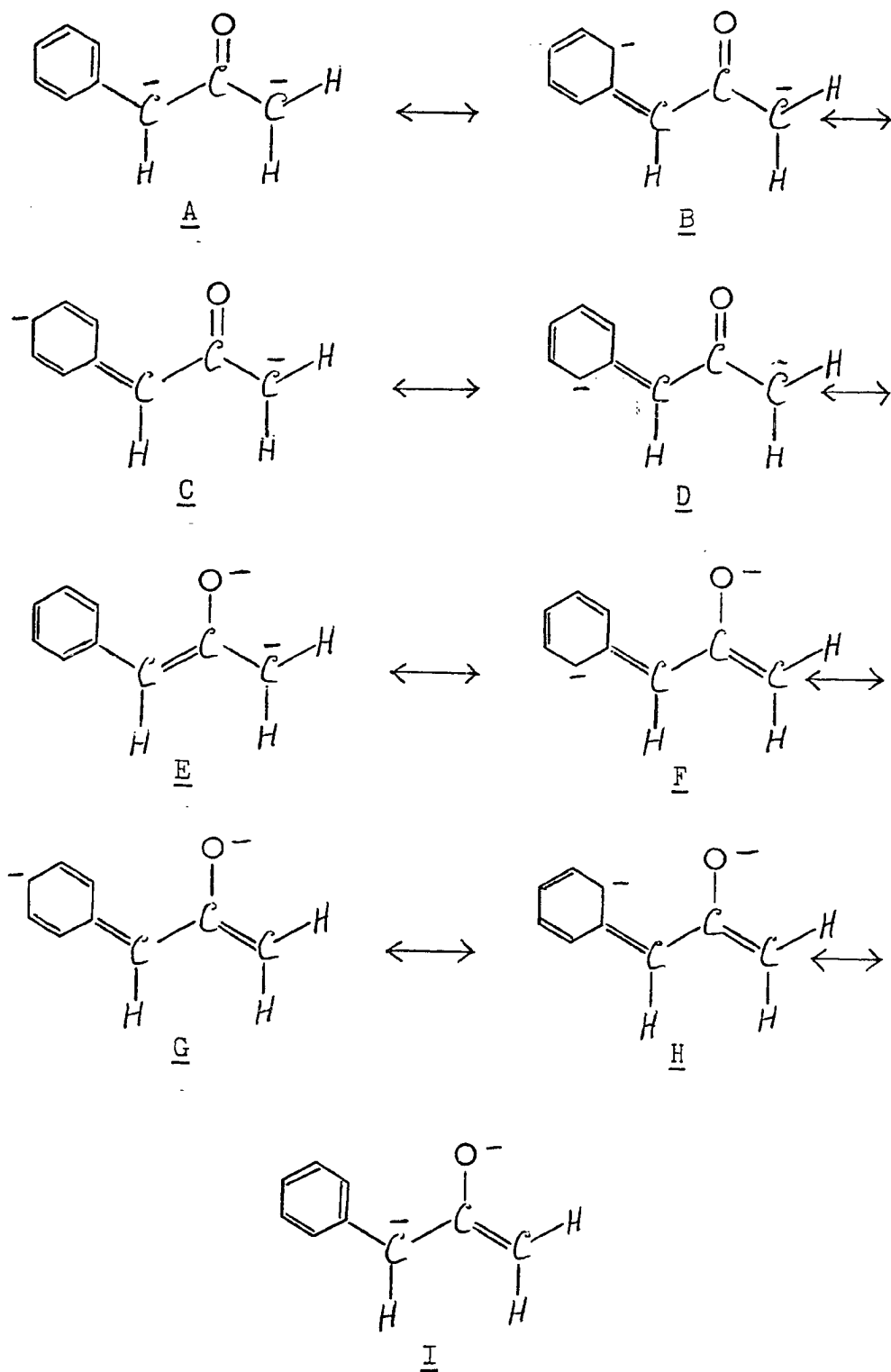
## V. DISCUSSION

The results in Table 2 show that alkylation at  $C_1$  of phenylacetone increases with decreasing reactivity of the alkyl iodide in an  $S_N2$  process<sup>13</sup>. Despite the fact that the  $C_1$  position is more hindered sterically than  $C_3$ , it still is the preferred site of alkylation. This is true for the less active ethyl and *n*-butyl iodides. This trend implies that  $C_1$  in the ambident dianion is more nucleophilic than  $C_3$ .

A previous nmr study<sup>11</sup> showed that the spectrum of the dianion of phenylacetone bears a very close resemblance with that of the allylbenzene monoanion<sup>15</sup>, f, in which the two terminal hydrogen atoms are shown to be non-equivalent. It also showed that the ring protons are shifted upfield relative to those in the original ketone.



In theory, the dianion of phenylacetone may be considered as a hybrid of the resonance structures shown below. Based on the electronegativity data of carbon (2.5) and oxygen (3.5)<sup>1</sup>, the atom of the latter in the hybrid

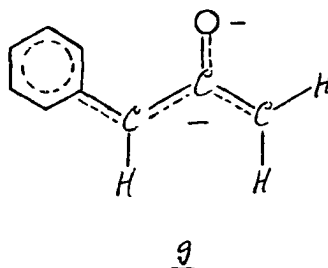




should be more associated with a negative charge than a double bond. So that the resonance structures A to D should contribute to the hybrid only to a very minor extent. Comparison of structures E and I leads to the conclusion that I is more stable than E. Structure I therefore, is expected to contribute more to the hybrid than structure E. It follows that the resemblance of the hybrid to the two resonance structures is more of I than of E. This leads to the conclusion that  $C_1$  has a greater electron density than  $C_3$ . For atoms of the same element, greater electron density results in greater polarizability (the tendency of an electron cloud to be distorted by an approaching electrophile), and hence, in greater nucleophilicity (the ability of an atom or group of atoms to donate a pair of electrons)<sup>14</sup>. Therefore,  $C_1$  in the dianion should be more nucleophilic than  $C_3$ . The results of alkylation are indeed in accord with this conclusion. Furthermore, the greater resemblance of the resonance hybrid to structure I also leads to the conclusion that  $C_3$  is more associated with a double bond than  $C_1$ . The nmr result is also in agreement with this conclusion.

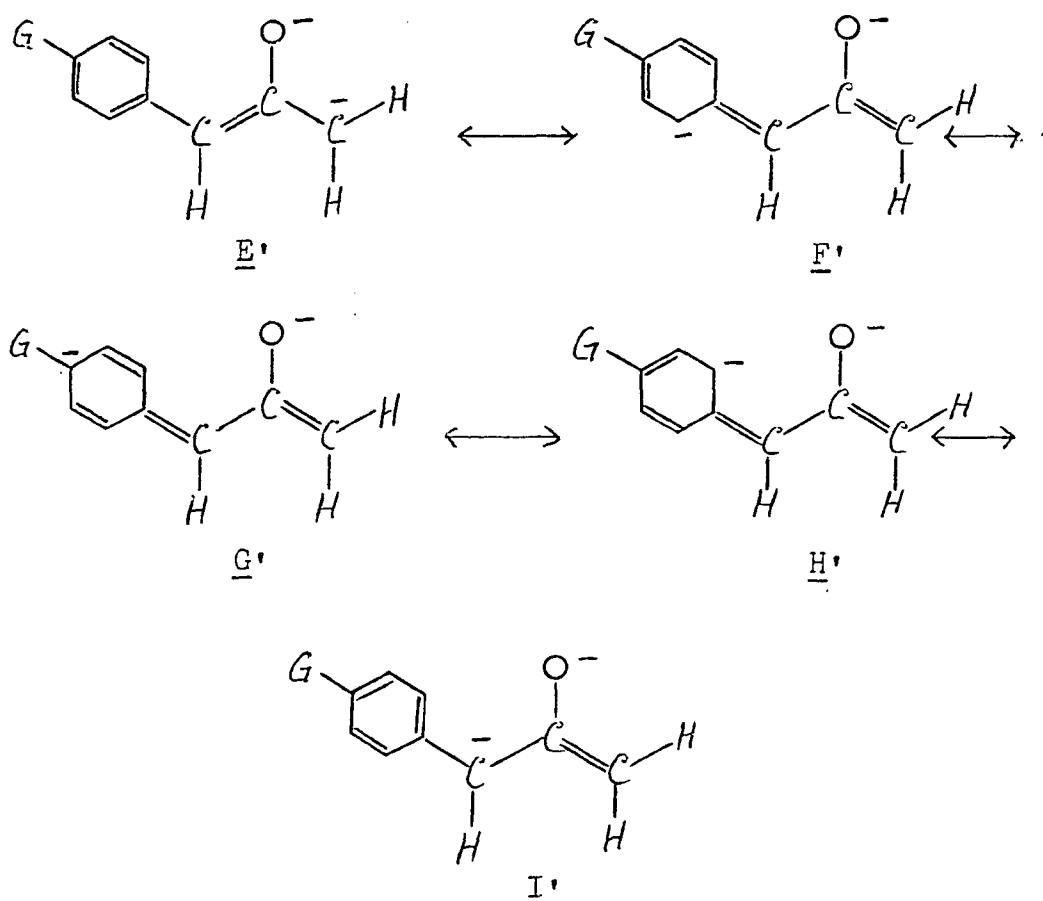
Based on the electronegativity data of the elements<sup>1</sup>, one of the negative charges in the dianion of phenylacetone may be considered as largely localized on oxygen. Based on the theory of resonance just described, the results of alkylation, and the nmr spectrum of the

dianion<sup>11</sup>, the second negative charge may be considered as being delocalized throughout the carbon chain and the phenyl ring. Thus, the dianion of phenylacetone may be represented by structure g, which has also been proposed recently by Bays<sup>16</sup>.



In theory, the influence of para-substituents on the alkylation sites of phenylacetone can also be evaluated on the basis of resonance. In this regard, the previous resonance structures, E to I, of the dianion of phenylacetone may only be recalled, in which the para-hydrogen is replaced with an electron-donating or an electron-withdrawing group, G, as shown below.

When G is an electron-donating group, the apparent inductive or resonance effect, or a combination of both, results in a greater destabilization of structures F' to I' relative to E'. As a consequence, contributions of those four structures to the resonance hybrid are diminished, and that of E' is increased correspondingly. The net effect results in the reduction of electron density at C<sub>1</sub> and enhancement at C<sub>3</sub> in the dianion. Therefore, alkyla-



tion at the former site is expected to decrease, and the latter to increase. The results of alkylation in Table 2 are indeed in accord with this conclusion. The electron-donating (by inductive) effect of the para-methyl substituent yielded essentially a 4% increase in  $C_3$  alkylation relative to the unsubstituted phenylacetone with each alkyl iodide used. An even more pronounced influence of charge on the alkylation sites of the dianion of phenylacetone is

displayed by a better electron donor (through resonance with the phenyl ring), the methoxy group, giving 6%, 8%, and 11% increases in terminal alkylation, relative to the unsubstituted phenylacetone, with methyl, ethyl, and n-butyl iodides respectively.

On the other hand, the effect of an electron-withdrawing group on the stability of the resonance structures F' to I' should be opposite to that of an electron-donating substituent. To the extent that no double bond character exists between  $C_1$  and the phenyl ring, increased stability of structures F' to I' should enhance further the electron density at  $C_1$  relative to that at  $C_3$ , resulting in a larger difference in charge density between the two sites compared to the corresponding difference in the dianion of the unsubstituted phenylacetone. Therefore, treatment of the dianion containing an electron-withdrawing group with an alkyl iodide should result in an increased alkylation at the  $C_1$  position, and a corresponding reduction at  $C_3$ . Unfortunately, no data could be gathered from the experiments involving the alkylation of para-chlorophenylacetone to support this conclusion. Thus, the influence of charge on the alkylation sites of phenylacetone may be assessed only on the basis of electron donation. Based on the results of alkylation of para-methyl- and para-methoxyphenylacetones therefore, it is concluded that an increase in

electron density in the dianion of phenylacetone by electron-donating groups at the para-position of the ring enhances the charge at  $C_3$  and hence, terminal alkylation.

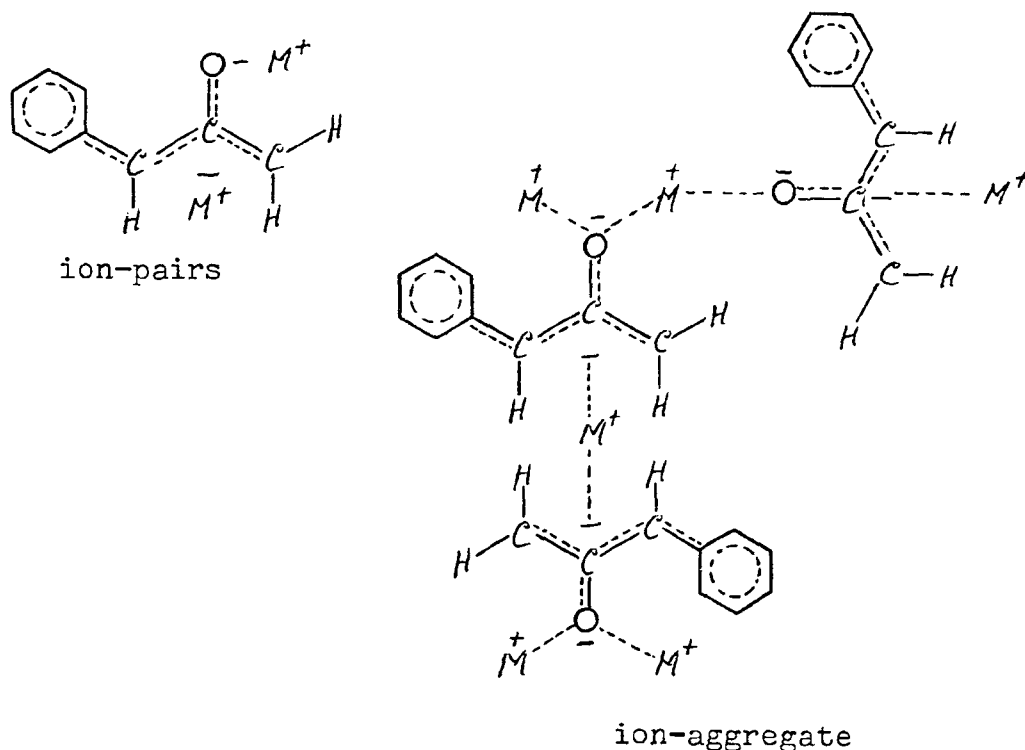
An observation worthy of note is the fact that the ratio of alkylation products of phenylacetone appears to be a function of the alkylating agent's activity. In a recent report by Bays<sup>16</sup> involving the alkylation of phenylacetone with methyl iodide, the author concluded that the reaction is nonregioselective by the fact that the  $C_1$  and  $C_3$  products were formed in almost equal amounts. The results of alkylation in Table 1 and in Table 2 indicate however, that the less active the alkylating agent the greater is the tendency to form the  $C_1$  product. For example, the data in Table 2 shows that the methyl iodide favored terminal alkylation slightly over  $C_1$ . Whereas the more bulky but less active ethyl and n-butyl iodides alkylated preferentially the more hindered  $C_1$  position. The latter results are definitely a display of regioselectivity in the reaction of the dianion.

The study of the protonation of the dianion of phenylacetone with one equivalent of water in tetrahydrofuran-hexane showed an exclusive attack of the reagent (water) at the terminal site<sup>11</sup>. As previously mentioned, the condensation of the dianion with para-anisaldehyde and chalcone occurred exclusively at  $C_3$ <sup>10</sup>. These results appear to suggest also that increasing activity of elec-

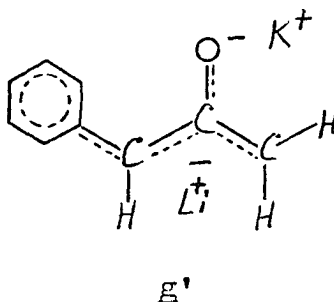
trophiles increases terminal alkylation, and hence, the regioselectivity of the reaction.

It may be well to consider that the oxygen atom in the dianion of phenylacetone bears essentially a negative charge, and thus, a potential site of alkylation. A competition for electrophiles may therefore be considered to exist between the carbon centers and the oxygen end. To understand the preference of alkylation between carbon and oxygen in the dianion, the following factors may be considered.

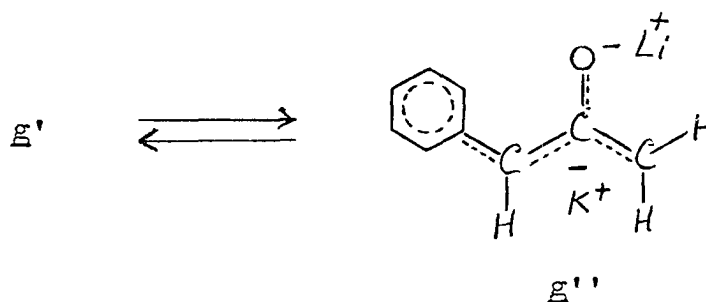
(1) In tetrahydrofuran, where solvation of the metal ions is not so significant, the dianion may be considered as being associated with the cations in ion-pairs or ion-aggregates as shown below<sup>17, 18</sup>. Based on the sequence of



adding the potassium hydride and the n-butyl lithium to the ketone, it may be presumed that the oxygen is associated with the potassium ion, and the carbon atoms with the lithium ion as shown in  $g'$ . Nevertheless, exchange of



cations within or between ion-pairs is possible. Thus, an equilibrium may be considered to exist between  $g'$  and the other possible ion-pairs,  $g''$ , as shown below. According



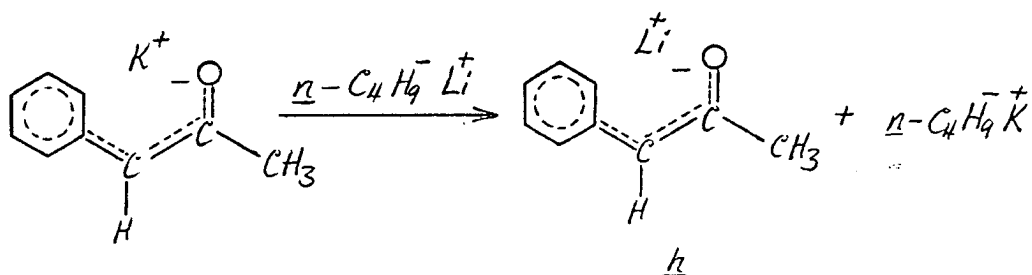
to the concept of soft and hard acids and bases, the lithium ion is a harder acid than the potassium ion, the former being smaller and hence, less polarizable than the latter. The carbanionic center in the ambident dianion is classified as a soft base, and the oxygen end as a hard base. Pearson has suggested the rule that hard acids bind preferentially to hard bases, and soft acids bind prefer-

entially to soft bases<sup>2</sup>. Therefore, both alkali metal ions are expected to have greater affinities toward the oxygen end than for the carbanionic sites. The solubility data of the alkali metal hydroxides in water indicate that lithium hydroxide is much less soluble than that of potassium<sup>22</sup>. Furthermore, the perchlorate of lithium is much more soluble in some common organic solvents such as, methanol, ethanol, ether, and acetone, than that of potassium<sup>23</sup>. These data imply that the Li-O bond has a greater covalent character than the K-O bond. In tetrahydrofuran, the stability of the more covalent Li-O bond should be greater than that of the K-O bond. This leads to the conclusion that  $g''$  should be the predominant ion-pairs. Thus, the equilibrium is shown to be shifted towards right.

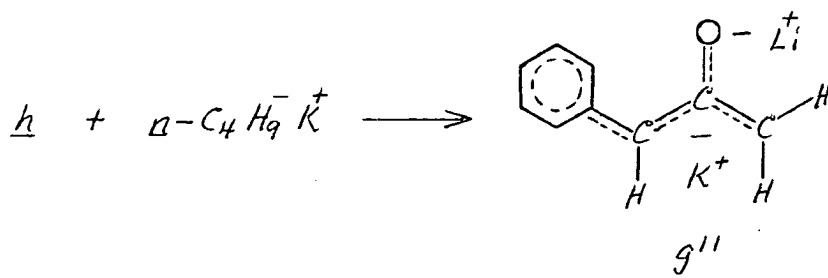


On the other hand, it has been reported that sodium and potassium t-butoxide underwent transmetalation with n-butyl lithium to form lithium t-butoxide and n-butyl sodium and potassium<sup>24</sup>. Furthermore, while lithium has been observed to be tightly bound to the oxygen atom of the phenylacetone enolate, potassium is only weakly bound. J. P. Bays has suggested that the enolate serves as the transmetalating agent, forming the lithium enolate and the more basic n-butyl potassium. Abstraction of the second proton from the enolate, h, by the n-butyl potassium leads





therefore, to the formation of the ion-pairs,  $g'$ ,<sup>16</sup>.



Based on the rule of soft and hard acids and bases, the solubility data of lithium and potassium hydroxides and perchlorates, and the results of transmetalation, it is concluded that the carbaionic centers in the ambident dianion are more active than the oxygen end. This results in a more favorable C-alkylation.

(2) Polarizability decreases with increasing electronegativity of an atom<sup>19</sup>. The fact that oxygen has a higher electronegativity than carbon implies that the former is less polarizable than the latter in the dianion. Since nucleophilicity increases with increasing polarizability<sup>14, 19</sup>, the carbon ends therefore, should be more nucleophilic than that of oxygen. This also favors C-alkylation over O-alkylation.

(3) Comparison of the bonds formed in the O-alkylation with those in the C-alkylation (Table 3) shows that the latter is considerably more stable<sup>20</sup>. In the processes shown, the activated complex in the alkylation step bears a significant resemblance with the final product<sup>21</sup>. It follows that the C-alkylation must be lower in energy than

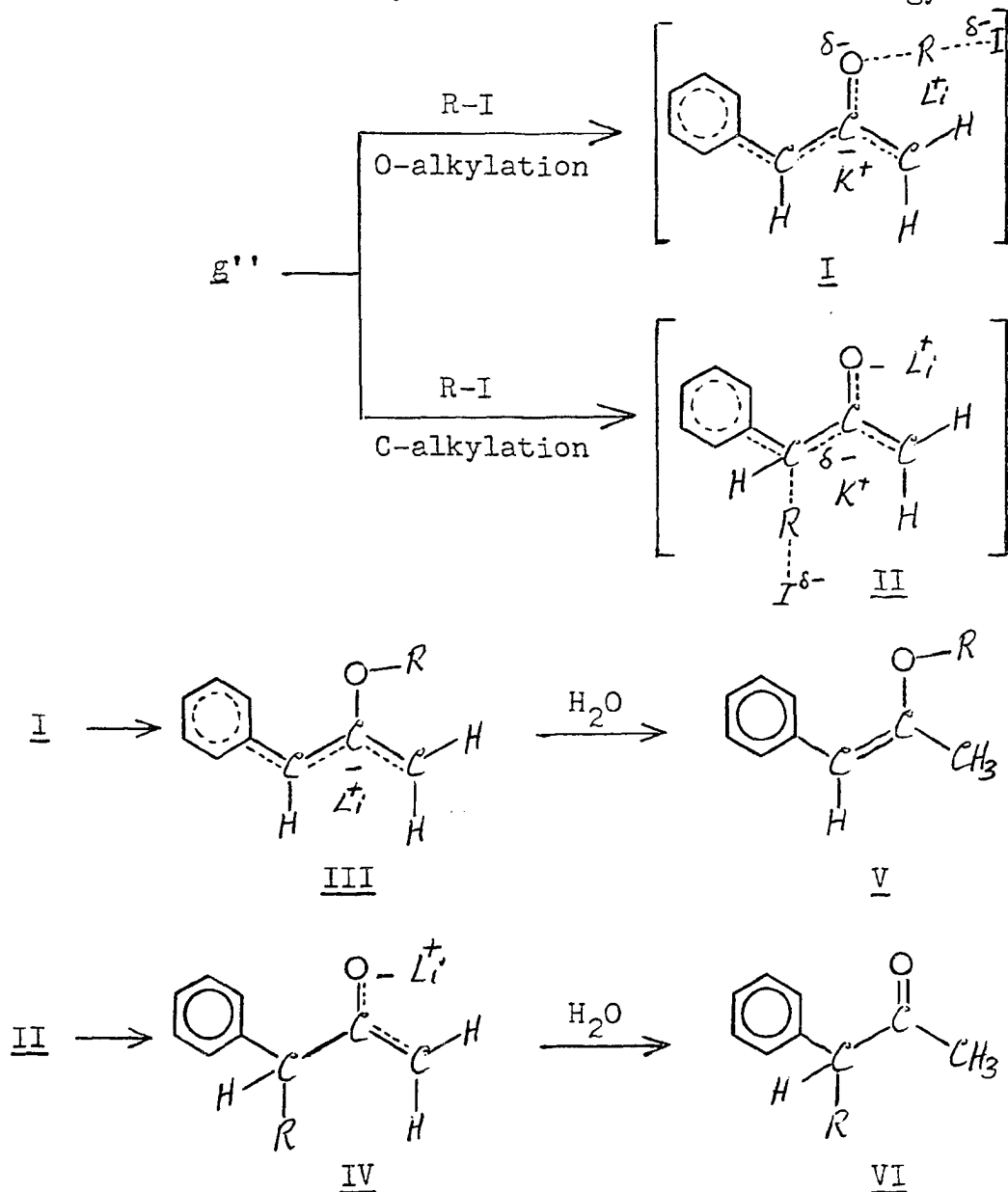
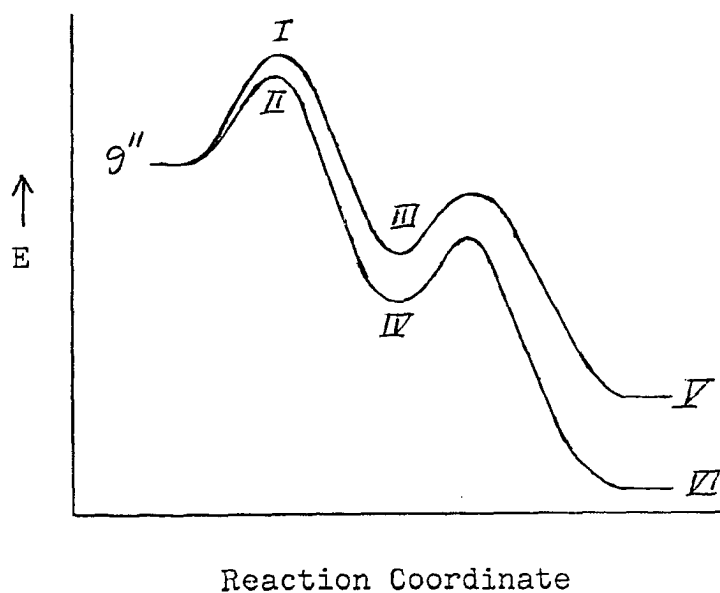


Table 3<sup>20</sup>  
Bond Energy

O-alkylation		C-alkylation	
Bond	E (Kcal/mol)	Bond	E (Kcal/mol)
C-O	79	C=O	173
C-O	79	C-C	80
C≡C	<145	C-C	80

the corresponding O-alkylation. Thus the following diagram shows that the former reaction is favored both kinetically and thermodynamically over the latter. The



total effect then of all three factors makes for a more favorable C-alkylation. The results of alkylation in this study showed essentially the C-alkylation products only. It has also been noted that O-alkylation in base-catalyzed reactions is unusual<sup>20</sup>.

## VI. EXPERIMENTAL

### A. Chemicals and Equipments

The para-methyl-, para-methoxy-, and the unsubstituted phenylacetones were purchased commercially, while the para-chloro compound was prepared in the laboratory. The potassium hydride was available as a 22% suspension in mineral oil, and the n-butyl lithium as a 2.4 M and a 2.6 M solutions in n-hexane. The methyl, ethyl, and n-butyl iodides were also obtained commercially.

All gas chromatograms were taken on a Varian Aero-graph series 2700. The nmr and mass spectrometer samples were run on Varian Associates Model A-60 Nuclear Magnetic Resonance and Dupont 21-490B Mass Spectrometers respectively. Chemical shifts in all nmr spectra were expressed in  $\delta$ ppm using tetramethyl silane as a reference, and the multiplicities were recorded as s, d, t, q, and m (where s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet). The elemental analyses of authentic samples were done by Galbraith Laboratories, and the melting points of solid derivatives were determined on a Thomas-Hoover melting point apparatus.

### B. General Procedure

#### 1. Preparation of 1-(4-chlorophenyl)-2-propanone<sup>25</sup>

(a) A three-neck, 1-liter, round-bottom flask was fitted with an electric heating mantle, a modified Dean and Stark water separator<sup>26</sup>, and a reflux condenser. Into the flask were added in this order: 200 ml of reagent grade toluene, 140 g (1.0 mol) of para-chlorobenzaldehyde, 90 g (1.1 mol) of nitroethane, and 20 ml of n-butylamine. With moderate stirring, the mixture was heated to produce a rapid reflux until the separation of water has ceased (the theoretical amount is 18 ml, collected in 15 to 20 hours).

(b) A three-neck, 3-liter, round-bottom flask was equipped with an electric heating mantle, a reflux condenser, a thermometer, a dropping funnel, and a high-speed whip stirrer. The cooled toluene solution from part (a) was placed in the flask, and 500 ml of water, 200 g of powdered iron (40 mesh was used), and 4 g of ferric chloride were added. The mixture was heated (with vigorous stirring) to about 75°C, and 360 ml of concentrated hydrochloric acid was added over a two-hour period (vigorous reflux was being maintained); heating and stirring were continued for an additional hour.

The reflux column was replaced with a distilling condenser, and the mixture was subjected to steam distillation until 7 to 10 liters of distillate had been collected. The toluene layer was removed, and the aqueous part was extracted three times with 300 ml portions of

fresh toluene. The combined toluene layers were agitated with a solution of 26 g of sodium hydrogen sulfite in 500 ml of water for 30 minutes. The organic layer was then washed with water, and the solvent was removed at water-pump pressure using a rotary evaporator and a hot water bath. Fractional distillation of the residual liquid under reduced pressure (less than 0.5 mm) with a Vigreux column, effected the purification of the product. The yield of the fraction collected between 78° and 80° C at 0.3 mm was 53 % based on the amount of para-chlorobenzaldehyde used.

## 2. Alkylation of phenylacetone and its para-substituted derivatives

A three-neck, 250-ml, round-bottom flask on a magnetic stirrer was fitted with a reflux condenser connected to a source of nitrogen gas, an addition funnel, and a ground-glass adapter, each of the latter two was fitted with a rubber septum. Approximately 10 g of 22 % potassium hydride in mineral oil was weighed, washed three times with 25 ml portions of n-pentane with the aid of a centrifuge, and transferred into the round-bottom flask with 60 ml of tetrahydrofuran (freshly distilled over sodium hydride). The mixture was stirred moderately under a slow but continuous flow of nitrogen gas. A phenylacetone was then introduced directly drop by drop to the mixture from a syringe through the ground-glass adapter until gas evolution stopped. The amount of the ketone used was determined from the weights of the filled syringe before and

after its addition. With constant stirring at room temperature, the mixture was allowed to stand for 30 minutes.

It was then cooled in an ice bath for 10 minutes, and 10 to 20 % excess of 2.4 or 2.6 M of n-butyl lithium in n-hexane was introduced drop by drop through the addition funnel. The mixture was allowed to stand further for an hour at room temperature. After cooling in an ice bath for another 10 minutes, one equivalent of an alkyl iodide in 10 ml of tetrahydrofuran was added drop by drop through a second addition funnel which replaced the ground-glass adapter. Stirring was continued for another hour at room temperature. Finally, the mixture was hydrolyzed slowly with 50 ml of water, and the resulting liquid layers were separated. The organic portion was dried over 8 to 10 g of anhydrous magnesium sulfate, filtered, and stripped of the solvent under water-pump pressure, using a rotary evaporator and a hot water bath. A gas chromatogram was obtained on the residual liquid.

### 3. Preparation of authentic samples

#### (a) Fractional distillation of alkylation mixture.

A fractionating column with a spinning band was fitted with a 50-ml, round-bottom flask and a still head which was connected to a vacuum pump. Six 13 x 100 mm test tubes were used as receivers for collecting fractions of distillate, and an oil bath for heating. The residual liquid from the alkylation reaction was transferred into the flask

and stirred. The pressure was reduced, and the column and the flask were then heated gradually with the metal coil and the oil bath respectively to obtain a distillation rate of about one ml per minute. The fractions were checked for purity by gas chromatography, and the impure samples were refractionated.

(b) Preparation of  $C_1$  alkylation product by alkylation of the monoanion of a phenylacetone. The procedure in the alkylation of phenylacetone and its para-substituted derivatives previously described was followed except that the use of n-butyl lithium and the time required with it was omitted. The alkylation product was obtained from the residual liquid by fractional distillation under reduced pressure (less than 0.5 mm).

(c) Preparation of  $C_3$  alkylation product from a corresponding benzaldehyde. The procedure in the preparation of para-chlorophenylacetone was followed except that the amounts of chemicals used were reduced by a factor of 5 to 20, depending on the amount of nitroalkane<sup>27</sup> available. The alkylation product was isolated by fractional distillation of the residual liquid.

### C. Alkylation of Phenylacetone and its para-Substituted Derivatives

#### 1. Formation of 3-phenyl-2-butanone (21) and 1-phenyl-2-butanone (22)

About 10 g of 22 % potassium hydride in mineral oil



were reacted with 6.02 g (0.0452 mol) of 1-phenyl-2-propa-  
none, and the mixture was then treated with 25 ml (0.0641  
mol) of 2.6 M n-butyl lithium in n-hexane, followed by the  
addition of 6.40 g (0.0452 mol) methyl iodide to give 73 %  
of (21) and (22). The peaks of the slightly impure samples  
in their gas chromatograms and nmr spectra were identical  
to those of (21a) and (22a) respectively. Gas chromato-  
graphic examination of the solvent-stripped alkylation  
mixture indicated a product composition of 44 % (21) and  
56 % (22).

## 2. Formation of 3-phenyl-2-pentanone (23) and 1-phenyl-2- pentanone (24)

About 10 g of 22 % potassium hydride in mineral oil  
were reacted with 7.56 g (0.0564 mol) of 1-phenyl-2-propa-  
none, and the mixture was then treated with 27 ml (0.0650  
mol) of 2.4 M n-butyl lithium in n-hexane, followed by  
8.01 g (0.0564 mol) of ethyl iodide to give 66 % of (23)  
and (24). The slightly impure samples had identical peaks,  
in both gas chromatograms and nmr spectra, to those of  
(23a) and (24a) respectively. Gas chromatographic examina-  
tion of the solvent-stripped alkylation mixture indicated  
a product composition of 69 % (23) and 31 % (24).

## 3. Formation of 3-phenyl-2-heptanone (25) and 1-phenyl-2- heptanone (26)

About 10 g of 22 % potassium hydride in mineral oil  
were reacted with 7.87 g (0.0588 mol) of 1-phenyl-2-propa-  
none, followed by the addition of 26 ml (0.0687 mol) of 2.6

M n-butyl lithium in n-hexane and 10.81 g (0.0588 mol) of n-butyl iodide to give 80% of (25) and (26). Gas chromatographic examination of the solvent-stripped alkylation mixture showed a product composition of 77% (25) and 23% (26).

Compound (25) was isolated from the mixture by fractional distillation: bp 59-60° (0.04 mm);  $n_D^{23}$  1.4960; molecular ion  $m/e$  190 (Calcd: 190); nmr ( $CCl_4$ )  $\delta$  0.7-1.5 (m, 7H, aliphatic CH), 1.6-2.0 (m, 2H, aliphatic CH), 1.93 (s, 3H,  $COCH_3$ ), 3.52 (t, 1H,  $ArCHCO$ ), 7.18 (s, 5H, aryl CH). Anal. Calcd for  $C_{13}H_{18}O$ : C, 82.10; H, 9.47. Found: C, 81.90; H, 9.41. Semicarbazone mp 156-157°.

Compound (26) had identical peaks, in both gas chromatogram and nmr spectrum, to those of (26a).

#### 4. Formation of 3-(4-methylphenyl)-2-butanone (27) and 1-(4-methylphenyl)-2-butanone (28)

About 10 g of 22% potassium hydride in mineral oil were reacted with 8.02 g (0.0538 mol) of 1-(4-methylphenyl)-2-propanone, which was then treated with 25 ml (0.0650 mol) of 2.6 M n-butyl lithium in n-hexane, followed by the addition of 7.66 g (0.0538 mol) methyl iodide to give 67% of (27) and (28). Gas chromatographic examination of the solvent-stripped alkylation mixture showed a product composition of 40% (27) and 60% (28).

Compound (27) was isolated from the mixture by fractional distillation: bp 49-50° (0.06 mm);  $n_D^{23}$  1.5052; molecular ion  $m/e$  162 (Calcd 162); nmr ( $CCl_4$ )  $\delta$  1.30 (d,

3H, CHCH<sub>3</sub>), 1.93 (s, 3H, COCH<sub>3</sub>), 2.30 (s, 3H, benzyl CH<sub>3</sub>), 3.62 (q, 1H, ArCHCO), 7.05 (s, 4H, aryl CH). Anal. Calcd for C<sub>11</sub>H<sub>14</sub>O: C, 81.48; H, 8.64. Found: C, 81.19; H, 8.60. Semicarbazone mp 181-182°. 2,4-Dinitrophenylhydrazone mp 122-123°.

Compound (28) was isolated from the alkylation mixture by fractional distillation: bp 55-56° (0.06 mm);  $n_D^{23}$  1.5086; molecular ion m/e 162 (Calcd 162); nmr (CCl<sub>4</sub>)  $\delta$  0.94 (t, 3H, CH<sub>2</sub>CH<sub>3</sub>), 2.28 (s, 3H, benzyl CH<sub>3</sub>), 2.34 (q, 2H, COCH<sub>2</sub>CH<sub>3</sub>), 3.50 (s, 2H, ArCH<sub>2</sub>CO), 7.02 (s, 4H, aryl CH). Anal. Calcd for C<sub>11</sub>H<sub>14</sub>O: C, 81.48; H, 8.64. Found: C, 79.88; H, 9.94. 2,4-Dinitrophenylhydrazone mp 115-117°. Anal. Calcd for C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>: C, 59.65; H, 5.27. Found: C, 60.51; H, 5.57.

#### 5. Formation of 3-(4-methylphenyl)-2-pentanone (29) and 1-(4-methylphenyl)-2-pentanone (30)

About 10 g of 22% potassium hydride in mineral oil were reacted with 8.17 g (0.0548 mol) of 1-(4-methylphenyl)-2-propanone, followed by the addition of 25 ml (0.066 mol) 2.6 M n-butyl lithium in n-hexane and 8.54 g (0.548 mol) of ethyl iodide to give 65% of (29) and (30). Gas chromatographic examination of the solvent-stripped mixture showed a product composition of 66% (29) and 34% (30).

Compound (29) was isolated from the mixture by fractional distillation: bp 51-52° (0.04 mm);  $n_D^{23}$  1.5015; molecular ion m/e 176 (Calcd 176); nmr (CCl<sub>4</sub>)  $\delta$  0.79 (t,

3H,  $\text{CH}_2\text{CH}_3$ ), 1.71 (m, 2H,  $\text{CHCH}_2\text{CH}_3$ ), 1.93 (s, 3H,  $\text{COCH}_3$ ), 2.30 (s, 3H, benzyl  $\text{CH}_3$ ), 3.39 (t, 1H,  $\text{ArCHCO}$ ), 7.05 (s, 4H, aryl CH). Anal. Calcd for  $\text{C}_{12}\text{H}_{16}\text{O}$ : C, 81.82; H, 9.09. Found: C, 81.56; H, 9.07. Semicarbazone mp  $171-172^\circ$ .  
2,4-Dinitrophenylhydrazone mp  $128-129^\circ$ .

Compound (30) had identical peaks, in both gas chromatogram and nmr spectrum, to those of (30a).

6. Formation of 3-(4-methylphenyl)-2-heptanone (31) and 1-(4-methylphenyl)-2-heptanone (32)

About 10 g of 22% potassium hydride in mineral oil were reacted with 7.98 g (0.0536 mol) of 1-(4-methylphenyl)-2-propanone, followed by the addition of 25 ml (0.065 mol) of 2.6 M n-butyl lithium in n-hexane and 9.86 g (0.0536 mol) of n-butyl iodide to give 64% of (31) and (32). Gas chromatographic examination of the solvent-stripped alkylation mixture showed a product composition of 73% (31) and 27% (32).

Compound (31) was isolated from the mixture by fractional distillation: bp  $72-73^\circ$  (0.05 mm);  $n_D^{23}$  1.4972; molecular ion  $m/e$  204 (Calcd 204); nmr ( $\text{CCl}_4$ )  $\delta$  0.7-1.6 (m, 9H, aliphatic CH), 1.6-2.0 (m, 2H, aliphatic CH), 1.93 (s, 3H,  $\text{COCH}_3$ ), 2.29 (s, 3H, benzyl  $\text{CH}_3$ ), 3.48 (t, 1H,  $\text{ArCHCO}$ ), 7.04 (s, 4H, aryl CH). Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}$ : C, 82.35; H, 9.80. Found: C, 81.37; H, 10.62. Semicarbazone mp  $166-167^\circ$ . Anal. Calcd for  $\text{C}_{15}\text{H}_{23}\text{N}_3\text{O}$ : C, 68.97; H, 8.80. Found: C, 69.04; H, 8.93. 2,4-Dinitrophenylhydrazone mp  $109-110^\circ$ .

Compound (32) had identical gas chromatogram and nmr spectrum to those of (32a).

7. Formation of 3-(4-methoxyphenyl)-2-butanone (33) and 1-(4-methoxyphenyl)-2-butanone (34)

About 10 g of 22% potassium hydride in mineral oil were reacted with 7.69 g (0.0468 mol) of 1-(4-methoxyphenyl)-2-propanone, followed by the addition of 25 ml (0.065 mol) of 2.6 M n-butyl lithium in n-hexane and 6.62 g (0.0468 mol) of methyl iodide to give 72% of (33) and (34). Gas chromatographic examination of the solvent-stripped alkylation mixture showed a product composition of 38% (33) and 62% (34). The peaks in their gas chromatograms and nmr spectra were identical to those of (33a) and (34a).

8. Formation of 3-(4-methoxyphenyl)-2-pentanone (35) and 1-(4-methoxyphenyl)-2-pentanone (36)

About 10 g of 22% potassium hydride in mineral oil were reacted with 9.67 g (0.0583 mol) of 1-(4-methoxyphenyl)-2-propanone, followed by the addition of 26 ml (0.068 mol) of 2.6 M n-butyl lithium in n-hexane and 9.08 g (0.0583 mol) of ethyl iodide to give 79% of (35) and (36). Gas chromatographic examination of the solvent-stripped alkylation mixture showed a product composition of 61% (35) and 39% (36).

Compound (35) was isolated from the mixture by fractional distillation: bp 74-75° (0.04 mm);  $n_D^{23}$  1.5108; molecular ion  $m/e$  192 (Calcd 192); nmr ( $CCl_4$ )  $\delta$  0.79 (t,

3H,  $\text{CH}_2\text{CH}_3$ ), 1.70 (m, 2H,  $\text{CHCH}_2\text{CH}_3$ ), 1.95 (s, 3H,  $\text{COCH}_3$ ), 3.39 (t, 1H,  $\text{ArCHCO}$ ), 3.75 (s, 3H,  $\text{OCH}_3$ ), 6.79 (d, 2H, aryl CH), 7.05 (d, 2H, aryl CH). Anal. Calcd for  $\text{C}_{12}\text{H}_{16}\text{O}_2$ : C, 75.00; H, 8.33. Found: C, 73.23; H, 8.20. Semicarbazone mp  $187-188^\circ$ . 2,4-Dinitrophenylhydrazone mp  $105-106^\circ$ . Anal. Calcd for  $\text{C}_{18}\text{H}_{20}\text{N}_4\text{O}_5$ : C, 58.06; H, 5.38. Found: C, 58.38; H, 5.46.

Compound (36) had identical gas chromatogram and nmr spectrum to those of (36a).

9. Formation of 3-(4-methoxyphenyl)-2-heptanone (37) and 1-(4-methoxyphenyl)-2-heptanone (38)

About 10 g of 22% potassium hydride in mineral oil were reacted with 8.98 g (0.0543 mol) of 1-(4-methoxyphenyl)-2-propanone, followed by the addition of 25 ml (0.065 mol) of 2.6 M n-butyl lithium in n-hexane and 9.98 g (0.0543 mol) of n-butyl iodide to give 73% of (37) and (38). Gas chromatographic examination of the solvent-stripped alkylation mixture showed a product composition of 66% (37) and 34% (38).

Compound (37) was isolated from the mixture by fractional distillation: bp  $87-88^\circ$  (0.02 mm);  $n_D^{23}$  1.5050; molecular ion  $m/e$  220 (Calcd 220); nmr ( $\text{CCl}_4$ )  $\delta$  0.7-1.6 (m, 9H, aliphatic CH), 1.6-2.0 (m, 2H, aliphatic CH), 1.95 (s, 3H,  $\text{COCH}_3$ ), 3.48 (t, 1H,  $\text{ArCHCO}$ ), 3.74 (s, 3H,  $\text{OCH}_3$ ), 6.81 (d, 2H, aryl CH), 7.05 (d, 2H, aryl CH). Anal. Calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_2$ : C, 76.36; H, 9.09. Found: C, 76.50; H, 9.06. Semicarbazone mp  $147-148^\circ$ .

Compound (38) had identical gas chromatogram and nmr spectrum to those of (38a).

10. Formation of 3-(4-chlorophenyl)-2-butanone (39) and 1-(4-chlorophenyl)-2-butanone (40)

About 7.5 g of 22% potassium hydride in mineral oil were reacted with 6.50 g (0.0386 mol) of 1-(4-chlorophenyl)-2-propanone, followed by the addition of 18 ml (0.047 mol) of 2.6 M n-butyl lithium in n-hexane and 5.52 g (0.0386 mol) of methyl iodide to give a complex mixture of products. Two of the peaks in the gas chromatogram were identical to those of (39a) and (40a) respectively. However, none of the components was isolated.

11. Formation of 3-(4-chlorophenyl)-2-pentanone (41) and 1-(4-chlorophenyl)-2-pentanone (42)

About 8.5 g of 22% potassium hydride in mineral oil were reacted with 7.31 g (0.0442 mol) of 1-(4-chlorophenyl)-2-propanone, followed by the addition of 20 ml (0.052 mol) of 2.6 M n-butyl lithium in n-hexane and 7.40 g (0.0442 mol) of ethyl iodide to give at least three gas chromatographic peaks, two of which were identical to those of (41a) and (42a) respectively. None of the components in the alkylation mixture was isolated.

12. Formation of 3-(4-chlorophenyl)-2-heptanone (43) and 1-(4-chlorophenyl)-2-heptanone (44)

About 7.5 g of 22% potassium hydride in mineral oil were reacted with 6.97 g (0.0402 mol) of 1-(4-chlorophenyl)-2-propanone, and the mixture was then treated with 19 ml (0.049 mol) of 2.6 M n-butyl lithium in n-hexane

followed by the addition of 7.61 g (0.0402 mol) of *n*-butyl iodide to give a mixture of (43), (44), and 30 to 40% 1-(4-chlorophenyl)-2-propanone. Two of the peaks in the gas chromatogram were identical to those of (43a) and (44a). No component was isolated from the mixture.

#### D. Preparation of Authentic Samples

##### 1. Formation of 3-phenyl-2-butanone (21a) from 1-phenyl-2-propanone

About 15 g of 22% potassium hydride in mineral oil were reacted with 11.58 g (0.0865 mol) of 1-phenyl-2-propanone, and the mixture was then treated with 12.30 g (0.0865 mol) of methyl iodide to give (21a): bp 46-47° (0.07 mm);  $n_D^{23}$  1.5036; molecular ion  $m/e$  148 (Calcd 148); nmr ( $CCl_4$ )  $\delta$  1.32 (d, 3H,  $CHCH_3$ ), 1.94 (s, 3H,  $COCH_3$ ), 3.67 (q, 1H,  $ArCHCO$ ), 7.20 (s, 5H, aryl CH). Anal. Calcd for  $C_{10}H_{12}O$ : C, 81.08; H, 8.11. Found: C, 80.94; H, 8.35. Semicarbazone mp 173-174°. 2,4-Dinitrophenylhydrazone mp 173-174°.

##### 2. Formation of 1-phenyl-2-butanone (22a) from benzaldehyde

A mixture of 21.2 g (0.200 mol) of benzaldehyde, 18.7 g (0.210 mol) of 1-nitropropane, and 4 ml of *n*-butylamine were refluxed vigorously, followed by reduction with 40 g (0.72 mol) of powdered iron and 72 ml of concentrated hydrochloric acid in the presence of 0.8 g of ferric chloride to give (22a): bp 46-47° (0.05 mm);  $n_D^{23}$  1.5202;



molecular ion  $m/e$  148 (Calcd 148); nmr ( $\text{CCl}_4$ )  $\delta$  0.95 (t, 3H,  $\text{CH}_2\text{CH}_3$ ), 2.35 (q, 2H,  $\text{CH}_2\text{CH}_3$ ), 3.56 (s, 2H,  $\text{ArCH}_2\text{CO}$ ), 7.17 (s, 5H, aryl CH). Anal. Calcd for  $\text{C}_{10}\text{H}_{12}\text{O}$ : C, 81.08; H, 8.11. Found: C, 79.77; H, 7.94. Semicarbazone mp 147-149°. 2,4-Dinitrophenylhydrazone mp 144-145°. Anal. Calcd for  $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O}_4$ : C, 58.54; H, 4.88. Found: C, 58.76; H, 5.16.

### 3. Formation of 3-phenyl-2-pentanone (23a) from 1-phenyl-2-propanone

About 15 g of 22% potassium hydride in mineral oil were reacted with 11.53 g (0.0861 mol) of 1-phenyl-2-propanone, and the mixture was then treated with 13.40 g (0.0861 mol) of ethyl iodide to give (23a): bp 51-52° (0.07 mm);  $n_D^{23}$  1.5000; molecular ion  $m/e$  162 (Calcd 162); nmr ( $\text{CCl}_4$ )  $\delta$  0.80 (t, 3H,  $\text{CH}_2\text{CH}_3$ ), 1.74 (m, 2H,  $\text{CHCH}_2\text{CH}_3$ ), 1.96 (s, 3H,  $\text{COCH}_3$ ), 3.46 (t, 1H,  $\text{ArCHCO}$ ), 7.19 (s, 5H, aryl CH). Anal. Calcd for  $\text{C}_{11}\text{H}_{14}\text{O}$ : C, 81.48; H, 8.64. Found: C, 81.36; H, 8.77. Semicarbazone mp 191-192°. 2,4-Dinitrophenylhydrazone mp 114-115°.

### 4. Formation of 1-phenyl-2-pentanone (24a) from benzaldehyde

A mixture of 17.0 g (0.160 mol) of benzaldehyde, 18.0 g (0.175 mol) of 1-nitrobutane, and 3.2 ml of *n*-butylamine were refluxed vigorously; the mixture was then reduced with 32 g (0.57 mol) of powdered iron and 58 ml of concentrated hydrochloric acid in the presence of 0.6 g of ferric chloride to give (24a): bp 48-49° (0.04 mm);  $n_D^{23}$

1.5078; molecular ion  $m/e$  162 (Calcd 162); nmr ( $\text{CCl}_4$ )  $\delta$  0.83 (t, 3H,  $\text{CH}_2\text{CH}_3$ ), 1.51 (m, 2H, aliphatic  $\text{CH}_2$ ), 2.32 (t, 2H,  $\text{COCH}_2\text{CH}_2$ ), 3.55 (s, 2H,  $\text{ArCH}_2\text{CO}$ ), 7.18 (s, 5H, aryl CH). Anal. Calcd for  $\text{C}_{11}\text{H}_{14}\text{O}$ : C, 81.48; H, 8.64. Found: C, 80.52; H, 8.48. Semicarbazone mp 165-168°. 2,4-Dinitrophenylhydrazone mp 130-131°. Anal. Calcd for  $\text{C}_{17}\text{H}_{18}\text{N}_4\text{O}_4$ : C, 59.65; H, 5.27. Found: C, 59.25; H, 5.33.

#### 5. Formation of 1-phenyl-2-heptanone (26a) from benzaldehyde

A mixture of 15.8 g (0.150 mol) of benzaldehyde, 19.6 g (0.150 mol) of 1-nitrohexane, and 3.0 ml of *n*-butylamine were refluxed vigorously; the mixture was then reduced with 30 g (0.54 mol) of powdered iron and 54 ml of concentrated hydrochloric acid in the presence of 0.6 g ferric chloride to give (26a): bp 69-70° (0.05 mm);  $n_D^{23}$  1.4980; molecular ion  $m/e$  190 (Calcd 190); nmr ( $\text{CCl}_4$ ) 0.7-1.7 (m, 9H, aliphatic CH), 2.33 (t, 2H,  $\text{COCH}_2\text{CH}_2$ ),  $\delta$  3.56 (s, 2H,  $\text{ArCH}_2\text{CO}$ ), 7.18 (s, 5H, aryl CH). Anal. Calcd for  $\text{C}_{13}\text{H}_{18}\text{O}$ : C, 82.10; H, 9.47. Found: C, 81.71; H, 9.23. Semicarbazone mp 125-128°.

#### 6. Formation of 1-(4-methylphenyl)-2-pentanone (30a) from para-tolualdehyde

A mixture of 8.4 g (0.070 mol) of *para*-tolualdehyde, 7.53 g (0.073 mol) of 1-nitrobutane, and 1.4 ml of *n*-butylamine were refluxed vigorously; the mixture was then reduced with 14 g of powdered iron and 20 ml of concentrated hydrochloric acid in the presence of 0.3 g of fer-

ric chloride to give (30a): bp 62-63° (0.04 mm);  $n_D^{23}$  1.5048; molecular ion m/e 176 (Calcd 176); nmr ( $CCl_4$ )  $\delta$  0.82 (t, 3H,  $CH_2CH_3$ ), 1.51 (m, 2H, aliphatic CH), 2.29 (s, 3H, benzyl  $CH_3$ ), 2.30 (t, 2H,  $COCH_2CH_2$ ), 3.49 (s, 2H,  $ArCH_2CO$ ), 7.02 (s, 4H, aryl CH). Anal. Calcd for  $C_{12}H_{16}O$ : C, 81.82; H, 9.09. Found: C, 81.64; H, 8.99. Semicarbazone mp 142-143°. 2,4-Dinitrophenylhydrazone mp 106-107°.

#### 7. Formation of 1-(4-methylphenyl)-2-heptanone (32a) from para-tolualdehyde

A mixture of 18.0 g (0.150 mol) of para-tolualdehyde, 19.6 g (0.150 mol) of 1-nitrohexane, and 3.0 ml of n-butylamine were refluxed vigorously; the mixture was then reduced with 30 g (0.54 mol) of powdered iron and 54 ml of concentrated hydrochloric acid in the presence of 0.6 g ferric chloride to give (32a): bp 82-83° (0.03 mm);  $n_D^{23}$  1.4960; molecular ion m/e 204 (Calcd 204); nmr ( $CCl_4$ )  $\delta$  0.7-1.7 (m, 9H, aliphatic CH), 2.90 (s, 3H, benzyl  $CH_3$ ), 2.9 (t, 2H,  $COCH_2CH_2$ ), 3.50 (s, 2H,  $ArCH_2CO$ ), 7.02 (s, 4H, aryl CH). Anal. Calcd for  $C_{14}H_{20}O$ : C, 82.35; H, 9.80. Found: C, 81.29; H, 10.56. Semicarbazone mp 100-104°. Anal. Calcd for  $C_{15}H_{23}N_3O$ : C, 68.97; H, 8.80. Found: C, 69.55; H, 8.87. 2,4-Dinitrophenylhydrazone mp 93-94°.

#### 8. Formation of 3-(4-methoxyphenyl)-2-butanone (33a) from 1-(4-methoxyphenyl)-2-propanone

About 15 g of 22% potassium hydride in mineral oil were reacted with 14.5 g (0.0885 mol) of 1-(4-methoxyphenyl)-2-propanone, and the mixture was then treated with 12.6 g (0.0885 mol) of methyl iodide to give (33a): bp

70-71° (0.04 mm);  $n_D^{23}$  1.5108; molecular ion  $m/e$  178 (Calcd 178); nmr ( $CCl_4$ )  $\delta$  1.28 (d, 3H,  $CH_2CH_3$ ), 1.93 (s, 3H,  $COCH_3$ ), 3.60 (q, 1H,  $CHCH_3$ ), 3.74 (s, 3H,  $OCH_3$ ), 6.80 (d, 2H, aryl CH), 7.06 (d, 2H, aryl CH). Anal Calcd for  $C_{11}H_{14}O_2$ : C, 74.16; H, 7.86. Found: C, 74.09; H, 8.08. Semicarbazone mp 184-185°. 2,4-Dinitrophenylhydrazone mp 135-136°.

9. Formation of 1-(4-methoxyphenyl)-2-butanone (34a) from para-anisaldehyde

A mixture of 27.2 g (0.200 mol) para-anisaldehyde, 18.7 g (0.210 mol) of 1-nitropropane, and 4 ml of n-butylamine were refluxed vigorously; the mixture was then reduced with 40 g (0.72 mol) of powdered iron and 72 ml of concentrated hydrochloric acid in the presence of 0.8 g ferric chloride to give (34a): bp 73-74° (0.03 mm);  $n_D^{23}$  1.5175; molecular ion  $m/e$  178 (Calcd 178); nmr ( $CCl_4$ )  $\delta$  0.94 (t, 3H,  $CH_2CH_3$ ), 2.35 (q, 2H,  $COCH_2CH_3$ ), 3.48 (s, 2H,  $ArCH_2CO$ ), 3.72 (s, 3H,  $OCH_3$ ), 6.76 (d, 2H, aryl CH), 7.02 (d, 2H, aryl CH). Anal. Calcd for  $C_{11}H_{14}O_2$ : C, 74.16; H, 7.86. Found: C, 73.77; H, 7.81. Semicarbazone mp 146-147°. 2,4-Dinitrophenylhydrazone mp 110-111°.

10. Formation of 1-(4-methoxyphenyl)-2-pentanone (36a) from para-anisaldehyde

A mixture of 13.7 g (0.100 mol) para-anisaldehyde, 11.8 g (0.114 mol) of 1-nitrobutane, and 2 ml of n-butylamine were refluxed vigorously; the mixture was then reduced with 20 g (0.36 mol) of powdered iron and 36 ml of

concentrated hydrochloric acid in the presence of 0.4 g ferric chloride to give (36a): bp  $81-82^{\circ}$  (0.04 mm);  $n_D^{23}$  1.5118; molecular ion  $m/e$  192 (Calcd 192); nmr ( $CCl_4$ )  $\delta$  0.82 (t, 3H,  $CH_2CH_3$ ), 1.51 (m, 2H, aliphatic  $CH_2$ ), 2.30 (t, 2H,  $COCH_2CH_2$ ), 3.48 (s, 2H,  $ArCH_2CO$ ), 3.72 (s, 3H,  $OCH_3$ ), 6.72 (d, 2H, aryl CH), 7.02 (d, 2H, aryl CH). Anal. Calcd for  $C_{12}H_{16}O_2$ : C, 75.00; H, 8.33. Found: C, 73.16; H, 7.99. Semicarbazone mp  $141-142^{\circ}$ . Anal. Calcd for  $C_{13}H_{19}N_3O_2$ : C, 62.65; H, 7.61. Found: C, 61.40; H, 7.36.

11. Formation of 1-(4-methoxyphenyl)-2-heptanone (38a) from para-anisaldehyde

A mixture of 21.4 g (0.150 mol) para-anisaldehyde, 19.6 g (0.150 mol) of 1-nitrohexane, and 3 ml of n-butylamine were refluxed vigorously; the mixture was then reduced with 30 g (0.54 mol) of powdered iron and 54 ml of concentrated hydrochloric acid in the presence of 0.6 g ferric chloride to give (38a): bp  $101-102^{\circ}$  (0.02 mm);  $n_D^{23}$  1.5020; molecular ion  $m/e$  220 (Calcd 220); nmr ( $CCl_4$ )  $\delta$  0.7-2.0 (m, 11H, aliphatic CH), 2.32 (t, 2H,  $COCH_2CH_2$ ), 3.48 (s, 2H,  $ArCH_2CO$ ), 3.73 (s, 3H,  $OCH_3$ ), 6.78 (d, 2H, aryl CH), 7.02 (d, 2H, aryl CH). Anal. Calcd for  $C_{14}H_{20}O_2$ : C, 76.36; H, 9.09. Found: C, 76.47; H, 9.30.

12. Formation of 3-(4-chlorophenyl)-2-butanone (39a) from 1-(4-chlorophenyl)-2-propanone

About 7 g of 22% potassium hydride in mineral oil were reacted with 6.65 g (0.0395 mol) of 1-(4-chlorophenyl)-2-propanone, and the mixture was then treated with

5.61 g (0.0395 mol) of methyl iodide to give (39a): bp 61-62° (0.04 mm);  $n_D^{23}$  1.5222; molecular ion m/e 182 (Calcd 182); nmr ( $\text{CCl}_4$ )  $\delta$  1.22 (d, 3H,  $\text{CHCH}_3$ ), 1.98 (s, 3H,  $\text{COCH}_3$ ), 3.68 (q, 1H,  $\text{CHCH}_3$ ), 7.24 (d, 4H, aryl CH). Anal. Calcd for  $\text{C}_{10}\text{H}_{11}\text{ClO}$ : C, 65.75; H, 6.03; Cl, 19.46. Found: C, 65.80; H, 6.16; Cl, 19.79. Semicarbazone mp 197-198°. 2,4-Dinitrophenylhydrazone mp 113-114°.

13. Formation of 1-(4-chlorophenyl)-2-butanone (40a) from para-chlorobenzaldehyde

A mixture of 28.0 g (0.200 mol) para-chlorobenzaldehyde, 18.7 g (0.210 mol) of 1-nitropropane, and 4 ml of n-butylamine were refluxed vigorously; the mixture was then reduced with 40 g (0.72 mol) of powdered iron and 72 ml of concentrated hydrochloric acid in the presence of 0.8 g ferric chloride to give (40a): bp 70-71° (0.04 mm);  $n_D^{23}$  1.5286; molecular ion m/e 182 (Calcd 182); nmr ( $\text{CCl}_4$ )  $\delta$  0.97 (t, 3H,  $\text{CH}_2\text{CH}_3$ ), 2.38 (q, 2H,  $\text{COCH}_2\text{CH}_3$ ), 3.56 (s, 2H,  $\text{ArCH}_2\text{CO}$ ), 7.14 (d, 4H, aryl CH). Anal. Calcd for  $\text{C}_{10}\text{H}_{11}\text{ClO}$ : C, 65.75; H, 6.03; Cl, 19.45. Found: C, 65.48; H, 6.10; Cl, 19.46. Semicarbazone mp 162-164°. 2,4-dinitrophenylhydrazone mp 125-126°.

14. Formation of 3-(4-chlorophenyl)-2-pentanone (41a) from 1-(4-chlorophenyl)-2-propanone

About 7 g of 22% potassium hydride in mineral oil were reacted with 6.35 g (0.0376 mol) of 1-(4-chlorophenyl)-2-propanone, and the mixture was then treated with 5.88 g (0.0376 mol) of ethyl iodide to give (41a): bp

67-68° (0.03 mm);  $n_D^{23}$  1.5150; molecular ion  $m/e$  196 (Calcd 196); nmr ( $CCl_4$ )  $\delta$  0.82 (t, 3H,  $CH_2CH_3$ ), 1.84 (m, 2H, aliphatic CH), 1.99 (s, 3H,  $COCH_3$ ), 3.48 (t, 1H,  $CHCH_2$ ), 7.20 (d, 4H, aryl CH). Anal. Calcd for  $C_{11}H_{13}ClO$ : C, 67.18; H, 6.62; Cl, 18.07. Found: C, 67.60; H, 6.10; Cl, 17.90. Semicarbazone mp 171-172°. 2,4-Dinitrophenylhydrazone mp 128-129°.

15. Formation of 1-(4-chlorophenyl)-2-pentanone (42a) from para-chlorobenzaldehyde

A mixture of 6.4 g (0.046 mol) para-chlorobenzaldehyde, 4.7 g (0.046 mol) of 1-nitrobutane, and 1 ml of n-butylamine were refluxed vigorously; the mixture was then reduced with 10 g (0.18 mol) of powdered iron and 18 ml of concentrated hydrochloric acid in the presence of 0.2 g of ferric chloride to give (42a): bp 75-76° (0.03 mm);  $n_D^{23}$  1.5212; molecular ion  $m/e$  196 (Calcd 196); nmr ( $CCl_4$ )  $\delta$  0.85 (t, 3H,  $CH_2CH_3$ ), 1.54 (m, 2H, aliphatic  $CH_2$ ), 2.35 (t, 2H,  $COCH_2CH_2$ ), 3.55 (s, 2H,  $ArCH_2CO$ ), 7.14 (d, 4H, aryl CH). Anal. Calcd for  $C_{11}H_{13}ClO$ : C, 67.18; H, 6.62; Cl, 18.07. Found: C, 66.56; H, 6.58; Cl, 17.59. Semicarbazone mp 128-133°. 2,4-Dinitrophenylhydrazone mp 95-98°. Anal. Calcd for  $C_{17}H_{17}ClN_4O_4$ : C, 54.18; H, 4.51. Found: C, 54.30; H, 4.67.

16. Formation of 3-(4-chlorophenyl)-2-heptanone (43a) from 1-(4-chlorophenyl)-2-propanone

About 7 g of 22% potassium hydride in mineral oil were reacted with 6.25 g (0.0370 mol) of 1-(4-chloro-

phenyl)-2-propanone, and the mixture was then treated with 6.82 g (0.0370 mol) of *n*-butyl iodide to give (43a): bp 84-85° (0.03 mm);  $n_D^{23}$  1.5070; molecular ion  $m/e$  224 (Calcd 224); nmr ( $CCl_4$ )  $\delta$  0.7-1.8 (m, 9H, aliphatic CH), 1.98 (s, 3H,  $COCH_3$ ), 3.55 (t, 1H,  $CHCH_2$ ), 7.19 (d, 4H, aryl CH). Anal. Calcd for  $C_{13}H_{17}ClO$ : C, 69.49; H, 7.57; Cl, 15.81. Found: C, 70.47; H, 7.73; Cl, 14.78. Semicarbazone mp 147-148°. Anal. Calcd for  $C_{14}H_{20}ClN_3O$ : C, 59.68; H, 7.12. Found: C, 60.23; H, 7.12. 2,4-Dinitrophenylhydrazone mp 111-112°.

17. Formation of 1-(4-chlorophenyl)-2-heptanone (44a) from para-chlorobenzaldehyde

A mixture of 8.0 g (0.057 mol) para-chlorobenzaldehyde, 7.5 g (0.057 mol) of 1-nitrohexane, and 1.2 ml of *n*-butylamine were refluxed vigorously; the mixture was then reduced with 13 g (0.25 mol) of powdered iron and 25 ml of concentrated hydrochloric acid in the presence of 0.3 g ferric chloride to give (44a): bp 90-91° (0.02 mm);  $n_D^{23}$  1.5114; molecular ion  $m/e$  224 (Calcd 224); nmr ( $CCl_4$ )  $\delta$  0.7-1.8 (m, 9H, aliphatic CH), 2.37 (t, 2H,  $COCH_2CH_2$ ), 3.55 (s, 2H,  $ArCH_2CO$ ), 7.15 (d, 4H, aryl CH). Anal. Calcd for  $C_{13}H_{17}ClO$ : C, 69.49; H, 7.57; Cl, 15.81. Found: C, 69.27; H, 7.48; Cl, 15.34.



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