A Study of Electronic and Steric Effects on the Course of an Aromatic Cyclodehydration Reaction *vs.* an Elbs Reaction

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The effect of substituents on the course of an aromatic cyclodehydration reaction and an Elbs reaction was investigated by synthesizing six 2-benzylphenyl 1- and 2-naphthyl ketones and subjecting each to reaction conditions which should favor one or the other of these reactions. The reaction products were analyzed and the results were interpreted.

Both the Elbs[2] reaction and the aromatic cyclodehydration reaction discovered by Bradsher[3] are well-known, valuable synthetic procedures. The usual conditions for an Elbs reaction involve high-temperature pyrolysis with no solvent or catalyst present. On the other hand, the Bradsher cyclodehydration reaction usually involves a relatively low temperature acid-catalyzed reaction in homogeneous solution. It was therefore rather surprising to find[4] that the homogeneous acid-catalyzed cyclization of 2-benzylphenyl 1-naphthyl ketone gave almost equal amounts of 9-(1-naphthyl)anthracene, the product expected from the aromatic cyclodehydration reaction, and 7-phenylbenz[*a*]anthracene, the product resulting from an Elbs reaction, the total yield being almost quantitative. It was further found that 2-(2-naphthylmethyl)phenyl 1-naphthyl ketone gave no aromatic cyclodehydration product, 12-naphthylbenz[*a*]anthracene, but only Elbs product, 7-(2-naphthyl)benz[*a*]anthracene. This brief, initial study[4] did not consider the effects of substituents on the course of these reactions.

In order to maximize the information which might be derived from the data, the series of ketones shown in Chart I was prepared, using well-documented methods.[5] In the case of the ketones bearing substituents, **3**–**6**, the substituent was put in the phenyl ring of the benzyl moiety and *para* to the predicted point of cyclization in order to maximize electronic effects.[6]

Using ketone **1** as a standard, the effects of the electron-donating CH_3 group and the electron-attracting CF_3 group can be observed by studying the reactions of ketones **3** and **5**. In each case the substituent is too far removed from the reaction site to cause a steric effect.

Each of the α-naphthyl ketones **1**, **3**, and **5** has an isomeric β-naphthyl counterpart, **2**, **4**, and **6**. Knowing the mechanism of the reaction,[6] we realize that by studying each pair, **1** and **2**, **3** and **4**, and **5** and **6**, we have removed electronic considerations and may now get information regarding the possible importance of steric effects.

Each of the six ketones was subjected to a given set of reaction conditions which would be expected to give aromatic cyclodehydration product or Elbs product, and the products of the reaction were identified.

A. Hydrobromic Acid–Glacial Acetic Acid Procedure.—Each of the ketones was allowed to react in a solution of hydrobromic and glacial acetic acids heated under reflux. If no reaction occurred after 15 hr, the reaction was repeated in a sealed Carius tube at 200° for 3 hr. The results of these experiments are summarized in Table I.

The 2-(3-methylbenzyl)phenyl 1- and 2-naphthyl ketones (**3** and **4**) gave somewhat higher yields of aromatic cyclodehydration product than the unsubstituted benzylphenyl naphthyl ketones (**1** and **2**). This might be explained on the basis of the electron release capability of the methyl group which increases the electron density at the position undergoing attack by the carbonium ion.[6] In contrasting ketones **2** with **1** and **4** with **3**, it can be seen that, when the linkage is through the 2-position of the naphthyl structure, the yields of aromatic cyclodehydration are very high. It would appear that the less sterically hindered ketones undergo reaction much more readily than their hindered counterparts. Finally, the presence of a trifluoromethyl group in **5** and **6** renders these structures essentially inert under the experimental conditions used.

B. Elbs Reaction.—Each of the ketones was mixed with powdered zinc and heated at 430° for 3 hr in the absence of oxygen. The same results are obtained if the zinc is omitted; however, heat transfer is probably aided when zinc is used since less charring occurs. The results of these experiments are summarized in Table II and are as one might have predicted with one notable exception. The formation of 2-methyl-10-(2-naphthyl)anthracene (**13**) from 2-(3-methylbenzyl)-phenyl-2-naphthyl ketone (**4**) was quite surprising.

C. Cyclodehydration with Alumina.—Each of the ketones was mixed with alumina and heated for 2.5 hr at 250°.[4] The results of these experiments are summarized in Table III and illustrate that cyclization into a naphthyl group is preferred over cyclization into a phenyl group and formation of a 7-substituted benz[*a*]anthracene is preferred over the corresponding 12 isomer. Ketones **1** and **2** give the product expected from an Elbs reaction, whereas ketones **3** and **4** give the product expected from the aromatic cyclodehydration reaction. Again the trifluoromethyl group supresses both cyclizations.

D. Cyclization with Liquid Hydrogen Fluoride.—Each of the ketones was mixed with liquid hydrogen fluoride and the solutions were allowed to stand at room temperature until the acid had evaporated. The results are summarized in Table IV. Apparently liquid hydrogen fluoride is a mild reagent for these

(1) Abstracted from the Doctorate Thesis of J. R. T. presented to the Virginia Polytechnic Institute, 1963.

(2) L. F. Fieser, *Org. Reactions*, **1**, 129 (1942).

(3) C. K. Bradsher, *J. Am. Chem. Soc.*, **62**, 486 (1940).

(4) F. A. Vingiello, A. Borkovec, and W. Zajac, Jr., *ibid.*, **80**, 1714 (1958).

(5) (a) F. A. Vingiello, J. G. Van Oot, and H. H. Hannabass, *ibid.*, **74**, 4546 (1952); (b) F. A. Vingiello and A. Borkovec, *ibid.*, **77**, 3413 (1955).

(6) This statement is based on a currently accepted mechanism for this reaction[3a] which reveals that any changes in electronic effects due to changes in the position of attachment of the naphthyl group, or the placing of substituents therein, would cancel and hence only steric factors would be important if such changes were made.

CHART I

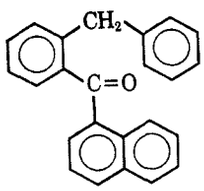
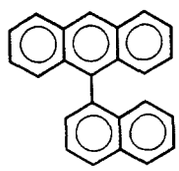
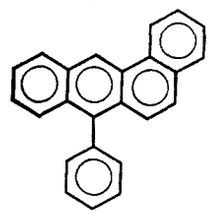
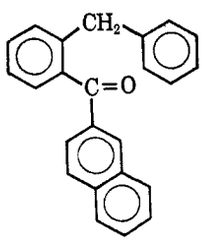
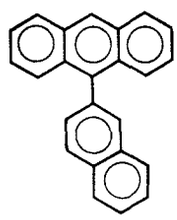
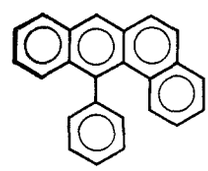
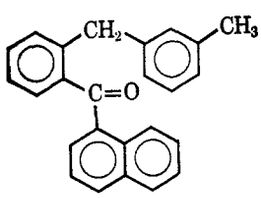
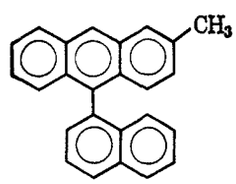
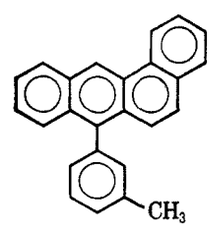
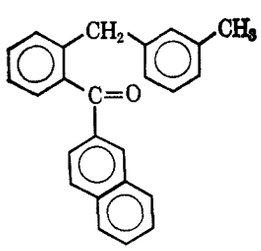
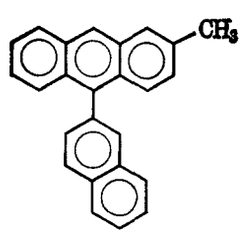
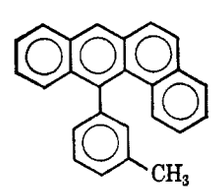
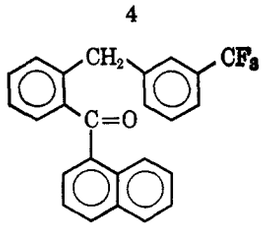
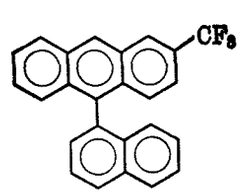
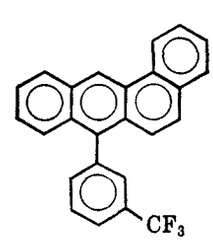
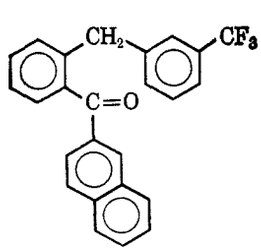
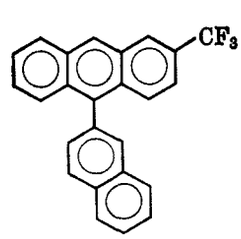
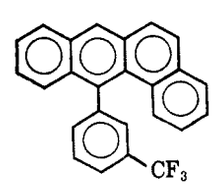
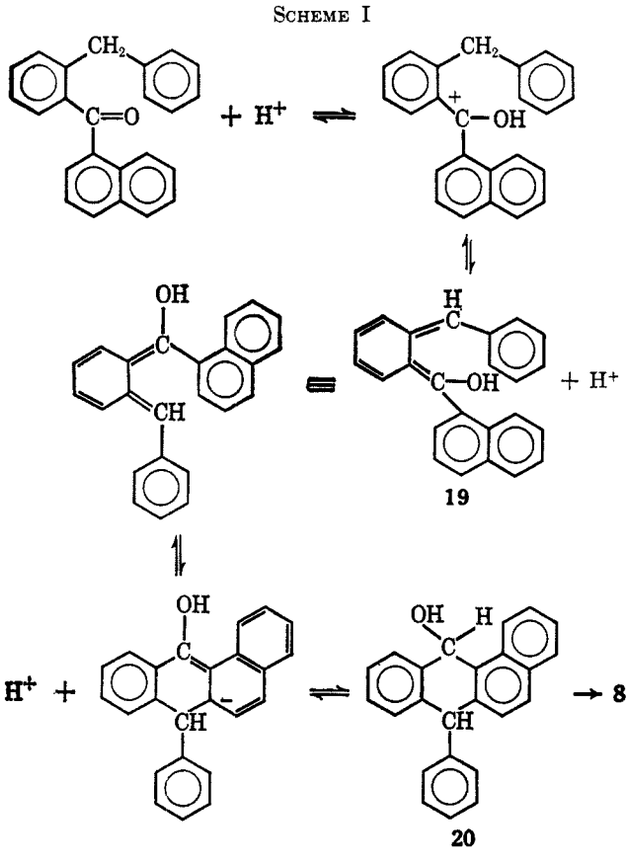
Ketone	Aromatic cyclodehydration product	Elbs reaction product
 1	 7	 8
 2	 9	 10
 3	 11	 12
 4	 13	 14
 5	 15	 16
 6	 17	 18

TABLE I

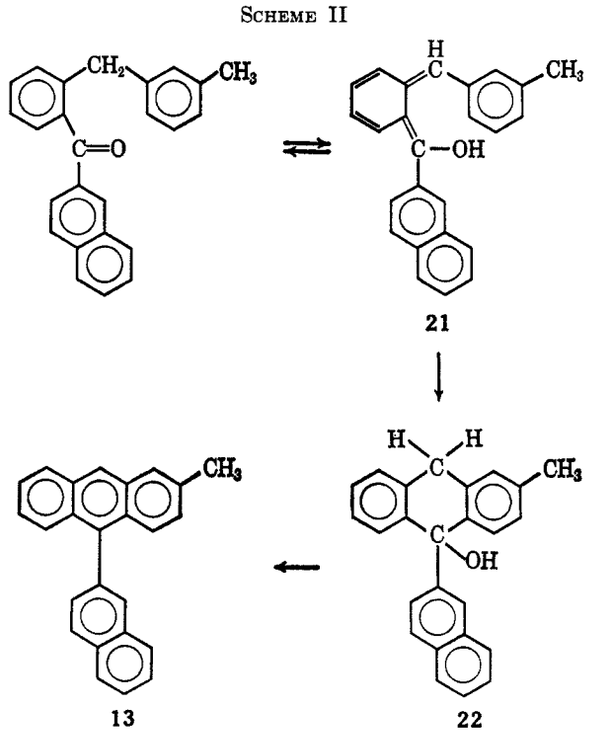
SUMMARY OF RESULTS OF HYDROBROMIC ACID–GLACIAL ACETIC ACID REACTIONS

Ketone used, amount, g, and conditions	Product and yield, g (%)		Starting material recovered, g
	Aromatic cyclodehydration	Elbs reaction	
2-Benzylphenyl 1-naphthyl ketone (**1**)	9-(1-Naphthyl)anthracene (**7**)	7-Phenylbenz[*a*]anthracene (**8**)	
2.0, sealed tube	0.2 (11)	0.2 (11)	...
1.5, reflux	...	...	1.1
2-Benzylphenyl 2-naphthyl ketone (**2**)	9-(2-Naphthyl)anthracene (**9**)	12-Phenylbenz[*a*]anthracene (**10**)	
1.5, reflux	1.2 (86)	...	0.1
2-(3-Methylbenzyl)phenyl 1-naphthyl ketone (**3**)	2-Methyl-10-(1-naphthyl)anthracene (**11**)	7-(3-Methylphenyl)benz[*a*]anthracene (**12**)	
4.0, sealed tube	1.3 (29)	...	...
2-(3-Methylbenzyl)phenyl 2-naphthyl ketone (**4**)	2-Methyl-10-(2-naphthyl)anthracene (**13**)	12-(3-Methylphenyl)benz[*a*]anthracene (**14**)	
1.5, reflux	1.3 (93)	...	...
2-(3-Trifluoromethylbenzyl)phenyl 1-napthyl ketone (**5**)	2-Trifluoromethyl-10-(1-naphthyl)-anthracene (**15**)	7-(3-Trifluoromethylphenyl)benz[*a*]-anthracene (**16**)	
3.0, sealed tube	...	...	1.9
1.6, reflux	...	...	1.4
2-(3-Trifluoromethylbenzyl)phenyl 2-naphthyl ketone (**6**)	2-Trifluoromethyl-10-(2-naphthyl)-anthracene (**17**)	12-(3-Trifluoromethylbenzyl)benz[*a*]-anthracene (**18**)	
1.5, sealed tube	...	...	0.9

SCHEME I



SCHEME II



cyclizations and only under the most favorable electronic and steric conditions does cyclization occur. Only aromatic cyclodehydration product was obtained. The favorable effect of the methyl group, the inhibiting effect of the trifluoromethyl group, and the importance of the steric factor are all clearly indicated.

The formation of 7-phenylbenz[*a*]anthracene when 2-benzylphenyl 1-naphthyl ketone is treated with hydrobromic and acetic acids is an unexpected result. A possible mechanism for this unusual reaction could begin with the reversible protonation of the ketone to give a Cook-type intermediate.[7] This might then cyclize with loss of a proton from the point of cyclization followed by regaining of the proton to give the anthranol **20** which one would expect would easily lose water transannularly to give the final product **8** (Scheme I).

The formation of 2-methyl-10-(2-naphthyl)anthracene *via* the pyrolysis of 2-(3-methylbenzyl)phenyl 2-naphthyl ketone is also unusual. This reaction may also proceed through a Cook-type intermediate,[7] **21**. This might then cyclize by attack on the electron-rich position *para* to the methyl group, followed by loss of a proton from that position and the addition of a proton to form the anthranol (**22**) which we would expect would easily lose water transannularly to give the final product **13** (Scheme II).

(7) J. W. Cook, *J. Chem. Soc.*, 487 (1931).

TABLE II

SUMMARY OF RESULTS OF ELBS REACTIONS[a]

Ketone	Product and yield, g (%)
2-Benzylphenyl 1-naphthyl ketone (1)	7-Phenylbenz[a]anthracene (8), 0.9 (32)
2-Benzylphenyl 2-naphthyl ketone (2)	12-Phenylbenz[a]anthracene (10), 0.3 (11)[b]
2-(3-Methylbenzyl)phenyl 1-naphthyl ketone (3)	7-(3-Methylphenyl)benz[a]anthracene (12), 0.3 (11)
2-(3-Methylbenzyl)phenyl 2-naphthyl ketone (4)	2-Methyl-10-(2-naphthyl)anthracene[c] (13), 0.8 (29)
2-(3-Trifluoromethylbenzyl)phenyl 1-naphthyl ketone (5)	No identifiable product
2-(3-Trifluoromethylbenzyl)phenyl 2-naphthyl ketone (6)	Starting material recovered, 0.2 g

[a] 3 g of ketone and 1 g of powdered zinc was heated for 3 hr at 430°. [b] 0.4 g of starting material was recovered. [c] It should be noted that this is the product expected from the aromatic cyclodehydration reaction; no Elbs product was found.

TABLE III

SUMMARY OF RESULTS OF CYCLODEHYDRATION REACTIONS USING ALUMINA[a]

Ketone	Product and yield, g (%)
2-Benzylphenyl 1-naphthyl ketone (1)	7-Phenylbenz[a]anthracene (8), 0.2 (14)
2-Benzylphenyl 2-naphthyl ketone (2)	12-Phenylbenz[a]anthracene (10), 0.1 (7)[b]
2-(3-Methylbenzyl)phenyl 1-naphthyl ketone (3)	2-Methyl-10-(1-naphthyl)anthracene (11), 0.2 (14)
2-(3-Methylbenzyl)phenyl 2-naphthyl ketone (4)	2-Methyl-10-(2-naphthyl)anthracene (13), 0.7 (50)
2-(3-Trifluoromethylbenzyl)phenyl 1-naphthyl ketone (5)	No product or starting material
2-(3-Trifluoromethylbenzyl)phenyl 2-naphthyl ketone (6)	No product or starting material

[a] 1.5 g of ketone and 15 g of alumina were heated for 2.5 hr at 250°. [b] 0.2 g of starting material was recovered.

TABLE IV

SUMMARY OF RESULTS OF LIQUID HYDROGEN FLUORIDE CYCLIZATIONS[a]

Ketone	Product and yield, g (%)	Starting material recovered, g
2-Benzylphenyl 1-naphthyl ketone (1)	...	1.1
2-Benzylphenyl 2-naphthyl ketone (2)	9-(2-Naphthyl)anthracene (9), 0.2 (14)	1.2
2-(3-Methylbenzyl)phenyl 1-naphthyl ketone (3)	2-Methyl-10-(1-naphthyl)anthracene (11), 0.4 (28)	0.6
2-(3-Methylbenzyl)phenyl 2-naphthyl ketone (4)	2-Methyl-10-(2-naphthyl)anthracene (13), 0.1 (72)	...
2-(3-Trifluoromethylbenzyl)phenyl 1-naphthyl ketone (5)	...	1.3
2-(3-Trifluoromethylbenzyl)phenyl 2-naphthyl ketone (6)	...	1.4

[a] 1.5 g of ketone was added to about 60 ml of liquid hydrogen fluoride and the solution was stirred at room temperature until the acid had evaporated.

TABLE V

NEW KETONES[a,b]

Ketone	Yield, %	Mp, °C	Bp, °C	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found
3	86	68–70	250–253	89.24	89.04	6.00	5.96
4	68	57.5–58	261–264	89.24	88.90	6.00	5.86
5	61	67–69	238–240	76.90	77.39	4.40	4.53
6	68	73–73.5	244–247	76.90	76.77	4.40	4.71

[a] All ketones had similar infrared absorption spectra and each showed a carbonyl peak at about 6.05 μ as expected. Distillations were performed at 1 mm. [b] Ketones 1 and 2 had been prepared earlier in our laboratory and the preparations are recorded in ref 4.

Experimental Section[8–10]

2-(3-Methylbenzyl)phenyl 1-Naphthyl Ketone (3).—A Grignard reagent was prepared from 37.5 g (0.18 mole) of 1-bromonaphthalene and 4.4 g (0.18 g-atom) of magnesium in 200 ml of dry ether. After the magnesium had reacted, the ether was replaced with a solution of 25 g (0.12 mole) of 2-(3-methylbenzyl)benzonitrile in 200 ml of dry toluene. The mixture was then heated under reflux overnight, and the adduct was decomposed with 5 *N* sulfuric acid. An additional 225 ml of 5 *N* sulfuric acid was added and the mixture was heated under reflux for 30 hr. The product was worked up in the usual way. The product distilled as a clear viscous, pale yellow oil, bp 250–253° (1 mm), yield 35.1 g (86%). The product was redistilled and an analytical sample was taken at 249° (1 mm).

Anal. Calcd for $C_{25}H_{20}O$: C. 89.24; H. 6.00. Found: C. 89.04; H. 5.96.

After standing several weeks, a duplicate analytical sample crystallized and had mp 68–70°.

The other ketones were prepared in a similar way. See Table V for the data on the new ketones.

The procedure for each of the four different cyclization experiments is illustrated below. The complete data are to be found in tables presented earlier.

Hydrobromic Acid–Glacial Acetic Acid Cyclization Procedure. A. 2-Methyl-9-(2-naphthyl)anthracene (13).—A mixture of 1.5 g of 2-(3-methylbenzyl)phenyl 2-naphthyl ketone, 15 ml of 48% hydrobromic acid, and 30 ml of glacial acetic acid was heated under reflux for 15 hr. The mixture was cooled and filtered, and the filtrate was extracted with benzene. The solid was dissolved in benzene and this solution was combined with the benzene extract. The solution was washed with water, then with 10% sodium hydroxide solution, and again with water. The benzene was removed by distillation, leaving a brown oil which crystallized when 95% ethanol was added. Two recrystallizations from ethanol gave 1.3 g (93%) of 2-methyl-9-(2-naphthyl)anthracene, mp 162–162.5°, which had an ultraviolet spectrum typical of an anthracene.

Anal. Calcd for $C_{25}H_{18}$: C, 94.32; H, 5.69. Found: C, 94.03; H, 5.90.

B. 2-Methyl-9-(1-naphthyl)anthracene (11).—A mixture of 4.0 g of 2-(3-methylbenzyl)phenyl 1-naphthyl ketone, 15 ml of

(8) Melting points are corrected; boiling points are not.

(9) Analyses were by Geller Laboratories, Bardonia, N. Y.

(10) The alumina used throughout this work was Fisher's alumina for chromatographic analysis, 80–200 mesh, and was dried at 350° (1 mm) for 1 hr before use.

48% hydrobromic acid, and 30 ml of glacial acetic acid was sealed in a Carius tube and heated for 3 hr at 200°. The product was worked up in the usual way and purified by chromatography on alumina with petroleum ether (bp 30–60°). The yield of **11** was 1.3 g (34%), mp 152–152.5°. The product had an ultraviolet spectrum typical of an anthracene.

Anal. Calcd for $C_{25}H_{18}$: C, 94.32; H, 5.69. Found: C, 94.46; H, 5.59.

Elbs Reaction Procedure.—A mixture of 3 g of 2-benzylphenyl 1-naphthyl ketone and 1 g of powdered zinc was heated for 3 hr at 415–430° in an atmosphere of nitrogen. The product was worked up in the usual way and purified by chromatography on alumina with petroleum ether. The product was 0.9 g (32%) of 7-phenylbenz[*a*]anthracene, mp 182–183°. No other products were isolated.

Cyclodehydration Procedure Using Alumina.—A mixture of 1.5 g of 2-benzylphenyl 1-naphthyl ketone and 15 g of alumina was heated at 250° for 2.5 hr at a pressure of 1 mm. After cooling, the alumina was poured onto a chromatography column packed with alumina and the product was eluted with petroleum ether. Only 7-phenylbenz[*a*]anthracene was obtained: 0.2 g (14%), mp 182–183°.

Cyclodehydration Procedure Using Liquid Hydrogen Fluoride.—The ketone, 1.5 g of 2-benzylphenyl 2-naphthyl ketone, was placed in a 125-ml polyethylene bottle and the bottle was half-filled with liquid hydrogen fluoride. During the addition, the mixture was stirred with a magnetic stirring bar. After the addition, the solution was allowed to stand without stirring until the hydrogen fluoride had evaporated. The oil was dissolved in benzene and washed with water. The oil that was left after removal of the benzene crystallized on addition of ethanol. Recrystallization of this material from ethanol gave 0.2 g (14%) of 9-(2-naphthyl)anthracene, mp 199.5–200°. Concentration of the mother liquor gave 1.2 g of starting material.

Alkylation of Unsymmetrical β-Diketones through Isomeric Disodio Salts in Liquid Ammonia. Structural Effects on Ease of Dianion Formation[1]

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A study was made of structural effects on the relative ease of secondary ionization at methyl, methylene, and methinyl sites of unsymmetrical β-diketones by sodium amide in liquid ammonia to form disodio salts. The relative ease of ionization at the secondary sites was phenylacetyl > acetyl > propionyl > isobutyryl. This was determined by alkylation of disodio salts of unsymmetrical diketones and analysis of the reaction mixtures for the isomeric alkylation products. Moreover, in an intermolecular comparison of secondary ionizations the relative ease of ionization at the methyl and γ-methylene sites of acetylacetone and dipropionylmethane, respectively, was found to be acetyl > propionyl, but in this intermolecular comparison the difference was not so great as that observed in the intramolecular one. These results show that many unsymmetrical β-diketones can be alkylated through only one of the two possible disodio salts to form a single product essentially uncontaminated by the isomeric one.

Alkylations at the terminal methyl group (a-position) of unsymmetrical β-diketone **1** with benzyl chloride has previously been effected by means of 2 molecular equiv of potassium amide in liquid ammonia, which converted **1** to dipotassio salt **1''**.[2,3] No alkylation at the b-position of **1** was observed.[2] Similarly, exclusive benzylation at the terminal methyl group of 2-acetylcyclohexanone and 2-acetylcyclopentanone was reported.[2]

$$\underset{\mathbf{1}}{\overset{\text{a}\quad\text{b}}{CH_3COCH_2COCH_2CH_2C_6H_5}} \qquad \underset{\mathbf{1''}}{\overset{\text{K}}{KCH_2COCHCOCH_2CH_2C_6H_5}}$$

We have now determined the relative extents of methylation at such a- and b-positions of four other unsymmetrical β-diketones through their disodio salts in liquid ammonia. The disodio salts were chosen rather than the dipotassio salts because, in contrast to the latter, which would probably undergo rapid metal–hydrogen exchange with the monopotassio salts of the alkylation products,[4] the disodio salts should exhibit such exchanges very slowly if at all.[4] Moreover, the disodio β-diketones appeared to be quite soluble in liquid ammonia, whereas dipotassio β-diketones often were not. The general procedure involved addition of the β-diketone to 2 molecular equiv of sodium amide in liquid ammonia, followed by 1 molecular equiv of methyl iodide. Thus, unsymmetrical β-diketone **2** underwent methylation at the a- and b-positions to form **3** and **4** to the extents of 89 and 11%, respectively (Scheme I).[3]

Similarly, unsymmetrical β-diketones **4** and **5** underwent methylation at the a- and b-positions to the relative extents of 99:1, and β-diketone **9** exhibited exclusive methylation at the b-position, the methylene hydrogen of which is activated by the phenyl group (Schemes II–IV). **9** also underwent exclusive alkylation at the b-position with the larger halides, *n*-butyl bromide and benzyl chloride. It is to be noted that two of the unsymmetrical β-diketones studied, **4** and **5**, were produced as one of the two possible alkylation products of **2** and **4**, respectively.

The relative amounts of the isomeric methylation products of unsymmetrical β-diketones **2** and **4**, and the *n*-butylation product of **9** were determined by vpc comparisons with authentic samples. The relative amounts of methylation products from **5** could not be determined by vpc since conditions were not found where the isomers could be separated. However, the product composition was determined by vpc of the neutral fraction of an alkaline hydrolysate. Only traces of pinacolone which would arise from b-isomer **8** could be observed; the major product was 3-methyl-2-butanone derived from a-isomer **7**. The validity of this method of analysis was demonstrated by the fact

(1) Supported by the National Science Foundation.

(2) T. M. Harris and C. R. Hauser, *J. Am. Chem. Soc.*, **81**, 1160 (1959).

(3) For convenience, mono- and dialkali salts are designated by prime (') and double prime ('), respectively, and only carbanion resonance forms are indicated even though other resonance forms may contribute more to the structures of the anions.

(4) With potassio salts but not with sodio salts proton transfers occur readily between diketone monoanions and dianions: see K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 61 (1965). In addition, the possibility exists particularly with potassio salts for direct or solvent-mediated intramolecular proton transfer within the dianions; for example, interconversion of **2a''** and **2b''** (Scheme I) might occur.