cm^{-1}. The nmr spectrum showed bands at τ 1.85 (aromatic proton β to the carbonyl), 2.3–2.8 (nine aromatic protons), 7.35 (J = 2 cps) (methylene protons), and 8.72 (*gem*-dimethyl protons).

Registry No.—2, 15982-09-9; **3**, 15982-10-2; **4**, 15982-11-3; **5**, 15982-12-4; **6**, 15982-13-5; **7**, 15982-14-6; **8**, 15982-41-9; **10**, 15982-42-0; **11**, 15982-43-1; **12**, 15982-44-2; **13**, 15982-45-3; **14**, 15982-46-4; **15**, 15982-47-5; **16** HCl, 15982-48-6; **17** HCl, 15982-49-7; **18** HCl, 15982-50-0; **19** HCl, 15982-51-1; **20** HCl, 15982-52-2; **21**, 15982-53-3; **22**, 15982-54-4; **23**, 15982-55-5; *cis*-2-(*o*-nitrobenzal)-4,4-dimethyl-1-tetralone, 15982-56-6; *trans*-2-(*o*-nitrobenzal)-4,4-dimethyl-1-tetralone, 15982-57-7.

Acknowledgment.—One of us, N. H. C., is very grateful for several useful discussions with Professor H. O. House during the writing of this article. He also wishes to thank the Department of Chemistry of the Massachusetts Institute of Technology for their kind hospitality during his tenure as guest of the institute in 1967. This work was supported in part by Grant No. CA02931 from the National Cancer institute of the U. S. Public Health Service.

Mobile Keto Allyl Systems. VI.[1a] Reaction of 3-Bromo-2-benzal-1-indanone with Amines

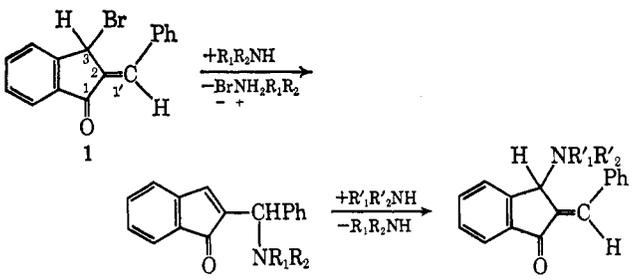
GEORGES MAURY, E.-MING WU, AND NORMAN H. CROMWELL[1b]

Department of Chemistry, University of Nebraksa, Lincoln, Nebraska 68508

Received October 24, 1967

The reaction of 3-bromo-2-benzal-1-indanone (**1**) with primary and secondary amines proceeds in two steps, giving initially 2-[α-(X-amino)benzyl]-1-indenones (**2**) as the kinetically favored products, and then 3-(X-amino)-2-benzal-1-indanones (**3**) as the thermodynamically stable isomers. With diisopropylamine, only the aminoindenone **2b** is isolated, and the reaction of **1** → **2b** has been found to be first order with respect to the bromoindanone and the amine; the rate is equal to the rate of consumption of the amine and to the rate of appearance of the bromide ion. These data are accommodated by a variant of an SN2′ mechanism in which the entry of the amino group and the departure of the bromide ion are nearly synchronous, but the carbon to nitrogen bond making is running slightly ahead of the carbon to halogen bond breaking.

In a previous paper[2] Cromwell and coworkers reported that 3-bromo-2-benzal-1-indanone (**1**) reacted with piperidine, morpholine, and cyclohexylamine, in the absence of solvent, to give the direct substitution products 3-(X-amino)-2-benzal-1-indanones, **3**. It was suspected, although not proved, that the reaction might proceed by an abnormal allylic substitution followed by rearrangement. Such a mechanism has recently been reported for the reaction of *t*-butylamine with *trans*-α-(bromomethyl)chalcone.[3] Therefore, it seemed desirable to reexamine the substitution of **1** by primary and secondary amines, particularly since this substrate has a fixed conformation and may involve the resonances of either the 2-benzal-1-indanone- or 2-benzyl-1-indenone systems in the reaction transition state.



2a, R_1 = H; R_2 = *t*-butyl
b, R_1 = R_2 = isopropyl
c, R_1 = R_2 = morpholino
d, R_1 = H; R_2 = cyclohexyl
e, R_1 = H; R_2 = *n*-butyl
f, R_1 = H; R_2 = phenyl
g, R_1 = methyl; R_2 = phenyl
h, R_1 = R_2 = piperidino
j, R_1 = R_2 = pyrrolidino
k, R_1 = H; R_2 = methyl

3a, R_1 = H; R_2 = *t*-butyl
b, R_1 = R_2 = isopropyl
c, R_1 = R_2 = morpholino
d, R_1 = H; R_2 = cyclohexyl
e, R_1 = H; R_2 = *n*-butyl
f, R_1 = H; R_2 = phenyl
g, R_1 = methyl; R_2 = phenyl
h, R_1 = R_2 = piperidino
j, R_1 = R_2 = pyrrolidino
k, R_1 = H; R_2 = methyl

Results

I. Thermodynamically Favored Products.—A series of experiments was first carried out to study the over-all course of the reaction. The bromo ketone **1** was allowed to react, for approximately 24 hr, with a number of amines including *t*-butylamine, diisopropylamine, *n*-butylamine, piperidine, morpholine, and cyclohexylamine in an apolar medium at room temperature. Under these conditions, it was observed that the nature of the isolated product depended upon the nature of the reacting amine. If the amine was bulky (*t*-butylamine, diisopropylamine) the compounds **2** or **3** were isolated. *t*-Butylamine (2 equiv) was treated with **1** in benzene solution to give 2-[α-(*t*-butylamino)benzyl]-1-indenone (**2a**). If 10 equiv of amine was used, 3-(*t*-butylamino)-2-benzal-1-indanone (**3a**) was formed; compound **2a** seemed to be an intermediate in this reaction since it reacted with *t*-butylamine to give the isomeric aminoindanone **3a**.[4] Spectroscopic evidence supported the structure of **2a**. The uv absorption (mainly at 238 and 244 mμ in *n*-hexane) was almost identical with that of 2-ethyl-1-indenone[2,5] but differed appreciably from that of 2-benzal-1-indanone and derivatives.[2] Further support for the indenone structure was provided by the ir carbonyl absorption at 1715 cm^{-1} in carbon tetrachloride.[6]

(1) (a) For paper V in this series, see N. H. Cromwell and E.-M. Wu, *J. Org. Chem.*, **33**, 1895 (1968). (b) The author to whom all correspondence concerning this article should be addressed.

(2) B. D. Pearson, R. P. Ayer, and N. H. Cromwell, *ibid.*, **27**, 3038 (1962).

(3) R. P. Rebman and N. H. Cromwell, *Tetrahedron Lett.*, 4833 (1962).

(4) N. H. Cromwell and E.-M. Wu, *ibid.*, 1499 (1966).

(5) N. H. Cromwell and R. P. Ayer, *J. Amer. Chem. Soc.*, **82**, 133 (1960).

(6) C. S. Marvel and C. W. Hinman, *ibid.*, **76**, 5435 (1954).

The diisopropylamino group, as compared with the *t*-butylamino group, seemed to favor the stability of the structure **2** under these reaction conditions. The bromo ketone **1** was treated with 2 (or 10) equiv of diisopropylamine at room temperature to give only the aminoindenone **2b** (R_1 = R_2 = isopropyl); the isomeric aminoindanone **3b** was never obtained in this experiment even at higher temperatures and in polar solvents.

With the less bulky amines, *n*-butylamine, cyclohexylamine, piperidine, or morpholine, only the nonrearranged products **3** were isolated under the same experimental conditions. Their ir and uv spectra were similar to those of 2-benzal-1-indanone or derivatives[2] and thus presented definite evidence for the assigned structures. The reaction of **1** with methanol was analogous and gave 3-methoxy-2-benzal-1-indanone.

II. Kinetically Favored Products.—The second approach was to follow the course of the reaction to detect any intermediate as well as to help in planning a kinetic study. This was carried out by using thin layer chromatography (tlc) and uv and nmr spectroscopy. Lower temperatures and apolar solvents were used to decrease the rate of the reaction. The series of reacting amines included morpholine, piperidine, pyrrolidine, cyclohexylamine, *n*-butylamine, monomethylamine, aniline, and N-methylaniline.

These reactions were first systematically followed by tlc. In most cases (morpholine, cyclohexylamine, *n*-butylamine, monomethylamine) it was possible to separate the spot of a bright yellow product (at higher R_f) from the noncolored spots of **1** and the aminoindanone **3**. It was observed that the colored spot appeared first (or simultaneously with **3**) then vanished as the amount of **3** increased. These colored spots were assigned to the corresponding aminoindenones (**2**) and were observed in every experiment (sometimes superimposed on the spot of **3**).

The preceding intermediates **2** were characterized, before isolation, using the great difference of uv absorption between the structures **2** and **3**. The reaction was quenched by dilution then analyzed by uv spectroscopy. In each case two very intense maxima appeared (in the earlier spectra) at about 237 and 242 mμ, as in the spectra of **2a** and **2b**.

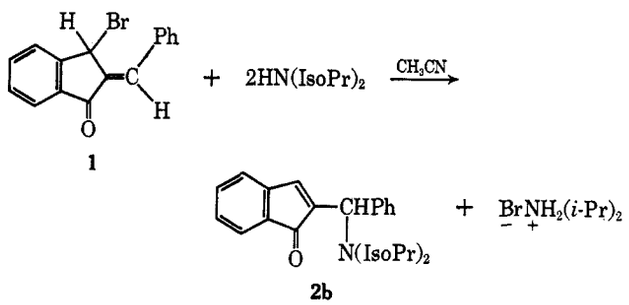
Finally, some of the intermediary aminoindenones **2** were isolated by quenching the reaction after mixing the reactants using chromatography on neutral alumina. Thus **2c** (R_1,R_2 = morpholino), **2d** (R_1 = H; R_2 = cyclohexyl), **2e** (R_1 = H; R_2 = *n*-butyl), **2f** (R_1 = H; R_2 = phenyl), and **2g** (R_1 = methyl; R_2 = phenyl) were isolated and immediately characterized by uv and nmr spectra because of their instability. However, it was not possible to isolate the aminoindenones **2h** (R_1, R_2 = piperidino), **2j** (R_1, R_2 = pyrrolidino), and **2k** (R_1 = H; R_2 = CH_3) because these compounds undergo reaction too rapidly with excess amine. The rates of the reactions **1** → **3** can be classified approximately as follows: piperidine > pyrrolidine ≫ monomethylamine ≃ *n*-butylamine ≫ morpholine > cyclohexylamine > aniline ~ N-methylaniline > *t*-butylamine > diisopropylamine.

It was thus established that, regardless of the nature of the amine, the reaction of **1** with amines involves an intermediary aminoindenone **2** in which the allylic system has been reversed. This intermediate is generally unstable and reacted further to give the stable aminoindanone **3**. The Hückel MO calculation method,[7] applied to 2-benzal-1-indanone and 2-benzyl-1-indenone, confirmed that the latter compound, which is related structurally to 1-indenone and cyclopentadienone, would be the less stable.[7]

The third phase of the study dealt with the investigation of the mechanism of the reaction **1** → **2**; the "amine-exchange reaction" **2** → **3** will be discussed in a following paper.

Either of two mechanisms can be offered to explain *a priori* the formation of the rearranged aminoindenones **2**: first, an abnormal nucleophilic substitution (S$_N$′) involving directly the halogenoallyl system and, second, a two-step process in which the α-enone system reacts (1,4-Michael addition) giving an adduct which is dehydrohalogenated in a second step. Consequently, we attempted to find an actual intermediate between **1** and **2**. The reactions of **1** with morpholine, cyclohexylamine, and aniline were repeated and followed simultaneously by tlc and uv spectroscopy, but in all three cases both methods showed that **1** and **3** were the only products.

We then investigated kinetically the reaction of the bromo ketone **1** with diisopropylamine. This particular example of aminoindenone formation was chosen because the reaction rate was the lowest observed, and because **2b** does not react further under the reaction conditions.[8]



A product study of the reaction was first carried out, at room temperature. In benzene as well as in acetonitrile a tlc study showed that **2b** appeared immediately and was the only product along with diisopropylamine hydrobromide. An nmr analysis of the crude material, after 24 hr of reaction, showed no unexpected product. In addition the same reaction was run in deuteriochloroform at about −5° and the reaction medium was constantly analyzed by nmr spectroscopy. In the first 10% of the reaction (before the hydrobromide precipitation) no evidence was found for any other product than **1** and **2b**, the starting amine and its hydrobromide.

The differences between the uv spectra of **1** and the aminoindenones **2** (see Figure 1) allowed us to follow the kinetics using uv spectroscopy. The results are recorded in Table I. As expected, the reaction showed second-order kinetics, first order in bromo ketone and

(7) We have carried out rough calculations according to the method suggested in A. Streitwieser, "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961, pp. 271–272.

(8) The special properties of the aminoindenone **2b** (related to the bulky diisopropylamino group) will be discussed in a following paper.

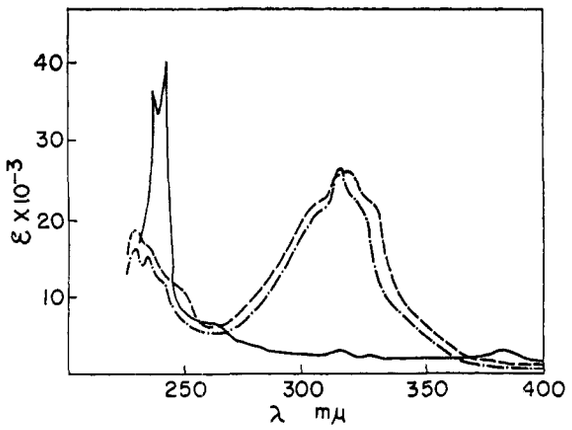


Figure 1.—The ultraviolet spectra in acetonitrile of **1**, ----; **2**, ——; and **4**, -·-·-.

TABLE I

VALUES FOR THE SECOND-ORDER RATE COEFFICIENTS K_2 IN THE REACTION OF 3-BROMO-2-BENZAL-1-INDANONE WITH DIISOPROPYLAMINE IN ACETONITRILE

Temperature, °C	[Bromo ketone] (mol/l.)	[Diisopropylamine] (mol/l.)	10^2K_2[a] (1 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}	$10^2K_2'$[b] (2 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}
15.6	0.00598	0.0500	2.3	2.4
18.7	0.00601	0.0489	2.9	2.9
18.7	0.00602	0.0449	2.7	2.7
30.0	0.1090	0.1090		4.6
30.2	0.00693	0.0342	4.8	5.0
30.4	0.00698	0.0223	5.0	5.3
30.4	0.00671	0.0411	5.0	5.1
44.1	0.00588	0.0299	9.9	10.5
44.9	0.00578	0.0244	8.6	9.3
44.9	0.00521	0.0352	11.5	12.0

[a] $K_2 = Ae^{-E/RT}$; $E = 9.0$ kcal/mol; $A = 1.6 \times 10^5$ l. mol^{-1} min^{-1}. [b] $K_2' = Ae^{-E/RT}$; $E = 9.3$ kcal/mol; $A = 2.5 \times 10^5$ l. mol^{-1} min^{-1}.

TABLE II

VALUES FOR THE SECOND-ORDER RATE COEFFICIENTS K_2 FOR BROMIDE ION FORMATION IN THE REACTION OF 3-BROMO-2-BENZAL-1-INDANONE WITH DIISOPROPYLAMINE IN ACETONITRILE

Temperature, °C	[Bromo ketone], mol/l.	[Diisopropylamine], mol/l.	10^2K_2 (1 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}	$10^2K_2'$ (2 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}
16.4	0.00503	0.0496	2.2	2.2
16.4	0.00607	0.0493	2.3	2.4
16.4	0.00622	0.0442	2.3	2.4
16.4	0.00706	0.0445	2.1	2.2
29.9	0.00628	0.0406	5.1	5.5
29.9	0.00679	0.0472	4.7	5.0
29.9	0.00689	0.0224	4.9	5.3
29.9	0.00731	0.0350	5.2	5.5
44.8	0.00529	0.0364	11.5	13.0
44.8	0.00618	0.0304	11.5	12.5

TABLE III

VALUES FOR THE SECOND-ORDER RATE COEFFICIENTS K_2 FOR AMINE CONSUMPTION IN THE REACTION OF 3-BROMO-2-BENZAL-1-INDANONE WITH DIISOPROPYLAMINE IN ACETONITRILE

Temperature, °C	[Bromo ketone], mol/l.	[Diisopropylamine], mol/l.	10^2K_2 (1 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}	$10^2K_2'$ (2 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}
18.1	0.00715	0.0440	2.7	2.8
18.1	0.00996	0.0403	2.5	2.7
18.1	0.0114	0.0577	2.5	2.7
18.1	0.0145	0.0610	2.5	2.7
30.0	0.00752	0.0347	5.1	5.6
30.0	0.00898	0.0260	4.9	5.6
30.0	0.0125	0.0584	5.2	5.7
30.0	0.0146	0.0496	4.7	5.5

in amine (the rate constants of an assumed reaction, first order only in **1**, showed considerable drifts). Therefore one molecule of amine is consumed in a bimolecular substitution and subsequently a second molecule of amine is protonated. Although the diisopropylamine hydrobromide remained completely in solution, its dissociation must be very limited and therefore the calculation of the rate constant should involve 2 equiv of amine/equiv of **1**.[9]

The kinetics of bromide ion formation in the same reaction was also followed. Assuming the equality of the observed concentration of bromide ions with the corresponding concentration of **1** having reacted, the rate constants have been calculated. It was found (Table II) that the kinetics are second order (first order with respect to **1** and the amine) and that the rate constants are nearly the same as in the first kinetic study.

In addition, we studied the kinetics of the diisopropylamine consumption in the same reaction. Table III shows the rate constants calculated by assuming that half the concentration of the consumed amine is equal to the concentration of **1** having reacted. Second-order kinetics were found; the rate constants were essentially the same as those for the two preceding kinetic studies.

Finally, in an attempt to determine to what extent the carbon to halogen bond breaking is involved in the transition state, we investigated the reaction of 3-chloro-2-benzal-1-indanone (**4**)[10] with diisopropylamine in acetonitrile. The product study (tlc and nmr spectrum) showed that the course of the reaction is very similar with that of the reaction with **1**; the only detected products were the aminoindenone **2b** and the diisopropylamine hydrochloride. Moreover, the reaction was followed by nmr analysis in deuteriochloroform and no other product was detected before the precipitation of the hydrochloride.

The uv spectra of **1** and **4** were very similar (see Figure 1) and we used uv spectroscopy to study the kinetics of the over-all reaction. The results (see Table IV) clearly supported second-order kinetics (first order in **4** and in amine), and the replacement of the bromine atom of **1** by a chlorine atom appeared to decrease the rate of the substitution by a factor of about 3.7 (at 30°).

(9) W. G. Young, I. D. Webb, and H. L. Goering, *J. Amer. Chem. Soc.* **74**, 1076 (1951).

(10) The synthesis of this compound will be reported in a forthcoming paper.

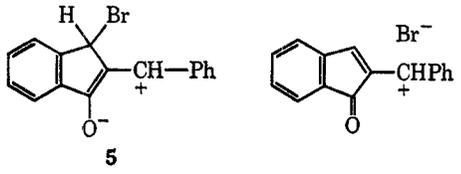
TABLE IV
VALUES FOR THE SECOND-ORDER RATE COEFFICIENTS K_2 IN THE REACTION OF 3-CHLORO-2-BENZAL-1-INDANONE WITH DIISOPROPYLAMINE IN ACETONITRILE

Temperature, ° C	[Bromoketone], mol/l.	[Diisopropylamine], mol/l.	10^2K_2 (1 equiv of amine/equiv of 1), l. mol^{-1} min^{-1}	$10^2K_2'$ (2 equiv of amine/equiv of 1), (l. mol^{-1} min^{-1}
29.9	0.0111	0.0258	1.2	1.4
29.9	0.0153	0.0487	1.2	1.4
29.9	0.0176	0.0416	1.2	1.5
29.9	0.0199	0.0544	1.2	1.4
29.9	0.0219	0.0622	1.2	1.3
29.9	0.0241	0.0490	1.1	1.3

Discussion

The preceding experimental results raised the following points for discussion: (1) The normal SN2 reaction is unfavored (if it exists) and the abnormal substitution predominates in each case. (2) The rate of the reaction depends on the nature of the reacting amine. (3) The reaction follows second-order kinetics; no evidence for the existence of an intermediate between **1** and **2** has been found.

The 3-(X-amino)-2-benzal-1-indanones **3** may be formed from **1** by two different reactions, either by a normal SN2 substitution or by the reaction of the first formed aminoindenones **2** with the amine in excess. However, no direct substitution product was isolated in the reaction of **1** with diisopropylamine where the intermediate **2b** is unable to react further with the excess of amine. Moreover, it was observed in the other cases that **2** is always formed either before **3** or simultaneously. Thus, the SN2 reaction appears to be unfavored. The easy occurrence of the abnormal substitution cannot be explained by steric reasons alone since the 3 position of 3-bromo-2-benzal-1-indanone seems to be nearly as accessible as its 1′ position. This is in agreement with the observed relative unimportance of the steric effects in the substitution of halogenoallyl systems by amines.[11] The electronic factor seems to be of major importance in our system. The electron-withdrawing effect of the carbonyl group attracts the exocyclic π electrons inside the five-membered ring because of the normal resonance effect in the ground state of the molecule (see structure **5**). Moreover, in the transition state, the presence of the positive charge on the lateral chain appears more likely.[7] These combined effects not only explain the orientation of the substitution but also the ease with which the reaction proceeds; see the kinetic and energetic constants.



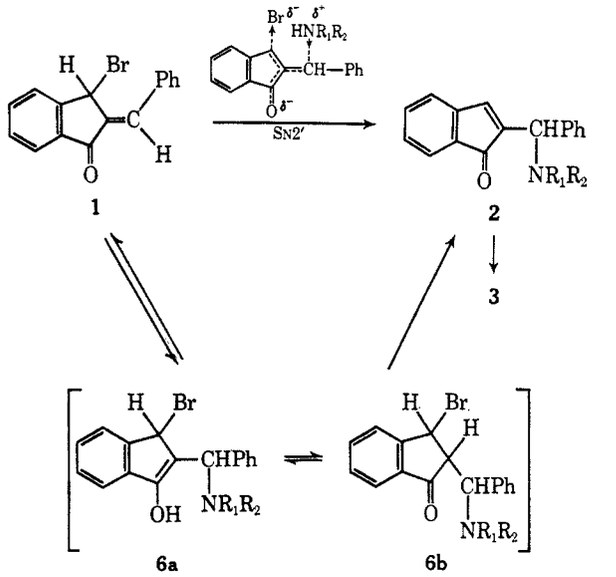
5

The nature of the amine does not change the course of the reaction **1** → **2** but it influences its rate. It was difficult to estimate even qualitatively the rate of the aminoindenone formation with the less bulky amines because of the speed of the reaction, **2** → **3** in these cases. Nevertheless, the steric factor seems to preponderate and the less bulky amines react more rapidly. The influence of the basicity of the amine was perceptible in the reactions of **1** with the aromatic amines; the rates were lower than with the normal aliphatic amines. These conclusions need to be made more precise on the basis of quantitative kinetic studies of the reaction.

The β-keto allyl system appears to be composed of two "crossed" simpler systems, the α-halogeno allyl system and the α,β-enone system.

If it is considered that the reaction involves mainly the α-halogeno allyl system, the preceding experimental data satisfy the criteria of DeWolfe and Young for an SN2′ mechanism,[11] namely, the formation of the abnormal product, the occurrence of second-order kinetics, and the absence of reactant or product rearrangement. Thus, the reaction may be of an SN2′ type; this implies a nearly concerted process and a transition state in which the exocyclic π electrons become partly endocyclic while the negative charge is dispersed to the leaving group and the oxygen of the carbonyl. It has been observed that the parent system of 3-haloalkylthiophene-1,1-dioxide (the allylic system here is also substituted by a strong electron-withdrawing group) reacts with primary and secondary amines in benzene to give SN2′-type reactions.[12a] The carbonyl group of 3-bromo-2-benzal-1-indanone is expected to greatly perturb the SN2′ reaction because it can absorb the developing negative charge. This effect is responsible for the relatively low decrease of the reaction rate when the bromine atom is replaced by the chlorine atom (a ratio k_{Br}/k_{Cl} = 40–50 is expected in the case of a "pure" SN2′ reaction).[12b] Thus the rate-determining process is only partly influenced by the departure of the halogeno group.

At the other limit, we can consider that only the α,β-enone system is concerned. The resulting 1,4 addition of a Michael-type adduct would involve the intermediates **6a** and, by ketonization, **6b**. In the



(11) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956).

(12) (a) F. G. Bordwell and coworkers, Northwestern University, Evanston, Ill., private communication, 1966. (b) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 30.

"pure 1,4 addition," the lifetime of the anionic oxygen is expected to be short because of the probable establishment of a hydrogen bond between the oxygen and the proton of the entering amine, and then protonation of the oxygen. The addition of amine would be followed by elimination of bromide ion. It has been shown that the rates of bromide ion production and amine consumption are equal (within the experimental error). Moreover, no intermediate **6** has been detected, and 2-benzal-1 indanone failed to react with diisopropylamine in the same conditions. Therefore the two-step mechanism appears unlikely. If an intermediate was involved the ratio K_{Br}/K_{Cl} might be very small, possibly ~ 1.

A more acceptable interpretation results from a consideration of the β-keto allyl system in its entirety. In a nearly concerted process, the amine attacks the 1′ position of the halogeno ketone, which is polarized as implied by **5**; before the complete development of the negative charge, the carbonyl reverts to type and induces the leaving of the bromide ion. Thus this mechanism can be considered as a highly perturbed SN2′ type in which the entering of the amino group and the departure of the halogeno ion are nearly synchronous, but the carbon to nitrogen bond making is running slightly ahead of the carbon to halogen bond breaking.

Although, it has been demonstrated in only one case,[13] it is generally accepted that the SN2′ mechanism involves a *cis* stereo relationship between the entering and the leaving groups in the transition state. Therefore, to test the SN2′ character of the reaction in our system, it would be interesting to carry out the reaction with an optical isomer of **1** and study the absolute configuration of the resulting aminoindenone **2**.

Experimental Section[14]

Reaction of 3-Bromo-2-benzal-1-indanone (1) with Amines. Thermodynamically Favored Products.—The bromo ketone **1** was prepared as previously[2] and its physical properties compared with those of an authentic sample; ultraviolet maxima (acetonitrile) were found at 230, 253, and 322 mμ (ε 16,500, 12,070, 27,200).

A. With *t*-Butylamine.—A 1.62-g sample of *t*-butylamine (0.022 mol) was added to a solution of 3.32 g (0.011 mol) of **1** in 1200 ml of *n*-hexane at room temperature. After 24 hr the solvent was evaporated and the crude product extracted with ether to separate the amino ketone. The evaporation of the solvent left a yellow solid which was recrystallized from *n*-hexane to give 1.6 g (48%) of 2-[α-(*t*-butylamino)benzyl]-1-indenone (**2a**) as a yellow solid, mp 83–85°; ultraviolet maxima (*n*-hexane) were found at 238, 244, 303, 314, 327, 389 mμ (ε 40,000, 41,600, 1100, 1200, 900, 800); an infrared absorption (CCl_4) appeared at 1715 cm^{-1} (C=O); and nmr peaks (CCl_4) were observed between τ 2.4 and 3.2 (9 H aromatic and 1 H vinylic), at 5.20 (1 H benzylic), and at 8.95 (9 H *t*-butyl).

Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.52. Found: C, 82.00; H, 7.24; N, 4.81.

The same reaction in benzene as solvent gave 62% of **2a** after 24 hr at room temperature. In acetonitrile, and under the same conditions, 32% of **2a** was isolated; in addition, 8% of 2-[α-(*t*-butylamino)benzyl]-1-indenone hydrobromide was separated, mp 185–187°; ultraviolet maxima (methanol) were found at 240, 245 mμ (ε 31,400, 35,600); an infrared absorption (KBr) appeared at 1712 cm^{-1} (C=O); and nmr peaks ($CDCl_3$) were observed between τ 2.0 and 3.9 (9 H aromatic and 1 H vinylic), at 4.67 (1 H benzylic), and at 8.55 (9 H *t*-butyl).

Anal. Calcd for $C_{20}H_{22}NOBr$: C, 64.51; H, 5.92; N, 3.77; Br, 21.51. Found: C, 63.95; H, 6.17; N, 3.89; Br, 21.63.

The same reaction from 1.5 g of **1** and 3.65 g of *t*-butylamine (10 equiv) in 40 ml of benzene at 25° gave, after 24 hr, 97% of *t*-butylamine hydrobromide and 81% of 3-*t*-(butylamino)-2-benzal-1-indanone (**3a**) as a pale yellow solid: mp 91–94°; ultraviolet maxima (isooctane) at 238, 245 (sh), 310 mμ (ε 14,400, 13,600, 24,200); infrared absorption (CCl_4) at 3380 (NH) and 1705 cm^{-1} (C=O); nmr peaks (CCl_4) between τ 2.0 and 2.8 (9 H aromatic and 1 H vinylic), at 4.63 (1 H methine, doublet, J = 2 cps), and at 9.11 (9 H *t*-butyl singlet).

Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.52. Found: C, 82.12; H, 7.22; N, 4.66.

The mother liquor was concentrated to dryness. The resulting oil was dissolved in ether and then treated with dry hydrogen chloride. A 0.4-g amount of hydrochloride of **3a** was obtained and recrystallized from 95% ethanol, mp 235–238°; ultraviolet maxima (methanol) were found at 232, 268 (sh), 324 mμ (ε 16,200, 8500, 25,500); an infrared absorption ($CHCl_3$) appeared at 1703 cm^{-1} (C=O); and nmr peaks ($CDCl_3$) were observed between τ 1.0 and 2.7 (9 H aromatic and 1 H vinylic), at 4.05 (1 H methine), and at 8.67 (9 H *t*-butyl).

Anal. Calcd for $C_{20}H_{22}NOCl$: C, 73.30; H, 7.02; N, 4.27; Cl, 10.81. Found: C, 73.44; H, 6.91; N, 4.33; Cl, 10.71.

B. With Diisopropylamine.—To a solution of 1.5 g of **1** in 60 ml of benzene 1.0 g of diisopropylamine (2 equiv) was added, at room temperature. After 27 hr, 0.62 g of diisopropylamine hydrobromide was collected and the solvent evaporated. The residue, dissolved in *n*-hexane, yielded 0.93 g (58%) of 2-(α-diisopropylaminobenzyl)-1-indenone (**2b**) as a red solid, mp 96–97° [petroleum ether (60–70°)]; ultraviolet maxima (acetonitrile) were found at 238, 242, 269, 312 (sh), 330 (sh), 404 mμ (ε 41,600, 46,450, 11,600, 1060, 840, 610); an infrared absorption (CCl_4) appeared at 1715 cm^{-1} (C=O); and nmr peaks ($CDCl_3$) were observed between τ 2.4 and 3.1 (9 H aromatic and 1 H vinylic), at 4.87 (1 H benzylic broad singlet), at 6.69 (2 H tertiary isopropyl, quintuplet, by the near superimposition of two quadruplets, J = 6.5 cps), and at 8.92 and 9.01 (12 H isopropyl, two doublets, J = 6.5 cps).

Anal. Calcd for $C_{22}H_{25}NO$: C, 82.72; H, 7.89; N, 4.38; mol wt, 319.5. Found: C, 82.88; H, 8.08; N, 4.53; mol wt, 331.

The same experiment, repeated with 10 equiv of diisopropylamine, yielded only the aminoindenone **2b** after 24 hr.

C. With *n*-Butylamine.—The same experiment was run with 1.2 g of **1** and 0.58 g of *n*-butylamine in 50 ml of benzene at 25° for 22 hr. The infrared spectrum (in CCl_4) of the oily residue showed absorptions at 1705 (C=O) and 1630 cm^{-1} (C=C); the nmr spectrum (in CCl_4) showed bands between τ 2.1 and 2.8 (9 H aromatic and 1 H vinylic), at 4.76 (1 H methine), and between 7.7 and 9.5 (10 H, *n*-butylaminogroup, multiplet).

The hydrochloride of 3-*n*-butylamino-2-benzal-1-indanone (**3e**) was obtained by treating an ether solution of the preceding residue with dry hydrogen chloride. The solid (1.1 g, 80%) was recrystallized from methanol–ether, mp 190–191°. An ultraviolet maximum (methanol) was found at 316 mμ (ε 34,400), and the carbonyl infrared absorption ($CHCl_3$) appeared at 1710 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}NOCl$: C, 73.30; H, 7.02; N, 4.27; Cl, 10.81. Found: C, 73.47; H, 7.18; N, 4.21; Cl, 10.70.

D. With Piperidine.—A 0.51-g amount of piperidine was dissolved in a solution of 0.93 g of **1** in 1.2 l. of *n*-hexane. After 20 hr at room temperature, 0.71 g (78%) of 3-piperidino-2-benzal-1-indanone (**3h**) was separated in the usual way, mp 141–143°. A mixture melting point determination with an authentic sample showed no depression.[2] Nmr peaks ($CDCl_3$) were found between τ 1.85 and 2.75 (9 H aromatic and 1 H vinylic), at 5.00 (1 H methine, doublet, J = 1.5 cps), at 7.5 (4 H, methylenes α to N, as a multiplet), and at 8.6 (6 H, methylenes, β and γ as a multiplet).

E. With Morpholine.—A 1.89-g sample of **1** left standing at room temperature for 16 hr with 1.05 g of morpholine in 75 ml of benzene produced 1.6 g (88%) of 3-morpholino-2-benzal-1-indanone (**3c**), mp 139–140°. A mixture melting point determination with an authentic sample showed no depression.[2] Nmr peaks ($CDCl_3$) were found between τ 1.9 and 2.75 (9 H aromatic and 1 H vinylic), at 4.92 (1 H methine, doublet, J = 1.5 cps),

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

(14) Melting points were read with a calibrated thermometer. Ultraviolet absorption spectra were determined with a Cary Model 11-MS spectrophotometer. Infrared spectra were measured with a Perkin-Elmer Model 21. Nmr spectra were determined with a Varian A-60 spectrophotometer.

at 6.4 (4 H, methylene groups α to 0) and at 7.4 (4 methylene groups α to N).

F. With Cyclohexylamine.—The same experiment was carried out with 1.5 g of **1** and 1.0 g (2 equiv) of cyclohexylamine in 60 ml of benzene at room temperature. A quantitative yield of cyclohexylamine hydrobromide was separated. After evaporation of the solvent the residue was extracted with *n*-hexane to give 1.45 g (91%) of 3-(cyclohexylamino)-2-benzal-1-indanone (**3d**) after recrystallization from methanol: mp 94–96°; ultraviolet maxima (isooctane) at 228, 235, 315 mμ (ε 13,600, 12,200, 21,900); infrared absorption (CCl_4) at 1705 cm^{-1} (C=O); nmr peaks (CCl_4) between τ 2.1 and 2.8 (9 H aromatic and 1 H vinylic), and 4.78 (1 H methine, doublet, J = 1.5 cps), at 7.5 (1 H, on carbon α to N), and between 8.6 and 9.1 (11 H cyclohexylamino).

Anal. Calcd for $C_{23}H_{23}NO$: C, 83.28; H, 7.25; N, 4.41. Found: C, 82.98; H, 7.51; N, 4.45.

Attempted Reaction. 2-Benzal-1-indanone with Diisopropylamine.—To a solution of 88 mg (4.10^{-4} mol) of 2-benzal-1-indanone in 5 ml of acetonitrile, 80 mg (2 equiv) of diisopropylamine were added at room temperature. The reaction was followed by tlc (silica gel, petroleum ether–ether 50:50) during 72 hr. No other compound than the reactants were detected. In addition, the nmr spectrum of a solution of 88 mg of 2-benzal-1-indanone and 80 mg of diisopropylamine in 0.5 ml of CD_3CN and 0.2 ml of $CDCl_3$ showed no change after 72 hr at room temperature.

Reaction of 1 with Methanol.—A 0.3-g sample of **1** in 20 ml of anhydrous methanol was refluxed for 24 hr. The evaporation of the solvent left an oil which crystallized. The recrystallization of the solid (methanol–ether) gave 0.22 g (71%) of 3-methoxy-2-benzal-1-indanone: mp 65–67°; ultraviolet maxima (methanol) found at 232, 328 mμ; infrared absorption (CCl_4) at 1708 cm^{-1} (C=O); nmr peaks (CCl_4) between τ 1.8 and 2.4 (9 H aromatic and 1 H vinylic), and 4.10 (1 H methine, doublet, J = 2 cps) and 7.15 (methyl).

Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.51; H, 5.88.

Reaction of 1 with Amines. Kinetically Favored Products. A. Tlc and Uv Analysis of the Reaction. General Procedure.—To a solution of 20 mg of **1** in 2 ml of the solvent (benzene–*n*-hexane, 50:50) 2 equiv of amine were added. In each case, the solution immediately became green-yellow and a white precipitate of the amine hydrobromide appeared. Shortly after the mixing of the reactants, a sample of the reaction medium was collected and "quenched" by dilution (at least 200 times) generally in chloroform or *n*-hexane. The resulting solution was then analyzed by uv spectroscopy. Simultaneously, the reaction was followed by thin layer chromatography on silica gel G, using mixtures of petroleum–ether and ether as the eluent.

1. With Morpholine.—The uv spectrum of the reaction medium showed two intense maxima at 242 and 248 mμ ($CHCl_3$) characteristic of the aminoindenone **2c**, and a weak maximum at 323 mμ assigned to **1** and **3c**. The tlc study (petroleum ether–ether 50:50) showed that the bromo ketone is consumed after 15 min. A bright yellow spot appeared, having the same R_f as a spot of **3c** but not its color; thus, the spots of the isomeric **2c** and **3c** were superimposed in this case.

2. With Piperidine.—In this case, the sample for the uv spectrum must be collected immediately after mixing the reactants. The uv spectrum (isooctane) showed two intense maxima at 238 and 244 mμ, characteristic of **2h** and two weaker maxima at 325 and 330 mμ assigned to **1** and **3h**. The tlc study (petroleum ether–ether 25:75) showed the presence (in the early moments of the reaction) of a bright yellow spot, at higher R_f, corresponding to the aminoindenone but having the same R_f as **3h**.

3. With Pyrrolidine.—Although very weak, the maxima at 235 and 243 mμ appear in the uv spectrum (*n*-hexane) of a sample collected immediately after mixing the reactants. After 15 min, the aminoindenone had vanished as seen in another uv spectrum in which the preceding maxima are absent. The tlc study (petroleum ether–ether 50:50) did not permit the separation of the spots of **2j** (bright yellow) and **3j** (noncolored).

4. With *n*-Butylamine.—The uv spectrum (isooctane) of the reaction medium showed the presence of **2e** at 235 and 242 mμ and of **1** and **3e** at about 320 mμ. The separation of **2e** (higher R_f) and **3e** was possible by tlc (petroleum ether–ether 50:50). It was observed that the aminoindenone has some stability under these conditions, and was still present in a sample collected 5 hr after the beginning of the reaction. After 15 hr, only **3e** was detected.

5. With Cyclohexylamine.—The sample for uv analysis was collected 1 hr after the beginning of the reaction. The aminoindenone **2d**, relatively stable under these conditions, was detected by its maxima at 239 and 245 mμ (chloroform). Compounds **2d** (yellow spot at higher R_f) and **3d** were separated by tlc (petroleum ether–ether 50:50).

6. With Monomethylamine.—The uv spectrum (*n*-hexane) of the reaction medium presented two intense maxima at 236 and 243 mμ (aminoindenone, **2k**) and a weaker maximum at 318 mμ (assigned to **1** and **3k**). The thin layer chromatogram showed the presence of three products, an aminoindenone product **2k** (yellow spot at higher R_f), the aminoindanone **3k**, and an unknown compound at lower R_f. The bromo ketone **1** was completely consumed after 30 min, whereas after 3 hr only **3k** remained in the reaction medium.

7. With Aniline.—The reaction was relatively slow since a significant amount of aminoindenone **2f** appeared only after 20 min. The maxima of the corresponding uv spectrum are in the range of 230–240 mμ. The tlc study showed that two main products appeared (yellow spots) after 15 min and were still present after 2 hr.

8. With *n*-Methylaniline.—This case parallels the preceding one. Two uv spectra run after 20 min and after 2 hr presented two intense maxima at 236 and 242 mμ (*n*-hexane) characteristic of the structure **2g**. By tlc it was observed that two yellow products appeared 10 min after mixing the reactants. After 1.5 hr, only one (at lower R_f) remained.

B. Isolation of the Aminoindenones 2.—The preceding reactions of **1** with amines were repeated on a larger scale and at lower temperature (0–5°). After filtration of the hydrobromide the reaction was quenched by evaporation of the solvent at room temperature. The remaining oil was dissolved in the minimum of benzene and chromatographed rapidly on a column of neutral alumina with benzene as eluent.

1. With Morpholine.—From 0.45 g of **1**, 0.23 g of hydrobromide was collected (90%) and 0.10 g of **2c** was separated by chromatography. The product, a green viscous unstable oil, was analyzed immediately by tlc and proved to be pure: ultraviolet maxima (*n*-hexane) at 238, 244, 316, 327 (sh), 387 mμ (ε 42,000, 44,000, 2300, 1600, 1000); nmr peaks ($CDCl_3$), between τ 2.3 and 3.1 (9 H aromatic and 1 H vinylic), at 5.71 (1 H benzylic, broad singlet), at 6.28 (4 H, methylenes α to O, complex triplet), and at 7.54 (4 H, methylenes α to N, multiplet).

2. With Cyclohexylamine.—The same experiment was carried out with 0.27 g of **1** and 0.21 g of cyclohexylamine in 15 ml of the same solvent. A 0.14-g amount of hydrobromide (85%) was collected. The chromatography gave 90 mg of a green-yellow, viscous oil which was proved to be pure **2d** by tlc (only one spot, the R_f of which is different from the R_f of the isomeric aminoindanone); ultraviolet maxima (*n*-hexane) were at 237, 243, 317, 375 mμ (ε 32,000, 33,000, 2500, 2200, 2500); nmr peaks ($CDCl_3$) were observed between τ 2.3 and 3.2 (9 H aromatic and 1 H vinylic), at 5.10 (1 H benzylic, doublet, J = 1.5 cps), between 7.3 and 9.2 (12 H cyclohexylamino), and at 7.62 (1 H, carbon α to N).

3. With *n*-Butylamine.—From the same experiment with 250 mg of **1** and 90 mg of *n*-butylamine (1.5 equiv) in 10 ml of the usual solvent, 90 mg of hydrobromide was removed by filtration (70%). The evaporation of the solvent gave an oil which was two times chromatographed; finally, 60 mg of a green-yellow, unstable oil were collected. A tlc study showed that the aminoindenone **2e** was present in the sample, with a slight amount of an impurity at higher R_f; several successive chromatographies of the same sample did not completely purify the aminoindenone. The isomeric aminoindanone **3e** was completely absent in the chromatogram. Ultraviolet maxima (*n*-hexane) were found at 237 and 243; nmr peaks of **2e** (in $CDCl_3$) were found at τ 5.31 (1 H benzylic, doublet, J = 1.5 cps) and at 7.43 (2 H methylene α to N, complex triplet).

4. Monomethylamine. First Experiment.—The usual experiment was carried out with 0.50 g of **1** and 0.21 g of monomethylamine (4 equiv) in 20 ml of solvent and 0.12 g of hydrobromide were collected (65%). The chromatography gave 0.30 g of a yellow oil. The nmr spectrum ($CDCl_3$) of this oil showed that the main product is compound **3k**, described hereafter. After 2 days in a refrigerator, a pale yellow solid precipitated and was recrystallized in *n*-hexane–benzene, mp 107° (homogeneity checked by tlc). Ultraviolet maxima (isooctane) were

found at 228, 231 (sh), 272 (sh), 309 and 321 (sh) mμ (ε 12,700, 12,000, 11,000, 23,000, and 17,500). This spectrum was characteristic of the structure **3k**. Nmr peaks ($CDCl_3$) were found between τ 1.9 and 2.8 (9 H aromatic and 1 H vinylic), at 4.67 (1 H methine, doublet, J = 1.7 cps), at 8.00 (3 H, N-methyl, singlet), and at 8.18 (1 H, NH).

Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.19; H, 6.18; N, 5.80.

Second Experiment.—The same procedure and the same amounts of reactants were used, except for monomethylamine of which 80 mg (1.5 equiv) were used. A 0.70-g amount of hydrobromide was collected (55%). The residue, after evaporation of the solvent, was analyzed by the usual technique. The chromatography gave the following results.

The first fraction (eluent, benzene) contained two products, A and B [R_f (A) > R_f (B)]; nmr peaks ($CDCl_3$) were found between τ 2.0 and 3.1 (aromatic H), at 4.23 (1 H, doublet), at 5.06 (2 H, singlet), at 6.13 (2 H, doublet), and at 7.92 (3 H, methyl). A partial assignment was possible since a small amount (20 mg) of B was purified and immediately analyzed by nmr ($CDCl_3$) spectroscopy; nmr peaks were found between τ 2.3 and 3.1 (20 H, aromatic and vinylic), at 5.05 (2 H, singlet), and at 7.86 (3 H, methyl). Tentatively, B seemed to be the diindenoamino compound resulting from the attack of **1** by **2k**. The second fraction upon tlc analysis showed the presence of three compounds B, C, and D. Compound D was identified by tlc as **3k**.

5. **With Aniline.**—Under the usual conditions with 0.50 g of **1** and 0.31 g of aniline (2 equiv) in 20 ml of solvent, 0.13 g (50%) of hydrobromide were collected after 15 min. Column chromatography of the crude product gave fraction 1, 120 mg of an orange solid A, pure by tlc; fraction 2, 50 mg of a mixture of two products, A and B [R_f (A) > R_f (B)]; fraction 3, 160 mg of an orange solid which was pure B. The solid A was recrystallized in *n*-hexane–benzene, mp 143–144°. The structure **2f** was assigned to this compound on the basis of the spectroscopic data. Ultraviolet maxima (*n*-hexane, saturated solution) were found at 237, 243, and 278 (sh) mμ; ($CHCl_3$) at 246, 285 (sh), 320 (sh) 334 (sh) and 409 mμ (ε 48,000, 4300, 1800, 1400, and 1000). Infrared absorption (CH_2Cl_2) was observed at 3370 (NH) and 1714 (C=O) cm^{-1}. Nmr peaks ($CDCl_3$) were seen between τ 2.4 and 3.5 (14 H aromatic and 1 H vinylic), at 4.66 (1 H benzylic, relatively broad singlet), and at 5.89 (NH; by adding D_2O, this peak is broadened and shifted).

Anal. Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.58; H, 5.60; N, 4.36.

The solid B was **3f**. It was recrystallized from *n*-hexane–benzene, mp 161–162°. Ultraviolet maxima (*n*-hexane) were found at 230 (sh), 237, 244, 300 (sh), 311, and 320 (sh) (ε 20,000, 22,000, 29,000, 25,500, 27,500, and 24,000). Nmr peaks ($CDCl_3$) were between τ 2.1 and 3.4 (14 H aromatic and 1 H vinylic), at 4.08 (1 H methine, doublet J = 1.5 cps), and at 6.11 (NH).

Anal. Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.79; H, 5.64; N, 4.50.

6. **With N-Methylaniline.**—From 0.50 g of **1** and 0.35 g of N-methylaniline (2 equiv) in 20 ml of solvent, 0.18 g (55%) of hydrobromide was separated after 30 min at room temperature. The chromatography gave fraction 1, 30 mg of brown-red, viscous oil, pure by tlc (product A); fraction 2, 110 mg of a mixture of A and B [R_f (A) > R_f (B)]; fraction 3, 220 mg of an orange solid (B) pure by tlc.

The aminoindenone **2g** (compound A) crystallized in a refrigerator, giving a red solid, mp 105–106° (*n*-hexane). Ultraviolet maxima ($CHCl_3$) were found at 243, 257 (sh), 295 (sh), 331 (sh), and 416 mμ (ε 42,000, 15,000, 3600, 9500, and 330). Ultraviolet maxima (*n*-hexane) were found at 237, 242, and 328 mμ (ε 43,000, 48,000, and 2000). Infrared absorptions (CH_2Cl_2) were found at 1723 cm^{-1} (C=O). Nmr peaks ($CDCl_3$) were seen between τ 2.4 and 3.3 (14 H aromatic and 1 H vinylic), at 4.00 (1 H benzylic, broad singlet), at 7.17 (3 H, N-methyl).

Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.30. Found: C, 85.09; H, 5.85; N, 4.35.

The solid B (**3g**) was recrystallized from *n*-hexane–benzene, mp 152–153°. Ultraviolet maxima (*n*-hexane) were found at 230 (sh), 236, 241, 305 (sh), 312, and 321 (sh) (ε 16,500, 18,000, 23,000, 24,500, 25,500, and 21,000). Nmr peaks ($CDCl_3$) were seen between τ 1.9 and 3.2 (14 H aromatic and 1 H vinylic), at 3.67 (1 H methine, broad singlet), and at 7.70 (3 H, N-methyl).

Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.30. Found: C, 84.87; H, 6.00; N, 4.32.

7. **With Piperidine.**—In this case it was not possible to isolate the corresponding aminoindenone. The reaction, carried out with 0.45 g of **1** and 0.27 g of piperidine, gave, after rapid chromatography, only 0.39 g (84%) of 3-piperidino-2-benzal-1-indanone (**3h**). The nmr spectrum was exactly superimposable with the spectrum of an authentic sample. Another experiment was run at lower temperature (−5°) with 130 mg of **1** and 80 mg of piperidine, in 0.6 ml of $CDCl_3$. The reaction medium was analyzed by nmr at −5°, immediately after mixing the reactants but only the signals of **1**, **3h**, and piperidine were detected.

8. **With Pyrrolidine.**—The experiment at 5° did not give the aminoindenone, but only **3j**. Nmr peaks ($CDCl_3$) were found between τ 1.9 and 2.6 (9 H aromatic and 1 H vinylic), at 4.48 (1 H methine, doublet, J = 1.6 cps), at 7.3 (4 H, methylene α to N, multiplet), and 8.3 (4 H, methylene β to N, multiplet).

Another experiment was run at −5° with 170 mg of **1** and 80 mg of pyrrolidine in 0.7 ml of $CDCl_3$. The nmr analysis at −10° showed the signals of **1**, **3j**, pyrrolidine, and **2j** (at 4.81, 1 H benzylic).

Kinetic Studies of the Reaction of 3-Halogeno-2-benzal-1-indanones 1 and 4 with Diisopropylamine in Acetonitrile. Product Study. Reaction of 3-Bromo-2-benzal-1-indanone (1) with Diisopropylamine.—To a solution of 0.75 g of **1** in 30 ml of acetonitrile, 0.50 g of diisopropylamine was added at room temperature. The reaction was followed by tlc (petroleum ether–ether 75:25). During 18 hr, only **1**, **2b**, the amine, and the hydrobromide were detected. A 0.33-g amount of diisopropylamine hydrobromide was filtered (72%); then, the evaporation of the solvent left 0.68 g of a red oil. A nmr spectrum of the crude product showed only the signals of **1** and the aminoindenone. The aminoindenone **2b** was purified by fast chromatography of the crude material on neutral alumina (eluent, benzene); a red solid (0.42 g) resulted, mp 95–96°, which was shown to be pure, by tlc and nmr analysis.

The same reaction was followed at lower temperature by nmr analysis. To a cooled solution of 72 mg of **1** in 0.5 ml of $CDCl_3$ in an nmr tube, 58 mg of diisopropylamine was rapidly added, and the reaction medium immediately analyzed by nmr spectroscopy at −5°. The solution turned pale red (color of the aminoindenone) as soon as the reactants were mixed. During 15 min only the signals of **1** and the amine were recorded. Then the signals of **2b** began to appear (benzylic H and isopropyl H). After 85 min, when the hydrobromide began to precipitate, no other signals than those of **1**, **2b**, diisopropylamine, and its hydrobromide were observed.

Reaction of 3-Chloro-2-benzal-1-indanone (4) with Diisopropylamine.—The chloro ketone **4** was prepared[10] from the action of chloride ions on the hydrochloride of **3b**. Ultraviolet maxima (*n*-hexane) were found at 229, 227 (sh), 235, 242 (sh), 307 (sh), 315, and 327 mμ (ε 15,000, 14,100, 14,000, 10,750, 22,850, 28,350, and 24,050).

The reaction of 20 mg of **4** and 32 mg of diisopropylamine (4 equiv) in 2.0 ml of acetonitrile was followed by tlc (petroleum ether–ether 50:50) at room temperature during 27 hr. Only the chloro ketone, the aminoindenone **2b**, diisopropylamine, and its hydrobromide were detected (the elution) of the plate must immediately follow the spotting because of the possible decomposition of **2b** under these conditions.

In another experiment, the reaction of 95 mg of **4** and 75 mg of diisopropylamine in 0.45 ml of $CDCl_3$ was followed by nmr at room temperature. The signals of the aminoindenone **2b** began to appear after 10 min. After 40 min, the hydrochloride of the amine precipitated. All the signals, in each spectrum, were assigned to **4**, **2b**, the amine, or its hydrobromide.

Fifteen hours after the beginning of the experiment, the mixture was poured into ether and the hydrochloride (40 mg, 78%) removed by filtration. The solvent was evaporated and the red solid residue was analyzed by nmr ($CDCl_3$) spectroscopy; the spectrum showed the peaks of the amine, the aminoindenone **2b**, and the chloro ketone. A subsequent tlc analysis confirmed the presence of **4** and **2b**; in addition, a slight amount of unidentified product was found (coming probably from the partial decomposition of the aminoindenone).

Kinetic Procedures.—The bromo ketone **1** was recrystallized from CCl_4 and its melting point, uv and nmr spectra, and thin layer chromatogram were identical with those of a pure sample. The purity of the chloro ketone **4** was verified on the basis of the analysis and the spectra. The diisopropylamine was distilled once from BaO, then fractionated twice with a Vigreux column. We used the acetonitrile (Spectrograde) of Eastman as solvent.

The stabilities of **1**, **4**, and **2b** were checked under the conditions of the kinetic runs. It was found that **1** and **4** are stable, whereas the aminoindenone **2b** showed a slight decomposition, at 45° after 12 hr. The dilution (100 times or more) at room temperature, quenched the studied reactions.

Two different techniques were used depending on the temperature. For the kinetics run at 30° or below, a sealed bulb containing the amine was crushed in the solution of **1** (or **4**); then the level was rapidly adjusted. Collecting of the samples was done by direct pipeting, and the reaction was quenched by dilution. At least eight measurements were made in each run. The kinetics run above 30° were carried out using the sealed-bulb method. The bulbs were filled with a special weight buret at low temperature to avoid the loss of amine.

In the case of the kinetics followed by uv spectroscopy, the concentrations of the reactant (**1** or **4**) and the product (**2b**) were deduced from the optical densities at four wavelengths. It was noted that only the optical densities of the maxima give significant results. From an average of these values the concentrations of reactant and product were calculated.

For each experiment the following expressions were plotted against time: $\log [a/(a - x)]$, $[1/(b - a)] \log [a(b - x)/b(a - x)]$ (second-order and 1 equiv of amine per 1 equiv of halogeno ketone); $[1/(b - 2a)] \log [a(b - 2x)/b(a - x)]$ (second-order and 2 equiv of amine per 1 equiv of halogeno ketone); a and b are the initial concentrations of the ketone and the amine respectively; x is the concentration of the product. The kinetic constants were determined by the least-squares method; the precision is estimated at about ±3%.

The titration of the bromide ions was carried out as follows. A sample (5 or 10 ml) of the reaction medium was poured into 80 ml of benzene. The bromide ions were carefully extracted three times with 15 ml of distilled water, and the organic solvents were removed under vacuum at room temperature. The bromide ions were titrated by Volhard's method. This procedure permits a selective titration of the bromide ions, without interference with any other component.

The amine-consumption was followed by titrating the remaining amine. The sample was poured in a separating funnel containing 10 ml of 4×10^{-2} *N* HCl solution covered by 70 ml of benzene. After shaking, the aqueous layer was collected and the benzene layer was extracted three times by 15 ml of distilled water. The organic solvents were removed from the water solution under vacuum and the remaining acid was titrated (using methyl red as indicator) by an 8×10^{-3} *N* solution of morpholine in methanol. This procedure prevented the formation of the hydrochloride of the aminoindenone **2b** and permitted the selective titration of the diisopropylamine.

Registry No.—**1**, 5387-50-8; **2a**, 5387-51-9; **2a** HBr, 15982-75-9; **2b**, 15982-76-0; **2c**, 15984-15-3; **2d**, 15982-77-1; **2e**, 15982-78-2; **2f**, 15982-79-3; **2g**, 15982-80-6; **3a**, 5387-52-0; **3a** HCl, 15982-82-8; **3c**, 15982-83-9; **3d**, 15982-84-0; **3e** HCl, 15982-85-1; **3f**, 15982-86-2; **3g**, 15982-87-3; **3h**, 16031-03-1; **3j**, 15982-88-4; **3k**, 15983-89-8; **4**, 15983-91-2; 3-methoxy-2-benzal-1-indanone, 15984-14-2.

Acknowledgments.—The senior author (N. H. C.) is grateful for the hospitality afforded him by the Department of Chemistry during his tenure in 1967 as a guest of the Massachusetts Institute of Technology and for helpful discussions with Professor H. O. House during the later phases of this investigation. We also wish to thank Professor G. A. Gallup for his suggestions in the programming of the MO calculations. The work was supported in part by Grant No. CA02931 from the National Cancer Institute of the U. S. Public Health Service.

Mobile Keto Allyl Systems. VII.[1a] Amine-Exchange Reactions in the Indanone–Indenone Series

GEORGES MAURY, E.-MING WU,[1b] AND NORMAN H. CROMWELL[1c]

Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68508

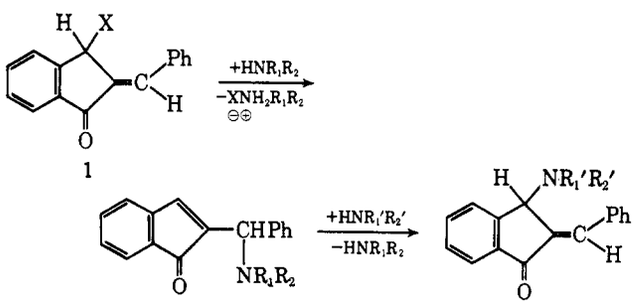
Received December 7, 1967

2-[α-(Substituted amino)benzyl]-1-indenones are shown to undergo a second-order amine-exchange reaction with certain amines to produce 3-substituted amino-2-benzal-1-indanones. For example, 2-[α-(diisopropylamino)-benzyl]-1-indenone undergoes this aminotropic allylic rearrangement with the less space-demanding amines (morpholine, piperidine, pyrrolidine, and *t*-butylamine) but not with diisopropylamine. The course of the reactions was followed by employing nmr, tlc, kinetic, and ultraviolet absorption techniques. It is proposed that these aminotropic allylic changes are best explained by a variant of an SN2′ mechanism. A novel amine-catalyzed prototropic rearrangement of the 3-(substituted amino)-2-benzal-1-indanones to 3-(substituted amino)-2-benzyl-1-indenones was also established.

In the preceding paper of this series,[1a] it has been shown that the reaction of 3-halogeno-2-benzal-1-indanones (**1**) with primary and secondary amines proceeds in two steps to give first the 2-(α-aminobenzyl)-1-indenones (**2**) then the isomeric 3-amino-2-benzal-1-indanones (**3**).

On the basis of various kinetic studies, a nearly concerted bimolecular mechanism was assigned to the first allylic rearrangement **1** → **2**. In the present paper, the results of our studies of the second allylic rearrangement **2** → **3** are reported.

The displacement of allylic amino groups with amines is expected to be relatively difficult, and reports of the use of an amine as the displacing reactant are very rare in the literature. Some allylamines resulting from the



2a, $R_1 = R_2 = i$-Pr
b, R_1 = H; $R_2 = t$-Bu
c, R_1 = H; $R_2 = i$-Pr

3a, R_1, R_2 = morpholino
b, R_1, R_2 = piperidino
c, R_1, R_2 = pyrrolidino
d, R_1 = H; $R_2 = t$-Bu
e, R_1 = H; $R_2 = i$-Pr

(1) (a) For paper VI in this series, see G. Maury, E.-M. Wu, and N. H. Cromwell, *J. Org. Chem.*, **33**, 1900 (1968); (b) Abstracted in part from the Ph.D. thesis of E.-M. Wu, University of Nebraska, Lincoln, Neb., 1966; (c) the author to whom all correspondence concerning this article should be addressed.