Mobile Keto Allyl Systems. XII.[1a] The Reaction of 2-(α-Bromobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene with Amines[1b]

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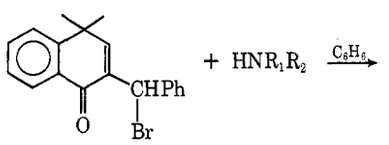
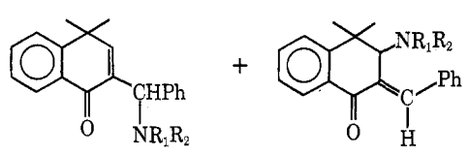
The title compound **1a** was found to react in benzene with 2 equiv of the following amines to yield the abnormal product of rearrangement–substitution, *trans*-2-benzal-3-amino-4,4-dimethyl-1-tetralone (**3**): isopropylamine, cyclohexylamine, morpholine, piperidine, and *sec*-butylamine. In the presence of an excess of amine, these first-formed amino ketones underwent an amine exchange reaction to yield the thermodynamically more stable amino ketones 2-[α-(amino)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2**). The bromo ketone **1a** reacts with more space-demanding amines, such as *tert*-butylamine, to yield both the normal product of direct substitution **2d** and the abnormal product of rearrangement–substitution **3d** by parallel pathways.

Hassner and Cromwell[2] were the first to report the reaction of 2-(α-bromobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**1a**) with amines. Using 2.32 molar equiv of piperidine and 2.13 molar equiv of morpholine in benzene solution, they obtained only the corresponding normal products **2a** and **2b**, respectively. Cromwell and Wu[3] extended these studies and found that **1a** gave normal products with an excess of piperidine and methylamine. Only with *tert*-butylamine did they observe an abnormal product, **3d**.



1a



2a, R_1R_2 = piperidine
b, R_1R_2 = morpholine
c, R_1 = H; R_2 = methyl
d, R_1 = H; R_2 = *tert*-butyl
e, R_1 = H; R_2 = isopropyl
f, R_1 = H; R_2 = cyclohexyl
g, R_1 = H; R_2 = *sec*-butyl

3a–g

It was decided, therefore, to treat **1a** with different amines at room temperature in benzene to attempt to determine the steric requirements of the reaction. An nmr spectrum of the crude reaction mixture was taken to determine if two products were obtained. The region between 250 and 300 Hz where the methine proton absorbances appear for **2d** and **3d** was carefully scanned at high amplitude. One signal indicated that one product was obtained. By this method, only products amounting to at least 10% of the total were observed.

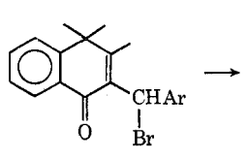
Results

Steric Requirements.—The reaction of **1a** with 10 molar equiv of isopropylamine, cyclohexylamine,[4] and *sec*-butylamine gave only the normal isomers **2e**, **2f**, and **2g**, respectively.

Adamantylamine and *tert*-octylamine (1,1,3,3-tetramethylbutylamine) reacted very slowly at room temperature with **1a** to give both the normal substitution product and the abnormal isomer, as observed by the nmr spectrum of the crude product mixture. The yields of crude oil were approximately 10–15% after several weeks. The two products could not be separated by column chromatography or tlc; so the products were not isolated or characterized. Diisopropylamine appeared to give no reaction after a week.

The procedure was repeated using slightly less than 2 molar equiv of piperidine, morpholine, isopropylamine, cyclohexylamine, and *sec*-butylamine in benzene. In each case, the only product was the abnormal amino ketone **3**, except in the reactions of piperidine and morpholine, in which cases the normal product **2** was also observed. When 1 molar equiv of piperidine or morpholine was added slowly to the stirred bromo ketone solution, the crude reaction mixture was shown by nmr analysis to consist entirely of abnormal amino ketone **3**.

It appeared that, if the amine was not very space-demanding, the first formed product was the abnormal isomer **3**, but the amine exchange reaction **3** to **2** was very fast. It was felt that by blocking the 2a position with an ortho methyl group on the benzyl ring, the rate of the amine exchange reaction could be reduced. As previously reported[4] 2-[α-bromo-*o*-methylbenzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**4**) reacted with 10 molar equiv of isopropylamine, cyclohexylamine, and *tert*-butylamine to yield both normal product **5** and abnormal product **6**. Using 2 molar equiv



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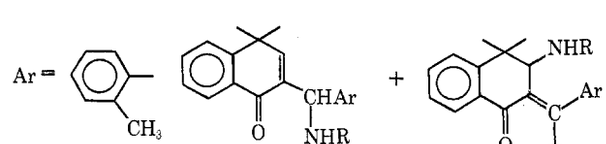


5a, R = isopropyl
b, R = cyclohexyl
c, R = *tert*-butyl

6a–c

(1) (a) For paper XI in this series, see A. D. George, E. Doomes, and N. H. Cromwell, *J. Org. Chem.*, **36**, 3918 (1971); (b) presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971.

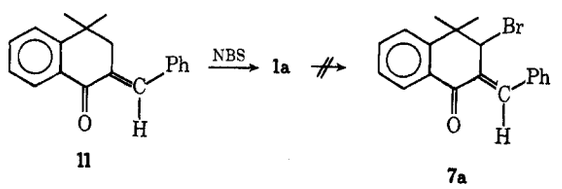
(2) A. Hassner and N. H. Cromwell, *J. Amer. Chem. Soc.*, **80**, 901 (1958).

(3) N. H. Cromwell and E. M. Wu, *J. Org. Chem.*, **33**, 1895 (1968).

(4) G. Glaros and N. H. Cromwell, *ibid.*, **36**, 3033 (1971).

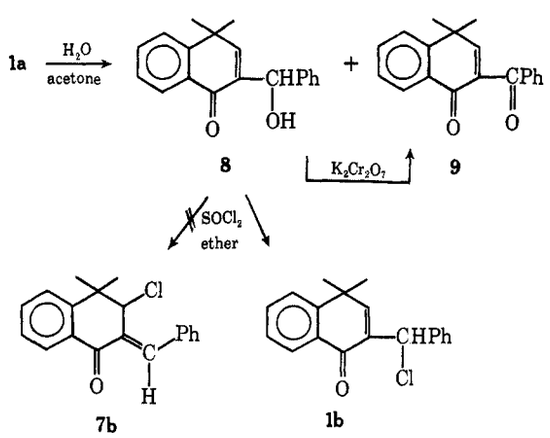
of isopropylamine and cyclohexylamine only the abnormal isomers **6a** and **6b**, respectively, were obtained.

Stability of Compounds.—Following the suggestion of DeWolfe and Young[5] the stability of all compounds was examined. The bromo ketone **1a** was stable under reaction conditions, with only slight decomposition taking place when stored in sunlight. There was no formation of the isomeric 2-benzal-3-bromo-4,4-dimethyl-1-tetralone (**7a**). This is not surprising, since the allylic system rearranges to the endocyclic structure during bromination.[3] It is known[6] that in the 4,4-dimethyl-1-tetralone system the endocyclic 2-benzyl isomer is thermodynamically more stable than the exocyclic 2-benzal isomer. In addition, if the reaction of **1a** with amines is stopped before completion, no evidence for **7a** is found.



11 **7a**

Attempts were made to prepare exocyclic chloro ketone **7b**. Bromo ketone **1a** was solvolyzed in aqueous acetone to 2-[α-hydroxybenzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**9**). This latter compound was identified by dichromate oxidation[7] of **8** to **9** and presumably arises during the solvolysis of **1a** by air oxidation of **8**.



7b **1b**

The allylic alcohol **8** was treated with thionyl chloride under conditions which are favorable for the SNi′ reaction[8] in hopes of obtaining 2-benzal-3-chloro-4,4-dimethyl-1-tetralone (**7b**). The only product observed was the previously reported[3] chloro ketone **1b**.

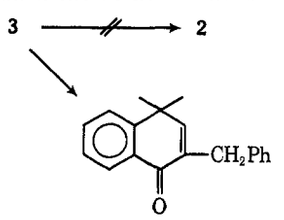
The normal products **2** were all stable under reaction conditions and with an excess of the corresponding amine present. Thus, the thermodynamically more stable isomers did not rearrange to the exocyclic unsaturated amino ketones **3**.

The exocyclic unsaturated amino ketones **3** are thermodynamically unstable relative to the endocyclic isomers **2**. All amino ketones **3** were stable, without added amine, to rearrangement to endocyclic unsaturated amino ketones **2** in $CDCl_3$ solution for periods up to 30 days. These amino ketones **3** having a hydrogen atom α to the nitrogen in the amino moiety decomposed slightly at room temperature to 2-benzyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**10**). This decomposition was quantitative at elevated temperatures.[4]

TABLE I
INFRARED AND ULTRAVIOLET DATA

	Ir,[a] cm⁻¹			Uv[b]	
Compd	C=O	C=C	C=C Ar	λ_{max}, nm	$\epsilon \times 10^{-3}$
2e	1660	1648	1600	257	7.95
				300 sh	2.2
2g	1660	1645	1601	257	10.55
				300 sh	2.8
3a	1660	1610	1600	287 sh	11.25
				303	11.9
3b	1670	1610	1600	285 sh	12.8
				302	13.85
3e	1670	1615	1600	280 sh	12.8
				298	14.2
3f	1660	1610	1595	280 sh	12.78
				298	13.93
3g	1675	1620	1600	282 sh	10.6
				294	11.4
8[c]	1655	1635	1600	254	10.65
				300 sh	2.45
9	1655		1600	257	18.27
				350	0.28
14	1670	1620	1600	237	13.2
				260 sh	11.6
				305	9.95
15	1675		1600	268	11.3
				302	7.7

[a] CCl_4 solution. [b] 95% ethanol. [c] Also OH 3620/84, 3600/87, and 3500/81 broad.



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All amino ketones **3** except **3d** reacted in a period of 1 week with added amine to yield the corresponding endocyclic unsaturated amino ketones **2**. In the case of the *tert*-butylamino ketone **3d**, the rearrangement was very slow. With a large excess of *tert*-butylamine in either C_6D_6, $CDCl_3$, or CD_3CN, only a trace of **2d** could be observed after 2 weeks at 40°.

During periodic nmr analysis of the reaction of **1a** with *tert*-butylamine in benzene, chloroform, and acetonitrile the ratio of amino ketone **2d** to **3d** did not change with time.[9] Thus, the presence of *tert*-butylamine hydrobromide did not appreciably alter the rate of the slow rearrangement of **3d** to **2d**.

$$3 + HNR_1R_2 \xrightarrow{C_6D_6} 2 + HNR_1R_2$$

While morpholine was found[10] to add to the exocyclic unsaturated ketone **11**, to an extent of 10%, it did not add to the endocyclic unsaturated ketone **10**. The ketone **10** prepared by the reaction scheme described previously[10] was allowed to react with *tert*-

(5) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956).
(6) N. H. Cromwell, R. P. Ayer, and P. W. Foster, *J. Amer. Chem. Soc.*, **82**, 130 (1960).
(7) L. T. Sandborn, "Organic Syntheses," Collect. Vol. I, H. Gilman, Ed., Wiley, New York, N. Y., 1941, p 340.
(8) F. F. Caserio, G. E. Dennis, R. H. DeWolfe, and W. G. Young, *J. Amer. Chem. Soc.*, **77**, 4182 (1955).
(9) G. Glaros and N. H. Cromwell, *J. Org. Chem.*, **37**, 867 (1972).
(10) A. Hassner and N. H. Cromwell, *J. Amer. Chem. Soc.*, **80**, 893 (1958).

TABLE II
ELEMENTAL ANALYSES

Compd	Calcd, % C	H	N	X	Found, % C	H	N	X
2e[a]	74.24	7.36	3.95	10.19[b]	74.27	7.42	4.08	10.48[b]
2g	82.84	8.16	4.20		82.71	8.16	4.34	
3a[c]	62.71	5.26	9.75		62.93	5.27	9.74	
3b	79.50	7.25	4.03		79.59	7.37	4.04	
3e	82.72	7.89	4.38		82.64	7.86	4.31	
3f	83.52	8.13	3.90		83.51	8.19	3.81	
3g[a]	74.67	7.62	3.78	9.58[b]	74.71	7.65	3.59	9.64[a]
8	81.98	6.52			81.78	6.56		
9	82.84	5.84			82.05	5.65		
14	82.84	8.16	4.20		82.63	8.16	4.11	
15[a]	76.16	7.87	3.42	8.65[b]	76.27	8.05	3.39	8.63[b]

[a] Hydrochloride salt. [b] Chlorine. [c] Picrate.

TABLE III
NMR SPECTRA[a,b]

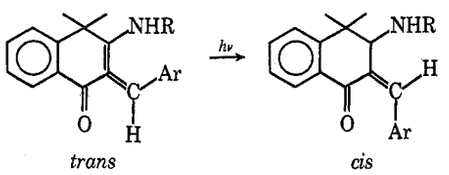
Compd	$(CH_3)_2C$	Methine	Vinyl	Amino
2e	86, 88	305	?[c]	d 65, J = 7 Hz, $(CH_3)_2CH$[d]–; s 95 NH; m 165 $(CH_3)_2CH$–
2g	82, 85	310	?[c]	m 40–95 $CH_3CH_2CHCH_3$; s 102 NH; m 150 $CH_3CH_2CHCH_3$
3a	81, 95	245	491	m 65–160 piperidino
3b	82, 95	246	496	m 125 $-(CH_2)_2=N$; m 202 $=(CH_2)_2=O$
3e	85, 96	245	480	d 29, J = 6 Hz; d 43, J = 6 Hz, $(CH_3)_2CH$;[d] s 48 NH; m 150, J = 6 Hz, $(CH_3)_2CH$–
3f	85, 96	247	482	m 30–140 cyclohexyl plus NH
3g	84, 97	249	482	m 15–75 CH_3CH_2–$CHCH_3$ plus NH; m 115–150 $CH_3CH_2CHCH_3$
8[e]	85	d 344 (J = 4 Hz)	d 408 (J = 1 Hz)	
9[f]	95	427		
14	84, 86	213	400	s 57 NH; s 65 *tert*-butyl
15[g]	84, 89	206	398	m 140–170 cyclohexyl plus NH

[a] All nmr spectra were taken in $CDCl_3$ and chemical shifts are reported in hertz, relative to internal TMS. [b] All compounds exhibited a multiplet downfield of the aromatic region assigned to the ring proton β to the carbonyl (483–504 Hz) and aromatic protons in the region 400–465 Hz. [c] Buried under the aromatic protons. [d] Nonequivalent methyls. [e] This compound also exhibited a signal which was lost upon addition of D_2O, d 238 Hz, J = 4 Hz, OH. [f] This compound exhibited a doublet of doublets at 460–475 Hz assigned to the ortho protons of the benzoyl group. [g] s 136 Hz, CH_3CH_3Ar–.

butylamine either alone or with sufficient benzene to dissolve all the ketone. No reaction took place after 2 weeks.

Structure of Compounds.—In this series of compounds, the position of the double bond, exocyclic or endocyclic, has been thoroughly studied by ir,[10] uv,[10] and nmr.[11,12] (See Tables I–III.) In general, the exocyclic unsaturated ketones have an intense long wavelength band, which is to be expected for the extended conjugation. Nmr has been found[11,12] to be definitive in determining both the position of the double bond and the stereochemistry about it. The diamagnetic anisotropy of the carbonyl group deshields the ring proton β to the carbonyl. This proton appears as a complex multiplet near 480 Hz.[11–13]

In *trans*-2-benzal-4,4-dimethyl-1-tetralones, the vinyl proton is in the same position relative to the carbonyl group as the β ring proton. Thus a downfield shift of this proton is observed, at approximately 460 Hz as predicted.[11] The cis isomer has its vinyl proton outside the deshielding cone of the carbonyl group and appears upfield at approximately 400 Hz.[14] All of the 2-benzal-4,4-dimethyl-1-tetralones studied have the vinyl proton absorbance downfield of the aromatic region. This includes the amino ketones **3** and **6**. Two of these trans compounds, **3d** and **6b**, were irradiated by the previously published procedure[11] to the corresponding *cis*-2-(substituted benzal)-3-amino-4,4-dimethyl-1-tetralones **14** and **15**, respectively. An upfield shift of the vinyl proton to approximately 400 Hz was observed, confirming the trans stereochemistry of the exocyclic double bond in **3d** and **6b**.



trans *cis*

3d, R = *tert*-butyl; Ar = Ph **14**
6b, R = cyclohexyl; Ar = *o*-CH_3Ph **15**

Discussion

There are two possible pathways for the reaction of **1a** with amines. With the less space-demanding amines, the first formed product is **3**. In the presence of an excess of amine, there is an amine exchange reaction with **3** to yield the amino ketones **2**. Thus, these normal substitution products arise *via* two rearrangement reactions rather than by direct substitution.

With the more space-demanding *tert*-butylamine, the rearrangement–substitution reaction is slowed

(11) D. N. Kevill, E. D. Weiler, and N. H. Cromwell, *J. Org. Chem.*, **29**, 1276 (1964).
(12) J.-L. Imbach, A. E. Pohland, E. D. Weiler, and N. H. Cromwell, *Tetrahedron*, **23**, 3931 (1967).
(13) For published spectra see G. Glaros and N. H. Cromwell, *J. Chem. Educ.*, **46**, 854 (1969).
(14) G. Glaros and N. H. Cromwell, *ibid.*, **48**, 204 (1971).

down to where direct substitution is competitive, and the rate of the amine exchange reaction is immeasurably slow. Thus, while small amines yield normal products *via* two consecutive rearrangement–substitution reactions, *tert*-butylamine reacts with bromo ketone **1a** *via* parallel direct substitution and rearrangement–substitution reactions, as had previously been suggested[3] (Scheme I).

The stability of **3d** in the presence of *tert*-butylamine when it is known to react with the less space-demanding amine piperidine[3] may be explained in terms of steric hindrance. The SN2′ reaction has been shown[15] to proceed with a cis orientation of entering and leaving group. If a cis orientation is a requirement for this reaction as well, two *tert*-butylamine groups entering and leaving cis to each other would present a very crowded transition state.[16] The facile aminotropic rearrangement with the less space-demanding piperidine[3] demonstrates that such a reaction is possible, but prevented with bulky amines.

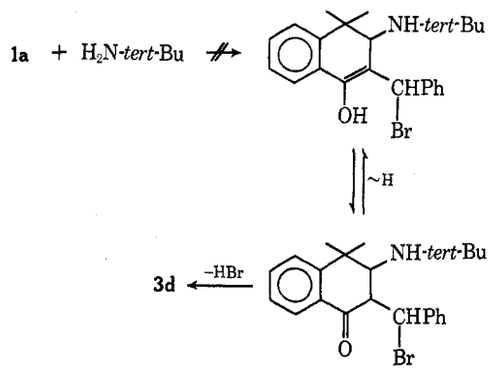
The stability of the bromo ketone **1a** under reaction conditions, toward rearrangement to the exocyclic structure **7a** precludes an SNi′–SN2 reaction sequence to explain the appearance of rearranged isomers **3**. That amino ketones **2** are thermodynamically more stable than amino ketones **3** and do not rearrange to **3** also precludes an SN2–SNi′ reaction sequence to explain the appearance of amino ketones **3**. That amines did not add in a 1,4 manner to the s-trans enone system present in the endocyclic unsaturated ketone **10** is not surprising and argues against a "1,4-addition–loss of amine and HBr" sequence to explain the appearance of amino ketones **3**.

Thus, the appearance of abnormal substitution products **3** is best explained in terms of a variant of an SN2′-type reaction. The nature of the transition state involved in this rearrangement reaction is discussed in the accompanying paper.[9]

Experimental Section[19,20]

Reaction of 1a with Amines (10 equiv).—The general procedure followed was that of Cromwell and Wu.[3] A solution of **1a**, mp 117–117.5° (lit.[2] mp 116.5–117.5°), and 10 molar equiv of amine in benzene was allowed to react at room temperature for periods of 3–14 days. The amine hydrobromide was recovered by filtration and the solvent was evaporated under reduced pressure to yield an oil. The oil was dissolved in ether and dry HCl gas was bubbled through the ethereal solution to precipitate the amino ketone hydrochloride. The amino ketone hydrochloride was filtered from the ether and dissolved in 95% ethanol.[21] The ethanolic solution was made basic with Na_2CO_3 solution and extracted with benzene. The benzene layer was separated, dried over $MgSO_4$, filtered free from drying agent, and evaporated under reduced pressure to yield an oil. This oil was analyzed by nmr and tlc and the pure amino ketones were isolated as described below.

SCHEME I
MICHAEL ADDITION–ELIMINATION SEQUENCE



A. With Isopropylamine.—The crude oil obtained in 38% yield showed two spots on tlc, but nmr analysis showed only 2-[α-(isopropylamino)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2e**) to be present. Repeated attempts to crystallize this compound failed, and it was analyzed as its hydrochloride salt, mp 232–233°.

B. With *sec*-Butylamine.—The crude oil obtained in 92% yield exhibited two spots on tlc, but nmr analysis showed it to consist of 2-[α-(*sec*-butylamino)benzyl]-1,4-dihydro-4,4-dimethylketonaphthalene (**2g**). The product crystallized slowly and was recrystallized from 95% ethanol to yield 47% of pale yellow needles, mp 66–68°.

C. With Diisopropylamine.—The reaction of **1a** with diisopropylamine was very slow. After 1 week, using 2 g (0.006 mol) of **1a** and 4.25 ml of amine in 20 ml of benzene, there was insufficient product for an nmr analysis.

D. With Adamantylamine.—Adamantylamine is a high-melting solid which was found to be only partially soluble in benzene, chloroform, and acetonitrile. To 1.7 g (0.005 mol) of bromo ketone **1a** is 25 ml of benzene was added 3 g (0.02 mol) of adamantylamine. Most of the amine did not go into solution, but the reaction was stirred at room temperature and worked up in the usual manner. Nmr analysis of the crude oil showed it to contain two products. From integrating the assumed methine signals, the ratio of nonrearranged product to rearranged product was found to be 21:79. Tlc showed two poorly resolved spots and column chromatography was unsuccessful in separating the two isomers.

E. With *tert*-Octylamine.—The reaction of bromo ketone **1a** with *tert*-octylamine was similar to that with adamantylamine. The reaction was slow, 18% crude oil was obtained after 2 weeks, and the products could not be separated on tlc or by column chromatography. Nmr analysis of the crude oil showed it to contain the nonrearranged product and the rearranged product in a ratio of 78:22.

Reaction of 1a with Amines (2 equiv).—The general procedure followed was the same as that described above, except that 2 equiv of amine were used.

A. With Isopropylamine.—From 1.7 g (0.005 mol) of **1a** and 0.6 g (0.01 mol) of isopropylamine in 25 ml of benzene, there was obtained 0.517 g (85%) of isopropylamine hydrobromide and 1.39 g (87%) of crude product. Nmr analysis of the crude product showed it to consist of *trans*-2-benzal-3-(isopropylamino)-4,4-dimethyl-1-tetralone (**3e**) with only a trace of nonrearranged product **2e**. The crude oil crystallized readily and was recrystallized from 95% ethanol to yield 0.798 g (50%) of pure **3e** as yellow crystals, mp 88–89°.

B. With Cyclohexylamine.—From 1.7 g (0.005 mol) of **1a** and 0.99 g (0.01 mol) of cyclohexylamine in 25 ml of benzene, there was obtained 0.68 g (76%) of cyclohexylamine hydrobromide. Nmr analysis of the crude solid which formed after removal of solvent showed it to consist entirely of *trans*-2-benzal-3-(cyclohexylamino)-4,4-dimethyl-1-tetralone (**3f**). The crude solid was recrystallized from 95% ethanol to yield 1.1 g (61%) of pure **3f** as yellow crystals, mp 94–95°.

(15) G. Stork and W. N. White, *J. Amer. Chem. Soc.*, **75**, 4119 (1953).

(16) A sensitivity to the steric requirements of the amine in similar aminotropic rearrangements has been observed in the indanone system[17] as well as in the chalcone system.[18]

(17) G. Maury, E. M. Wu, and N. H. Cromwell, *J. Org. Chem.*, **33**, 1907 (1968).

(18) N. H. Cromwell, K. Matsumoto, and A. D. George, *ibid.*, **36**, 272 (1971).

(19) Melting points were taken by the capillary method in a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were obtained as CCl_4 solutions using a Perkin-Elmer Model 237 spectrophotometer. Ultraviolet spectra were taken on a Cary Model 14 recording spectrophotometer. Proton magnetic resonance spectra were obtained on a Varian A-60 or A-60D spectrometer employing $CDCl_3$ solutions and are reported in Hertz relative to internal TMS (0.0 Hz). Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

(20) All physical data on new compounds are presented in Tables I–III.

(21) If the hydrochloride was hygroscopic and formed a gummy mass, the ether was decanted off and the hydrochloride was washed with fresh ether.

C. With *sec*-Butylamine.—From 1.7 g (0.005 mol) of **1a** and 0.73 g (0.01 mol) of *sec*-butylamine in 25 ml of benzene, there was obtained 0.54 g (75%) of *sec*-butylamine hydrobromide. Nmr analysis of the crude product showed it to consist of *trans*-2-benzal-3-(*sec*-butylamino)-4,4-dimethyl-1-tetralone (**3g**). This crude oil could not be crystallized when triturated with petroleum ether (bp 30–60°) or ethanol. The oil was analyzed as its hydrochloride salt, mp 176–177°.

D. With Morpholine.—From 1.7 g (0.005 mol) of **1a** and 0.87 g (0.01 mol) of morpholine in 25 ml of benzene, there was obtained 0.856 g (102% wet) of morpholine hydrobromide. Nmr analysis of the crude product showed it to consist of *trans*-2-benzal-3-morpholino-4,4-dimethyl-1-tetralone (**3b**) and 2-[α-(morpholino)-benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2b**) in a ratio of 50:50. Tlc showed two spots of similar R_f value. Chromatography of the mixture on a Florisil column eluting with benzene gave a first fraction enriched in **3b**. Recrystallization of this enriched fraction yielded 0.218 g (12.5%) of pure **3b** as yellow crystals, mp 147–149°.

E. With Piperidine.—From 1.7 g (0.005 mol) of **1a** and 0.85 g (0.01 mol) of piperidine in 25 ml of benzene, there was obtained 0.74 g (89%) of piperidine hydrobromide. Nmr analyses of the crude product showed it to consist of *trans*-2-benzal-3-piperidino-4,4-dimethyl-1-tetralone (**3a**) and 2-[α-(piperidino)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**2a**) in a ratio of 50:50. Chromatography on a column of Florisil eluting with benzene afforded **3a** as a yellow oil, analyzed as its picrate salt, mp 184–185° dec.

Further elution with ethyl acetate yielded **2a** as a yellow solid. Recrystallization from 95% ethanol yielded pure **2a**, mp 103–104° (lit.[2] mp 102–103°).

Reaction of 1a with Amines (1 equiv).—The general procedure followed is described above, except that only 1 equiv of amine was used. The amine was added as a solution in 10 ml of benzene over a period of 1 hr. The reaction was worked up after stirring for an additional 1 hr at room temperature.

A. With Morpholine.—From 1.7 g (0.005 mol) of **1a** and 0.49 g (0.0056 mol) of morpholine in 25 ml of benzene, there was obtained 0.218 g (52%) of morpholine hydrobromide. Nmr analysis of the crude product showed it to consist entirely of the rearrangement–substitution product *trans*-2-benzal-3-(morpholino)-4,4-dimethyl-1-tetralone (**3b**), which was recrystallized from 95% ethanol to yield pure **3b**, mp 148–150°.

B. With Piperidine.—From 1.7 g (0.005 mol) of **1a** and 0.424 g (0.005 mol) of piperidine in 25 ml of benzene, there was obtained 0.252 g (60%) of piperidine hydrobromide. Nmr analysis showed the yellow oil to consist entirely of *trans*-2-benzal-3-(piperidino)-4,4-dimethyl-1-tetralone (**3a**).

Reaction of 4 with Amines (2 equiv).—The general procedure followed is described above, except that 2 equiv of amine were used.

A. With Isopropylamine.—From 1.72 g (0.005 mol) of **4** and 0.59 g (0.0098 mol) of isopropylamine in 25 ml of benzene, there was obtained 0.443 g (63%) of isopropylamine hydrobromide. Nmr analysis of the crude product showed it to consist entirely of *trans*-2-*o*-methylbenzal-3-(isopropylamino)-4,4-dimethyl-1-tetralone (**6a**). The product was recrystallized from 95% ethanol to yield 0.78 g (47%) of pure **6a**, mp 95–96° (lit.[4] mp 96–97°).

B. With Cyclohexylamine.—From 1.7 g (0.005 mol) of **4** and 0.987 g (0.01 mol) of cyclohexylamine in 25 ml of benzene there was obtained 0.64 g (71%) of cyclohexylamine hydrobromide. Nmr analysis of the crude product showed it to consist entirely of *trans*-2-*o*-methylbenzal-3-(cyclohexylamino)-4,4-dimethyl-1-tetralone (**6b**). The crude product was recrystallized from 95% ethanol to yield 1.133 g (61%) of pure **6b** as yellow crystals, mp 116–117° (lit.[4] mp 116–117.5°).

Reactions of Abnormal Substitution Products (3) with Amines.—The general procedure involved weighing approximately 100 mg of the amino ketone **3** into an nmr tube and adding 0.25 ml of C_6D_6 and approximately 1 equiv of the corresponding amine. The nmr spectrum was then recorded and the region between 200 and 350 Hz was scanned periodically. For compounds **3** having the amino moiety isopropyl, cyclohexyl, morpholino, piperidino, and *sec*-butyl the rearrangement to amino ketone **2** was essentially quantitative in 1 week. There was only a trace of **2d** observed with **3d** and *tert*-butylamine in CD_3CN at 45° after 2 weeks.

Solvolysis of 1a.—A 3.41-g (0.01 mol) sample of **1a** was dissolved in 50 ml of reagent grade acetone and 15 ml of deionized water. The mixture was stirred at room temperature for 3 days, the solvent was removed under reduced pressure, and the residue was extracted with ether. The ether layer was separated, dried over $MgSO_4$, filtered, and evaporated to yield a colorless oil which crystallized upon trituration with petroleum ether, yielding 2.1 g (75%) of a white solid. Nmr analysis showed this crude product to contain two compounds identified as 2-[α-(hydroxy)benzyl]-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**8**) and 2-benzoyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**9**) in a ratio of 79:21. Recrystallization from ether or petroleum ether gave a mixture enriched in the diketone **9**. Column chromatography on alumina (Woelm activity I) eluting with benzene gave a first fraction also enriched in **9**. The enriched fraction was recrystallized until nmr and melting point showed it to be pure **9**, mp 153–154°.

Further elution with benzene yielded alcohol **8** as colorless plates, mp 116–118°.

Oxidation of Alcohol 8.—The procedure followed was essentially that recorded in the literature.[7] To a stirred mixture of 0.34 g of concentrated H_2SO_4, 0.406 g of $K_2Cr_2O_7$, and 2.5 ml of water was added 0.5514 g (0.00198 mol) of the alcohol **8**. Acetone (4 ml) was then added to dissolve all the alcohol and the mixture was stirred for 15 min. The reaction mixture was extracted with ether; the ether was washed with water, NaOH solution, and water and dried over $MgSO_4$. After filtering the dried ether solution, the ether was evaporated and the solid which remained was recrystallized from ether to yield 0.188 g (34%) of the diketone **9**, mp 153–154°, with an nmr spectrum superimposable on that of the product obtained previously from the solvolysis of **1a**.

Reaction of 8 with Thionyl Chloride. Attempted Synthesis of 2-Benzal-3-chloro-4,4-dimethyl-1-tetralone (7b). A.—Thionyl chloride (1.33 g, 0.007 mol) was added dropwise to 2.0 g (0.0060 mol) of alcohol **8** in 20 ml of chloroform. The mixture was stirred for 4 hr and the solvent was removed under reduced pressure. Cooling the residue in an ice bath yielded 0.8 g (39%) of a colorless compound, mp 108–109°, which had an nmr spectrum superimposable with that of 2-(α-chlorobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**1b**) prepared as previously described,[3] mp 108–109° (lit.[3] mp 107–108°).

B.—The procedure followed was that recorded in the literature.[8] When 0.12 g (0.001 mol) of thionyl chloride was added dropwise to an ice bath cooled solution of 0.278 g (0.001 mol) of alcohol **8** in 25 ml of dried ether, only the previously prepared chloro ketone **1b** was again observed.

Irradiation of Trans Exocyclic Amino Ketones.—The procedure followed has been previously published.[11] Irradiation of a methanolic solution of *trans*-amino ketone using a B-100A Blakray source, followed by evaporation of the solvent under reduced pressure, yielded the corresponding *cis*-amino ketones.

***cis*-2-Benzal-3-(*tert*-butylamino)-4,4-dimethyl-1-tetralone (14).**—Irradiation of a 0.5-g sample of **3d**[3] in chloroform, followed by evaporation of the solvent, yielded 0.22 g (44%) of **14** as deep yellow crystals, mp 140–142°.

***cis*-2-(*o*-Methylbenzal)-3-(cyclohexylamino)-4,4-dimethyl-1-tetralone (15).**—Irradiation of 0.374 g of **6b**[4] yielded 42% of **15** as a yellow oil. This oil could not be crystallized and was analyzed as its hydrochloride salt, mp 187–188°.

Control Experiments. Stability of Compounds. A. Bromo Ketone 1a.—Approximately 100 mg of **1a** was dissolved in 0.25–0.30 ml of C_6D_6, $CDCl_3$, or CD_3CN in nmr sample tubes. The nmr tubes were sealed and placed in a constant-temperature bath at 45°. The nmr spectrum was recorded periodically and no change was observed for periods up to 2 weeks.

B. Nonrearranged Products 2.—The amino ketones **2** were found to be stable when kept in the pure state or in solution. Amino ketone **2** was stable when dissolved in benzene and heated to 135° for 4 hr.[4]

C. Abnormal Substitution Products 3.—In a typical experiment, approximately 100 mg of amino ketone **3** was dissolved in 0.25 ml of $CDCl_3$ and the nmr spectrum was recorded periodically. In each case except for **3d** there was some decomposition to 2-benzyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**10**), but no evidence was obtained for rearrangement to the corresponding amino ketones **2**. These control experiments were conducted at room temperature for 30 days.

D. Endocyclic Double Bond.—A 0.66-g (0.0025 mol) sample of 2-benzyl-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene (**10**) was placed in a test tube and 1.4 g of *tert*-butylamine was added. The test tube was sealed and allowed to stand at room temperature for 2 weeks. The tube was opened, the amine was removed

under reduced pressure, and the contents were analyzed. Nmr and tlc showed no compounds present except **10**.

In another experiment, 0.66 g (0.0025 mol) of **10**, 1.4 g of *tert*-butylamine, and enough benzene to dissolve all the ketone were placed in a test tube and the tube was sealed. After 2 weeks at room temperature, nmr and tlc analysis showed that no reaction had taken place.

Registry No.—**1a**, 33224-47-4; **2a**, 33224-50-9; **2b**, 33224-51-0; **2e**, 33224-52-1; **2e** HCl, 33224-53-2; **2g**, 33224-54-3; **3a**, 33224-55-4; **3a** picrate, 33224-56-5; **3b**, 33224-57-6; **3e**, 33240-01-6; **3f**, 33240-02-7; **3g**, 33240-03-8; **3g** HCl, 33303-98-9; **6a**, 30765-51-6; **6b**, 30765-50-5; **8**, 33240-06-1; **9**, 33240-07-2; **14**, 33240-08-3; **15**, 33240-09-4; **15** HCl, 33240-10-7.

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Mobile Keto Allyl Systems. XIII.[1] The Kinetics and Mechanism of the Reaction of 2-(α-Halobenzyl)-1,4-dihydro-4,4-dimethyl-1-ketonaphthalene with *tert*-Butylamine[2]

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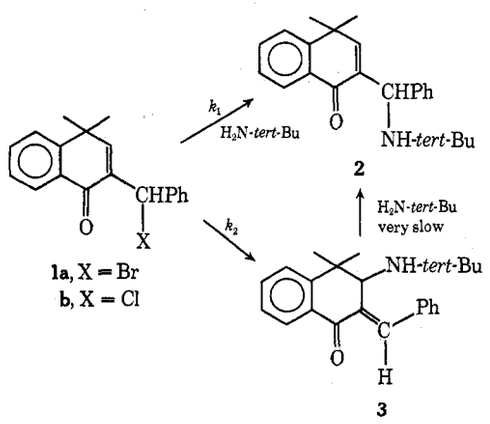
The title compound **1** was found to react with *tert*-butylamine by parallel reactions which obeyed second-order kinetics, first order in **1** and amine. The reaction yielding direct substitution product **2** is characterized by a large solvent effect ($k_{CH_3CN}/k_{C_6H_6}$ = 124), large leaving group effect (k_{Br}/k_{Cl} = 110), and an activation energy of 15–17 kcal/mol. These data are consistent with a normal SN2 displacement reaction. The reaction yielding abnormal substitution product is characterized by a small solvent effect ($k_{CH_3CN}/k_{C_6H_6}$ = 11), a small leaving group effect (k_{Br}/k_{Cl} = 5.5), and an activation energy of 12–13 kcal/mol. Although not ruling out the possibility of a dipolar intermediate being involved, the data are best interpreted in terms of a variant of an SN2′-type reaction in which the entering of the amino group and the departure of the halogen ion are concerted, but the carbon to nitrogen bond making is running ahead of carbon to halogen bond breaking, and the carbonyl group serves to disperse some of the developing negative charge.

In earlier papers[1,3] in this series it was shown that the halo ketone **1** reacts with *tert*-butylamine to yield two products **2** and **3** by parallel pathways. Compounds **1**, **2**, and **3** were shown to be stable under reaction conditions to rearrangement or decomposition. Because of the stability of these compounds, and because the rearrangement–substitution reaction could be compared with the direct substitution process, it was decided to study the kinetics of the reaction of halo ketone **1** with *tert*-butylamine.



Method.—Compounds **1** and **2** have very similar ir and uv spectra;[3] so both of these methods are unsatisfactory to follow the kinetics of the reaction. Halide titration would give only the overall rate constants $(k_1 + k_2) = k$; so this method is unsatisfactory also. Since the methine proton absorbance of **1** appears near 400 Hz, the methine proton absorbance of **2** appears near 300 Hz, and the methine proton absorbance of **3** appears near 250 Hz[3], it was decided to use nmr to follow the rate of the reaction. The assumption was made that the sum of the concentrations of **1**, **2**, and **3** at any time was a constant and equal to the initial concentration of **1**. Thus, $[1]_0 = [1]_t + [2]_t + [3]_t$ and the individual rate constants k_1 and k_2 could be obtained.

The use of nmr to follow kinetics places certain restrictions on the system. First, large quantities of reactants must be used to get strong enough signals for accurate measurements. Secondly, the method is relatively insensitive; consequently greater errors are introduced when one species is present to a much greater extent than another, as occurs in the beginning and end of a reaction. Lastly, although good correlation may be obtained for the overall rate constant k, the error involved in determining the ratio of **2** to **3** causes a greater error to be introduced in determining the individual rate constants k_1 and k_2. With these restrictions in mind we determined the kinetics of the reaction of **1** with *tert*-butylamine under various conditions. Because of the inaccuracy of the method we have been very cautious about comparing a rate constant we obtained with one obtained by other workers. Instead, we have tried to make comparisons in our system as various factors governing the rate of reaction are changed, such as temperature, solvent, and leaving group.

(1) For paper XII in this series, see G. Glaros and N. H. Cromwell, *J. Org. Chem.*, **37**, 862 (1972).

(2) Presented at the 162nd National Meeting of the American Chemical Society, Washington, D. C., Sept 1971.

(3) N. H. Cromwell and E. M. Wu, *J. Org. Chem.*, **33**, 1895 (1968).