Registry No.—**3**, 1003-41-4; **5**, 18542-89-7; **7**, 1073-80-9; **9**, 694-85-9; **15**, 6104-45-6; **16**, 18542-92-2; **17**, 2228-30-0; **18**, 18542-94-4; **19**, 2701-45-3; **21**, 18661-77-3; 3,5-dimethyl-4-pyrathione, 18542-95-5; 3,5-dimethyl-4-thiapyrathione, 18542-87-5.

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Mobile Keto Allyl Systems. VIII.[1a] Properties of 2-(α-Aminobenzyl)-1-indenones

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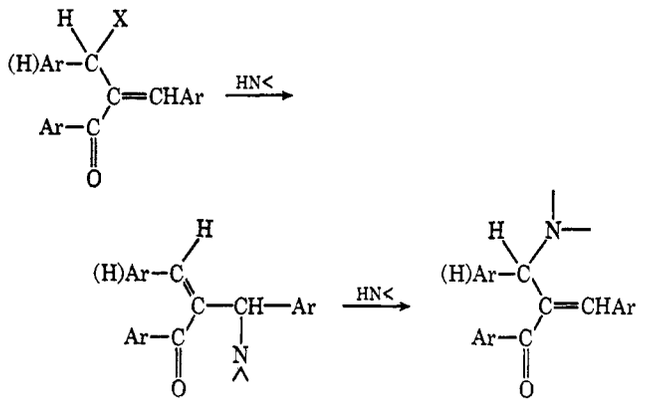
2-(α-Isopropylaminobenzyl)-1-indenone (**1a**) rearranges to the allylic isomer **2a** in the absence of added amine. Evidence supporting the intermolecularity of the rearrangement is presented; the results of kinetic studies support the occurrence of a chain reaction initiated by released amine. The aminoindenones **1b** and **1c** have specific properties associated with steric hindrance in the molecule; for instance, in contrast to the other indenones **1**, the hydrohalides of **1b** and **1c** rearrange to the corresponding 3-halo-2-benzal-1-indanones.

The ability of β-keto allyl systems to rearrange has been illustrated in the course of several studies involving the substitution of allyl halides by amines[2,3] or in the amine exchange reaction of allylamines.[1a,3] These investigations showed the occurrence of a variant



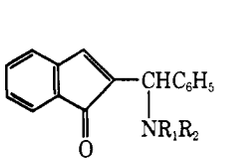
of an SN2′ mechanism with a transition state in which bond making is running slightly ahead of bond breaking. The orientation and the ease of the rearrangements have been attributed to the combined electron-withdrawing effects of the carbonyl and the halogen (or the amino) groups.

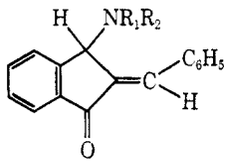
It has now been found that the presence of added amine is not necessary to induce the allylic rearrangement of the indenone **1** to the indanone **2**. Initial results in this series showed that the behavior of the aminoindenones **1** was apparently different from that of the aminobenzylacrylophenones;[3] therefore, the new rearrangement **1** → **2** was extensively studied. Another important item of interest in the chemistry of 2-(α-aminobenzyl)-1-indenones is the special properties of compounds **1** when the amino groups are very bulky; these effects have been associated with steric hindrance and are consistent with previous kinetic results[1a] as well as conclusions drawn from the study of the nmr spectra of **1** and **2**.

(1) (a) For paper VII in this series see G. Maury, E.-M. Wu, and N. H. Cromwell, *J. Org. Chem.*, **33**, 1907 (1968). (b) The author to whom all correspondence concerning this article should be addressed.

(2) G. Maury, E.-M. Wu, and N. H. Cromwell, *ibid.*, **33**, 1900 (1968).

(3) R. P. Rebman and N. H. Cromwell, *Tetrahedron Lett.*, 4833 (1965); N. H. Cromwell and R. P. Rebman, *J. Org. Chem.*, **32**, 3830 (1967).





1a, R_1 = H; R_2 = *i*-Pr
b, R_1 = R_2 = *i*-Pr
c, R_1 = *iso*-Pr; R_2 = cyclohexyl
d, R_1 = H; R_2 = *t*-But
e, R_1 = Me; R_2 = *i*-Pr
g, R_1 = H; R_2 = benzyl

2a, R_1 = H; R_2 = *i*-Pr
d, R_1 = H; R_2 = *t*-But
e, R_1 = Me; R_2 = *i*-Pr
f, R_1 = H; R_2 = *sec*-But
g, R_1 = H; R_2 = benzyl
h, R_1 = C_6H_5; R_2 = *i*-Pr

Results and Discussion

Rearrangement of 2-(α-Aminobenzyl)-1-indenones in the Absence of Added Amine.—2-(α-Isopropylaminobenzyl)-1-indenone rearranged slowly in chloroform at room temperature to give the isomeric 3-isopropylamino-2-benzal-1-indanone. The indanone **2a** was the only product detected by nmr or thin layer chromatographic analysis. The same reaction occurred, at different rates at room temperature, in dry acetonitrile, benzene, and *n*-hexane, and no other product than **2a** was found.

To investigate the mechanisms of the rearrangement, the kinetics of the preceeding reactions were followed in different solvents and at different concentrations. Nmr and uv spectroscopies were used in these studies because of the wide differences in the absorptivities of the compounds **1a** and **2a**.[1a] Characteristic kinetic curves are shown in Figure 1.

Each curve begins with an "induction period," the length of which depends upon the solvent and the starting concentration of **1a**; the middle part of the curves is very nearly a straight line, whereas the end approaches asymptotically the value of the initial concentration of **1a**. The addition of small amounts of dibenzoyl peroxide increases the rate of the rearrangement in chloroform or in acetonitrile, but no decrease in rate was observed upon addition of a radical inhibitor ruling out the possibility of a radical reaction; it is possible that the decomposition products of dibenzoyl peroxide initiate parallel nucleophilic reactions. The addition of small quantities of water has no effect on the rate within the experimental error.

The question first to be discussed is whether the

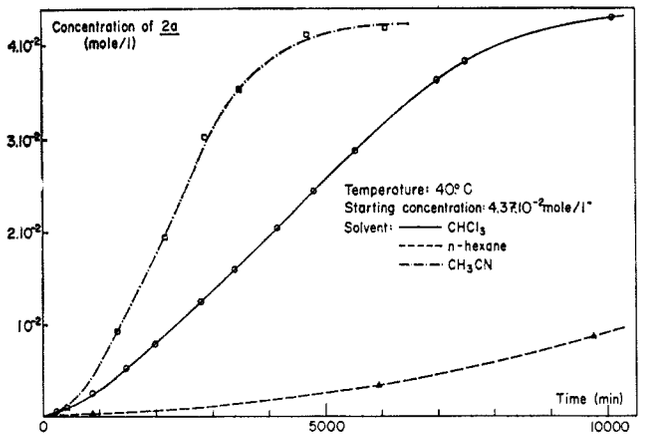
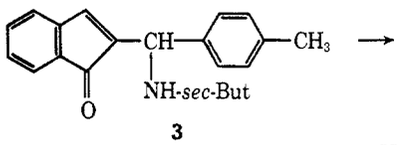


Figure 1.—Kinetic curves of the rearrangement reaction of **1a** to **2a**.

rearrangement is intra- or intermolecular, although the existence of a strained four-membered-ring intermediate (in the intramolecular mechanism) seems unlikely in this series; the occurrence of an SN1 isomerization[4] is also unfavored owing to the relative instability of the anion NR_1R_2. To answer this question,



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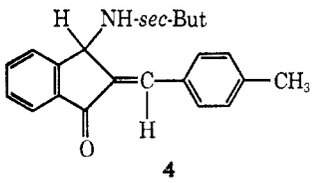

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a "crossover" experiment was carried out. The aminoindenone **3** undergoes the same rearrangement as **1a**, at a comparable rate in chloroform; the only detected product was **4**. 3-*sec*-Butylamino-2-benzal-1-indanone (**2f**) and 3-isopropylamino-2-*p*-methylbenzal-1-indanone (**5**), the expected "crossed products," were prepared as previously described.[2] A 1:1 mixture of **1a** and **3**, in deuteriochloroform at 22°, was observed by nmr; at the end of the reaction, the nmr spectrum showed the presence of the four possible aminoindanones, **2a** and **5** being the major products. These results were confirmed by mass spectrometry which indicated that **2f** and/or **5** were present in the crude product of reaction since a molecular peak at *m/e* 291 appears in the spectrum. Although, the intramolecularity of the rearrangement is not formally ruled out by the preceding results, they strongly suggest that it is intermolecular.

The intermolecularity of the rearrangement and the shape of the kinetic curves imply that several reactions take place. No free isopropylamine was detected in the rearrangement of **1a**, but it is expected that it reacts with **1a** as soon as released (the kinetic constant of the corresponding second-order reaction of **1a** with isopropylamine is 8.5×10^{-2} l. mol^{-1} min^{-1} at 23° in chloroform[1a]). The presence of amine in the reaction medium would explain the increase of the rearrangement rate in solvents of increasing polarity. The released amine acts as a catalyst and its relatively high reactivity explains the acceleration of the reaction after the induction period; at the end of the reaction, the decrease in concentration of **1a** and amine slows down the reaction. Thus the "propagation stage" of the reaction can be represented by **1** + amine → **2** + amine.

The shape of the kinetic curves suggests that a slow reaction initially takes place and initiates the rearrangement by releasing isopropylamine. A possible initiation reaction would be the nucleophilic attack of **1a** in position 3, by traces of water; a similar process, using an amine as initiator, was described previously.[1a] However, this path is not likely the major one since the rate of the rearrangement of **1a** is not influenced by addition of water and the results are reproducible, within the experimental error. On the other hand, the aminoindenone **1a** can itself initiate the reaction if its nitrogen attacks the position 3 of another molecule of **1a**, releasing isopropylamine for further reaction with **1a**; this is supported by the fact that the slope at the middle part of the curve increases with increasing starting concentration of **1a**. The condensation product, containing a 1-indenone and a 2-benzal-1-indanone moiety, can also react with the amine, giving two molecules of indanone **2a**. Condensation products of this type have been observed in the reaction of 3-bromo-2-benzal-1-indanone with methylamine[2] and of 1,3-dichloro-2(*p*-phenylbenzoyl)propane with *t*-butylamine.[5] The rearrangement of **1a** appears therefore similar to a chain reaction, with an initiation process (release of isopropylamine), a propagation process (reaction of **1a** with the amine), and a termination process (reaction of the amine with the condensation product).

The preceding rearrangement is not limited to the case of **1a**. Compounds **1** (R_1 = H; R_2 = cyclohexyl) and **1** (R_1, R_2 = morpholino), liquid at room temperature, rearrange in dry atmosphere, after their purification by chromatography. In acetonitrile or chloroform, **1d** and **1e** also rearrange at 60 and 20°, respectively. These rearrangements were not fully investigated but nmr and tlc showed that the corresponding aminoindanone **2** is the major or the only product. It is proposed that a chain mechanism occurs in which the propagation stage is basically the same as that in the case of **1a**, while the reaction is initiated by any nucleophile present and/or by the aminoindenone **1** itself when the nitrogen atom is disubstituted.

In contrast, the indenones **1b** and **1c** do not give the preceding autocatalytic rearrangement since they do not react with the corresponding amine. If temperature is increased, **1b** and **1c** decompose slowly in solution giving mainly 2-benzal-1-indanone and the corresponding amine; vapor phase chromatography (vpc) of **1b** and **1c** also resulted in decomposition, and the same products were detected. The course of the reaction is independent of the nature of the solvent. A kinetic study of the reaction in benzene at 60° showed no induction period, the rate of decomposition of the indenone was found to decrease with time, and addition of dibenzoyl peroxide did not affect the rate of reaction. Since the aminoindenone **1d** (which rearranges very slowly to **2d**) does not show any sign of decom-

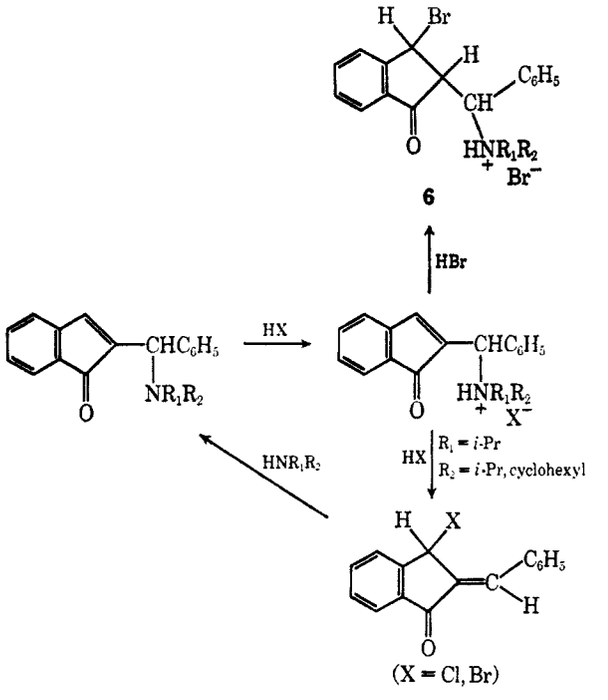
(4) R. M. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 753 (1956).

(5) E. Doomes and N. H. Cromwell, unpublished results.

position to 2-benzal-1-indanone at 60°, it is suggested that the decomposition of **1b** and **1c** is induced, directly and indirectly, by the steric hindrance related to the very bulky amino groups. The existence of several unidentified secondary products prevents us, at this stage, from choosing between the possible mechanisms of decomposition. An homolytic scission of the C–N bond may be involved. Another possible explanation would be the existence of an interaction between the carbonyl and the tertiary proton of an isopropylamino group, leading to a fragmentation of the molecule to a Schiff base and an homoenolate ion immediately protonated.

Reactions of Indenones 1 with Halogeno Acids.—The aminoindenones **1b** and **1c** present other special properties related to the bulky amino groups. Diisopylamine in excess does not react further with the aminoindenone **1b** and the corresponding 3-amino-2-benzal-1-indanone has not been prepared or even detected.[2] This was rationalized by assuming the existence of steric hindrance between the entering and leaving amino groups supposed to be *cis* to each other in the transition state of the reaction.[1a]

The reaction of halogeno acids on **1b** and **1c** is also specific at room temperature. If the solvent is ether and an excess of halogeno acid avoided, the hydrohalide of **1b**, as of any indenone **1**, is obtained. Left in contact with an excess of the corresponding halogeno acid in ether, the hydrochlorides or hydrobromides of **1b** or **1c** very readily rearrange at room temperature to give quantitative yields of amine hydrohalide and 3-halogeno-2-benzal-1-indanone. Since the yield and the purity of the halogeno ketone are excellent, this method has been applied to prepare the previously unknown 3-chloro-2-benzal-1-indanone used in kinetic studies.[2] In chloroform, the hydrohalide salts of **1b** or **1c** remained in solution but the same products were obtained in similar yields.



In contrast, no 3-bromo-2-benzal-1-indanone was formed in the reaction of **1a** or **1d** with an excess of HBr in chloroform at room temperature. The only product obtained in each case was shown to be the corresponding hydrobromide of 3-bromo-2-(α-X-aminobenzyl)-1-indanone **6**, resulting from addition of HBr to the double bond. The course of the reaction is similar in noncyclic β-keto allylamino systems.[6]

The reactivity of the 3 position of aminoindenones **1** is likely to increase by protonation of the nitrogen since it enhances its electron-withdrawing effect. In the case of **1a**, **1d**, and probably the aminoindenones **1** having less bulky amino groups, the addition of HBr to the olefinic bond occurs without rearrangement at room temperature; the *trans*-addition product is expected to be favored because of the probable existence of more extensive steric interactions in the *cis* isomer.

The steric hindrance associated with the amino group in the aminoindenones **1b** and **1c** is likely to increase by protonation of the nitrogen. This in turn increases the ability of the amino groups to leave and explains the specific behavior of the two preceding aminoindenones. The possible mechanisms include a two-step reaction with actual formation of an intermediate **6** and elimination of a molecule of amine, or a variant of an SN2′ mechanism in which no intermediate is formed and the breaking of the C–N bond immediately follows the formation of the C–Br bond in the transition state. The observed relative stability of compounds **6** on one hand and the potential ability of the amino groups in **1b** and **1c** to eliminate after absorption of the negative charge in the transition state on the other hand suggest that the SN2′ mechanism is more probable.

Nmr Spectra of the Indenones 1 and the Indanones 2.—The nmr spectra of the prepared aminoindenones **1** and aminoindanones **2** have been studied, particularly to detect the influence of the bulky amino groups. The results are reported in Table I.

The benzylic proton in **2** appears always deshielded compared with the benzylic proton in **1**, although these corresponding protons have nearly equivalent electronic environments. Since the phenyl group of the lateral chain is likely to be in the plane of the molecule **2**, its deshielding action on H_3 is expected to be more intense than the deshielding action of the free rotating phenyl group on the benzylic proton in **1**, even though the latter proton is nearer the plane of the molecule (in the favored rotamer; see later text) than H_3 in **2**. The preceding relation between the chemical shifts of the benzylic protons may be used to indentify the two isomers **1** and **2**. In both **1** and **2**, the benzylic proton signals are doublets or broad singlets, and the splitting results from an allylic coupling with the styryl proton; no significant benzylic coupling is involved since, in the similar case of 3-bromo-2-benzal-1-indanone, the coupling completely vanishes on deuteration of the benzal proton. The allylic coupling constant is always larger for **2** than for the isomeric **1**, and it is in the range 1.5–1.8 Hz for the aminoindanones **2**. This suggests that, in every case, the rotamer corresponding to the C_2–C_1' bond in **1**, and having the amino or the phenyl group nearly perpendicular to the plane

(6) (a) N. H. Cromwell and E. Doomes, *Tetrahedron Lett.*, 4037 (1966); (b) J.-L. Imbach, E. Doomes, R. P. Rebman, and N. H. Cromwell, *J. Org. Chem.*, **32**, 78 (1967).

TABLE I

NMR SPECTRA OF INDENONES 1 AND INDANONES 2 (DEUTERIOCHLOROFORM)

		Indenones 1			Indanones 2		
R_1	R_2	Benzylic H[a]	R_1	R_2[b]	Benzylic H[b]	R_1	R_2[b]
H[c]	Me				4.67 (1.7)	8.18	8.00
H[c]	*n*-But	5.31 (1.6)	8.20	Multiplet	4.76[d]		Multiplet
H	*t*-But	5.14 (1.1)	8.60	8.92	4.55 (1.8)	8.32	9.11
H[c]	C_6H_5	4.66 (<0.8)	5.89		4.08 (1.6)	6.11	
H[c]	Cyclohexyl	5.10 (1.5)	8.35	Multiplet	4.78[d] (1.7)	7.5	Multiplet
H	$CH_2C_6H_5$	5.22 (1.4)	7.38	6.27	4.75 (1.7)	8.03	6.74–6.90[e]
H[f]	*i*-Pr	5.17 (1.3)	8.33	8.92–8.98	4.68 (1.7)	8.13	9.10–9.24
Pyrrolidino		4.81			4.48 (1.6)	7.3 (α)	8.3 (β)
Piperidino[c]					5.00 (1.5)	7.5 (α)	8.6 (β, γ)
Morpholino[c]		5.71 (<0.8)	6.3 (β)	7.5 (α)	4.92 (1.6)	6.4 (β)	7.4 (α)
Me[c]	C_6H_5	4.00 (1.2)	7.17		3.67 (1.5)	7.70	
Me	*i*-Pr	5.38 (0.8)	7.90	8.98	4.68 (1.8)	8.13	9.10–9.24
i-Pr[c]	*i*-Pr	4.87 (<0.8)		8.92–9.01			
Cyclohexyl	*i*-Pr	4.85 (1.0)	8.4	8.93–9.06			
C_6H_5	*i*-Pr				3.74		9.03–9.11

[a] These signals are doublets or broad singlets; the numbers in parentheses are the corresponding allylic coupling constants. [b] Two values of chemical shift in this column indicate that two identical groups (benzylic H or isopropyl methyl) are magnetically nonequivalent. [c] Reference 2. [d] In carbon tetrachloride. [e] Coupling constant, J = 11.7 Hz. [f] Reference 1a.

of the indenone ring, is favored.[7] The value of the allylic coupling constant is relatively low when the nitrogen in **1** is disubstituted by very bulky groups (as in **1b** and **1c**), suggesting that the favored rotamer has the benzylic proton in the plane of the molecule.[8] However, this discussion does not take into account other factors (the polarities of the different rotamers for example) which also may influence the population of rotamers.

It has also been found that, in the nmr spectra of the aminoindenones **1** and aminoindanones **2** having isopropylamino groups, the isopropyl methyl protons are usually magnetically nonequivalent.[9] A systematic solvent- and temperature-effect study showed that the magnetic nonequivalence increases regularly with decreasing temperature in the case of **1b** and **1c**, suggesting a restriction in the conformational mobility compared with **1a** and **1e**. An opposite effect (nonequivalence decreasing with decreasing temperature) has been observed for compounds **1a**, **1e**, and **2e** in acetonitrile and methylene dichloride, whereas this effect is reversed for **1e** and **2e** in benzene.[9]

Experimental Section[10]

Preparations of 2-(α-Aminobenzyl)-1-indenones (1).—The preparation of several aminoindenones **1** (**1a**, **1b**, **1d**, etc.) has been already described,[1a] and the same general procedure was used to prepare the following indenones.

A. 2-(α-Methylisopropylaminobenzyl)-1-indenone (1e) was prepared from 1.5 g of 3-bromo-2-benzal-1-indanone (5×10^{-3} mol) and 0.88 g of methylisopropylamine (2.2 equiv). The hydrobromide was separated by addition of ether (0.42 g, 55%). A fraction of 1.1 g of a yellow oil (75%) was obtained after two successive chromatographies on alumina (eluent, benzene). The oil crystallized as a yellow solid which was shown to be pure by tlc: mp 85–87° (unstable at room temperature). Uv maxima (*n*-hexane) were found at 239, 245, 299, 320, 330 (sh), 374 mμ (ε 38,000, 36,300, 1850, 2000, 1750, 1600).

B. 2-(α-Cyclohexylisopropylaminobenzyl)-1-indenone (1c) was obtained from 1.50 g of 3-bromo-2-benzal-1-indanone (5×10^{-3} mol) and 1.70 g of cyclohexylisopropylamine (2.2 equiv). After 12 hr at room temperature, 0.92 g of amine hydrobromide (83%) was filtered, and tlc on the residue after evaporation of the solvent (2.0 g of a black-red oil) showed only one spot (ether–petroleum ether 50:50). The oil crystallized as a yellow solid: mp 104–105° dec. Uv maxima were found at 237, 242, 257 (sh), 318, 330, 391 mμ (ε 40,000, 45,000, 5300, 1000, 850, 850).

Anal. Calcd for $C_{25}H_{29}NO$: C, 83.52; H, 8.13; N, 3.90. Found: C, 83.50; H, 8.04; N, 3.86.

C. 2-(α-Benzylaminobenzyl)-1-indenone (1g) was prepared from 1.50 g (5×10^{-3} mol) of 3-bromo-2-benzal-1-indanone and 1.08 g of benzylamine (2 equiv). A 0.85-g amount of amine hydrobromide was collected (90%). After fast evaporation of the solvent, two successive chromatographies gave a yellow oil which was shown to be a mixture of **1g** and **2g** by tlc. The nmr spectrum ($CDCl_3$) of the sample showed that the proportion of **1g** was about 95%: 1 H methine at τ 5.22 (doublet, J = 1.4 Hz), 2 H aminobenzylic at 6.27 (sharp singlet), and NH at 7.38.

Preparation of 3-Amino-2-benzal-1-indanones (2).—The general procedure has been given previously with the preparation of several indanones **2** (**2a**, **2d**, etc.).[1a]

A. 3-Methylisopropylamino-2-benzal-1-indanone (2e).—To a solution of 1.0 g of a 95% pure sample of **1e** (the impurity being **2e**) in 15 ml of benzene, 1.0 g of methylisopropylamine was added. After 15 hr at room temperature, the solvent was evaporated and the solid residue (0.82 g) was recrystallized twice in *n*-hexane–benzene. A yellow solid was obtained: mp 96–97° (pure in tlc). Uv maxima were found at 228, 232 (sh), 259 300 (sh), 312, 322 mμ (ε 14,000, 13,000, 9200, 11,900, 24,500, 20,000).

Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.34; H, 7.39; N, 5.01.

B. 3-Benzylamino-2-benzal-1-indanone (2g).—From 1.0 g of 3-bromo-2-benzal-1-indanone (3.4×10^{-3} mol) and 1.08 g of benzylamine (3 equiv). After 4 days at room tmperature, 0.57 g of amine hydrobromide was filtered (90%). The oil residue, after evaporation of the solvent, crystallized slowly giving 0.40 g (36%) of a white-yellow solid, which was recrystallized in *n*-hexane–benzene: mp 103–104°. Tlc showed that the solid (**2g**) was pure, and that traces of several unidentified compounds were present in the mother liquor. The uv maxima in the spectrum of **2g** (*n*-hexane) were found at 228, 265 (sh), 310, 326 (sh) mμ (ε 14,500, 10,000, 22,500, 15,000).

Anal. Calcd for $C_{23}H_{19}NO$: C, 84.89; H, 5.89; N, 4.30. Found: C, 84.91; H, 6.05; N, 4.32.

C. 3-Phenylisopropylamino-2-benzal-1-indanone (2h) was obtained from 1.50 g of 3-bromo-2-benzal-1-indanone and 1.65 g of phenylisopropylamine (2.4 equiv). After 1.5 hr at room tem-

(7) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p 107.

(8) A. A. Bothner-By, D. Naar-Colin, and H. Gunther, *J. Amer. Chem. Soc.*, **84**, 2748 (1962).

(9) G. Maury and N. H. Cromwell, results to be published in detail separately.

(10) Melting points were not corrected. Uv spectra were determined with a Cary Model 11-MS spectrophotometer. Ir spectra were measured with a Perkin-Elmer Model 237. Nmr spectra were determined with a Varian A-60 spectrometer; the chemical shifts are given in τ units with TMS as internal reference. Mass spectra were obtained with a Hitachi Model RMU-6D.

perature, tlc showed that the reaction was over. An orange-yellow solid was filtered (1.4 g, 78%), washed with water, dried, and recrystallized in *n*-hexane–benzene: mp 180–182° (pure in tlc). Uv maxima (*n*-hexane) were found at 231, 238, 259, 307, 317, 331 mμ (ε 14,700, 14,200, 20,600, 24,800, 26,500, 21,700).

Anal. Calcd for $C_{25}H_{23}NO$: C, 84.95; H, 6.56; N, 3.96. Found: C, 85.14; H, 6.66; N, 4.03.

D. 3-*sec*-Butylamino-2-benzal-1-indanone (2f) was prepared from 1.0 g of 3-bromo-2-benzal-1-indanone and 0.73 g of *sec*-butylamine (3 equiv). After 42 hr at room temperature, 0.45 g (86%) of amine hydrobromide was filtered. The residue, after evaporation of the solvent, was chromatographed on alumina (eluent, benzene); 0.70 g (71%) of an orange oil was obtained (pure in tlc). Uv maxima (*n*-hexane) were found at 231, 237, 262, 315, 325 (sh) mμ (ε 12,400, 12,200, 11,400, 21,000, 16,600). Nmr peaks ($CDCl_3$) were found between τ 2.0 and 2.8 (9 H aromatic + 1 H vinylic), at 4.76 (1 H methine, broad singlet), at 7.45 (1 H tertiary of the *sec*-butyl group, multiplet), at 8.38 (NH), between 8.5 and 9.7 (8 H of *sec*-butyl group, multiplet).

Rearrangement of the Aminoindenone 1a. A. Product Study.—An approximately 15% (w/v) solution of **1a** (pure and dry sample), in a solvent (acetonitrile-d_3, deuteriochloroform, benzene, or *n*-hexane) dried on alumina, was kept at room temperature in a sealed nmr tube. Observation by nmr showed, in each case, only the formation of the isomeric aminoindanone **2a** (H methine or methyl peaks). The rearrangement was completed in about 75, 150 and 170 hr in acetonitrile-d_3, deuteriochloroform, and benzene, respectively; in *n*-hexane, the reaction was slower and the product **2a** precipitated early preventing further nmr observation. Tlc (ether–petroleum ether, 50:50) confirmed the result of the nmr analysis in each case. Besides the spots of **1a** and **2a**, a very weak spot was, however, sometimes present at lower R_f on silica gel; it may have resulted from partial reaction of **2a** with silica gel.

B. Kinetic Studies.—The rearrangement of **1a** was studied kinetically by using uv and nmr spectroscopies. The kinetic procedures using uv spectroscopy have been previously reported[2] and were used without modification. In kinetics involving nmr spectroscopy, the solution of **1a** (volume determined at the end of the experiment) was kept in a sealed nmr tube, in a constant-temperature bath, except when the nmr spectra were run; the manual or electronic integrations of characteristic signals (H methine and methyls) gave the curves representing the variation of the concentrations of **1a** and **2a** with time. Regardless of the conditions, the curves [concentrations of **2a–f** (time)] had the general shape shown in Figure 1. At 40° and with an initial concentration of **1a** = 4.37×10^{-2} mol/l., the slope of the middle part of the curve was 2.2 times smaller in chloroform than in acetonitrile and considerably smaller in *n*-hexane where the precipitation of **2a** occurred after about 30% of the reaction. The addition of dibenzoyl peroxide (9×10^{-4} mol/l.) increased the slope of the middle part of the curve 3.3 times in chloroform and 2 times in acetonitrile. At the same temperature and initial concentration in acetonitrile, the addition of a radical inhibitor (5×10^{-4} mol/l. of diphenylpicrylhydrazyl) increased 1.4 times the value of the slope; under the same conditions, the curves obtained after addition of water (1.1×10^{-2} or 4.4×10^{-2} mol/l.) can be considered identical with the reference curve, within the experimental error. A study of the influence of the initial concentration in chloroform at 40° gave the following results (initial concentration in mol/l., slope at the middle part of the curve in mol $l.^{-1}$ min^{-1}, time at half-reaction in minutes): 3.7×10^{-2}, 5.6×10^{-6}, 4200; 4.4×10^{-2}, 5.9×10^{-6}, 4200; 7.7×10^{-2}, 1.2×10^{-5}, 4300; 8.9×10^{-2}, 1.6×10^{-5}, 3500; 8.5×10^{-1}, 4×10^{-4}, 1700; 1.0, 4.2×10^{-4}, 1600. It must be noted that the rearrangement is too slow to influence appreciably the rate of the second-order reaction of **1a** with isopropylamine when one or several equivalents of amine are present.[1a]

Crossover Experiment. A. 3-Bromo-2-*p*-methylbenzal-1-indanone.—A solution of 2.0 g of 2-*p*-methylbenzal-1-indanone (8.5×10^{-3} mol), 1.50 g (1 equiv) of N-bromosuccinimide, and 0.1 g of dibenzoyl peroxide in 70 ml of carbon tetrachloride was refluxed for 2.5 hr under an ir lamp. After filtration of the succinimide and evaporation of the solvent, 1.70 g (64%) of a white solid was obtained. Recrystallization in *n*-hexane–benzene gave a solid and ony one spot was seen in its tlc chromatogram: mp 135–140°. Uv maxima (*n*-hexane) were found at 240, 248 (sh), 328, 340 (sh) mμ (ε 16,000, 13,000, 19,000, 16,000). Nmr peaks ($CDCl_3$) were found between τ 1.9 and 2.8 (8 H aromatic and 1 H vinylic), at 3.59 (1 H methine, broad singlet), at 7.60 (3 H methyl); in addition, a very weak peak was found at 5.46 which may be due to an isomer.

B. 3-Isopropylamino-2-*p*-methylbenzal-1-indanone (5) was obtained from 0.40 g of 3-bromo-2-*p*-methyl-benzal-1-indanone (1.3×10^{-3} mol) and 0.24 g of isopropylamine (3 equiv). After 24 hr at room temperature, 0.15 g of hydrobromide (82%) was filtered, and the solvent was evaporated leaving 0.27 g of a yellow solid (71%) recrystallized in *n*-hexane–ether: mp 89–91° (pure in tlc). Uv maxima (*n*-hexane) were found at 237, 244, 263 (sh), 326, 340 (sh) mμ (ε 14,200, 13,800, 9300, 25,000, 22,500). Nmr peaks ($CDCl_3$) were found between τ 1.9 and 2.8 (8 H aromatic + 1 H vinylic), at 4.71 (1 H methine, doublet, J = 1.6 Hz), at 7.19 (1 H tertiary isopropyl, quintet), at 7.62 (3 H methyl), at 8.38 (NH), at 9.08 (3 H isopropyl methyl, J = 6.6 Hz), at 9.22 (3 H isopropyl methyl, J = 6.6 Hz).

Anal. Calcd for $C_{20}H_{21}NO$: C, 82.44; H, 7.26; N, 4.81. Found: C, 82.44; H, 7.40; N, 4.91.

C. 3-*sec*-Butylamino-2-*p*-methylbenzal-1-indanone (4) was prepared from 0.75 g of 3-bromo-2-*p*-methyl-benzal-1-indanone (2.5×10^{-3} mol) and 0.52 g of *sec*-butylamine (2.8 equiv). After 3 days, 0.38 g (98%) of hydrobromide was filtered, and the solvent was evaporated. The residue (0.72 g) was chromatographed twice on alumina (eluent, benzene). A yellow oil crystallizing as an solid was obtained: mp 78–79° (recrystallization in *n*-hexane). Nmr peaks ($CDCl_3$) were found between τ 2.0 and 2.9 (8 H aromatic + 1 H vinylic), at 4.66 (1 H methine, broad singlet), at 7.60 (3 H methyl) at 7.40 (1 H tertiary *sec*-butyl, multiplet), at 8.20 (NH), between 8.5 and 9.5 (8 H *sec*-butyl, multiplet).

Anal. Calcd for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.64; H, 7.73; N, 4.53.

D. 2-(α-*sec*-Butylamino-*p*-methylbenzyl)-1-indenone (3) resulted from the reaction of 0.50 g of 3-bromo-2-*p*-methylbenzal-1-indanone (1.6×10^{-3} mol) and 0.35 g of *sec*-butylamine (3 equiv) in 10 ml of benzene, at 0°. After 5 min, 0.11 g (45%) of amine hydrobromide was filtered and the solvent was quickly evaporated. The residue was chromatographed twice on alumina giving 0.17 g (37%) of a yellow-green oil which was shown to be pure by tlc and nmr. Nmr peaks ($CDCl_3$) were found between τ 2.4 and 3.0 (8 H aromatic + 1 H vinylic), at 5.12 (1 H methine, broad singlet), at 7.44 (1 H tertiary, *sec*-butyl, multiplet), at 7.66 (3 H methyl), at 8.32 (NH), between 8.1 and 9.3 (8 H *sec*-butyl, multiplet).

Rearrangement of the Indenone 3.—A solution of 0.10 g of **3** freshly prepared (and pure in tlc) in 0.4 ml of $CDCl_3$ (dried on alumina), was kept at 22°. Nmr spectra, run at intervals of time, showed that the isomeric indanone **4** began to appear after 20 hr (H methine at τ 4.63, and methyl at 7.57). After 120 hr, the indenone **3** had completely vanished, and only **4** was detected by nmr. A thin layer chromatogram on the crude mixture, after evaporation of the solvent, showed only the presence of indanone **4** (same R_f as that of an authentic sample) and traces of **3**.

E. Crossover Experiment.—A 0.28-g sample of the indenone **1a** and 0.28 g of the indenone **3** (pure samples dried under vacuum-were dissolved in 0.50 ml of deuteriochloroform passed on alumina; the resulting solution was poured into an nmr tube which was sealed and kept at 23°. The reaction medium was analyzed by nmr until the end of the reaction after about 140 hr. The signals of **2a, 2f, 4,** and **5** were present in the last nmr spectrum, and no other product was detected. Analyzing the relative intensities of the aliphatic methyl peaks (all in a relatively narrow range, and sometimes overlapping) it was found that the concentration of **2a** > concentration of **5** > concentration of **4** > concentration of **2f**. Confirmation of these results was sought by applying other techniques.

The solvent was evaporated giving a brown oil which crystallized slowly and partially. A tlc analysis (ether–petroleum ether, 50:50, or ether–benzene, 20:80) failed to separate the spots of the corresponding aminoindanones. Vpc (SE-30 or Apiezon columns) could not be used because the aminoindanones decompose in the injector (200°).

A mass spectrum of the crude mixture gave the following significant peaks: *m/e* 305, 291, 277, 276, 262, 248, 234, 72, 58. The peaks at *m/e* 305, 291, and 277 are the molecular peaks of **4, 2f, 5,** and **2a** (compared with the mass spectra of the authentic samples) thus proving the presence of the corresponding indanones (particularly **2f** and/or **5**) in the mixture.

Thermal Decomposition of 1b and 1c.—A solution of 1.0 g of

1b in 40 ml of dry benzene was kept in a sealed tube 22 hr at 90°. The evaporation gave 0.88 g of a dark oil which crystallized on addition of petroleum ether giving 0.46 g of 2-benzal-1-indanone (65%), mp 112–113°. Uv absorption (methanol) was found at 229, 280 (sh), 319 mμ (ε 7900, 8900, 26,700); an nmr spectrum was exactly superimposable on that of 2-benzal-1-indanone.

In another experiment, a solution of 0.12 g of **1b** in 0.40 ml of dry benzene at 60° in a sealed nmr tube was followed kinetically by nmr. No induction period was found, and the decomposition rate of **1b** and the rate of appearance of 2-benzal-1-indanone decreased with increasing time. The major reaction products (2-benzal-1-indanone and diisopropylamine) began to appear after 20 hr, and after 120 hr no starting material remained; the yields, determined by nmr, were 55% 2-benzal-1-indanone and 45% diisopropylamine. The presence of these products was confirmed by vpc analysis (SE-30 column); injection of an ethereal solution of **1b** or **1c** (detector temperature 200°) resulted in decomposition giving 2-benzal-1-indanone and the corresponding amine. A tlc study of the crude product (ether–petroleum ether, 50:50) showed traces of eight unidentified decomposition products, along with the two major products. Within the experimental error, no change in rate (compared with the reference run) was observed on addition of dibenzoyl peroxide (2×10^{-2} mol/l.) or diphenylpicrylhydrazyl (1.3×10^{-2} mol/l.).

The preceding reaction occurs also in chloroform; after 18 days at room temperature, approximately half the starting aminoindenone **1b** decomposed. In acetonitrile, after 24 hr at 90°, 0.10 g of 2-benzal-1-indanone (54%) was obtained from 0.27 g of **1b**.

The reaction is similar for the case of the indenone **1c**. A solution of 80 mg of **1c** in 0.40 ml of dry benzene was kept at 60° in a sealed nmr tube, and the reaction was followed kinetically by nmr. The reaction was faster than in the case of **1b** and was over in 70 hr; the main products were 2-benzal-1-indanone and cyclohexylisopropylamine. This result was confirmed by vpc under the same conditions as used for **1b**. A tlc analysis showed the presence of traces of five unidentified compounds.

Reactions of the Aminoindenones 1 with Halogeno Acids. A. Halides of Compounds 1.—The hydrochlorides or hydrobromides of the indenones **1** were prepared by bubbling the dry halogeno acid into an ethereal solution of **1** until precipitation of the yellow salt was complete. The hydrobromide of **1d** has been described previously.[2] The hydrobromide of **1a** had the following properties: mp 157–158°; ir absorption (Fluorolube) was found at ν 1710 (C=O) and 1600 cm^{-1} (Ar); uv absorption (chloroform) was found at 241, 245, 327 mμ (ε 36,400, 40,700, 2500) and this is charactristic of the absorption of the indenone nucleus.[2] The hydrochloride of **1b** was immediately filtered after precipitation, abundantly washed with ether: mp 95–98° dec; uv absorption (acetonitrile) was found at 242, 247, 413 mμ.

B. Rearrangements of Halides of 1b and 1c in Presence of an Excess of Halogeno Acid.—Into a solution of 2.25 g of **1b** (7×10^{-3} mol) in 200 ml of dry ether, dry hydrogen chloride was bubbled until saturation. The yellow hydrochloride precipitated first and the mixture was stirred for 3 hr at room temperature. A white precipitate of diisopropylamine hydrochloride was filtered (0.90 g, 94%): mp 215–216° (chloroform). The evaporation of ether left 1.72 g of 3-chloro-2-benzal-1-indanone as a white solid (yield, 97%), which was washed with water, dried, and recrystallized in ether: mp 114–116°. The crude and the pure samples both showed only one spot in tlc (ether–petroleum ether, 50:50). Nmr peaks were found between τ 2.0 and 2.8 (9 H aromtic + 1 H vinylic), at 3.83 (1 H methine, doublet, J = 1.3 Hz). The uv absorption of this compound has been previously reported.[2]

Anal. Calcd for $C_{16}H_{11}ClO$: C, 75.45; H, 4.35; Cl, 13.93. Found: C, 75.62; H, 4.25; Cl, 13.97.

A parallel experiment was carried out with 0.25 g of **1b** in 50 ml of dry ether saturated by dry hydrogen bromide. The yellow hydrobromide precipitated and almost immediately decomposed to give 0.11 g of diisopropylamine hydrobromide (84%). The evaporation of the solvent left 0.22 g of 3-bromo-2-benzal-1-indanone (93%) which was shown to be pure by tlc: mp 116–117°. The nmr spectrum ($CDCl_3$) is exactly superimposable on the spectrum of an authentical sample. The same reaction repeated from 0.30 g of **1b** in 20 ml of chloroform gave the same results; 0.27 g of 3-bromo-2-benzal-1-indanone (96%) was obtained, as the only product, and shown to be pure by tlc analysis and by nmr.

A 0.87-g sample of **1c** was dissolved in 100 ml of dry ether and the solution was saturated by dry hydrogen chloride. The yellow hydrochloride precipitate then seemed to dissolve. The solution was stirred 12 hr at room temperature. A 0.42-g sample of cyclohexylisopropylamine hydrochloride was filtered (98%). The evaporation of the solvent gave 0.53 g of 3-chloro-2-benzal-1-indanone (90%) recrystallized from carbon tetrachloride-ether: mp 113–114°; mmp 113° with an authentic sample. It was shown by tlc that the sample was pure and that the chloro ketone was the only product of reaction. The nmr spectrum of the sample is superimposable on that of an authentic sample.

A parallel experiment using 0.87 g of **1c** in 100 ml of dry ether saturated with hydrogen bromide gave first the hydrobromide of **1c** which immediately decomposed to give 0.52 g of the hydrobromide of the amine (97%) and 0.72 g of 3-bromo-2-benzal-1-indanone (98%) recrystallized from carbon tetrachloride–ether: mp 119–120°; mp 120°. The sample was shown to be pure by tlc. The nmr spectrum of the product is exactly superimposable on that of an authentic sample.

C. Preparation of Compounds 6.—A 0.31-g sample of **1d** was dissolved in 20 ml of chloroform and the solution was saturated with dry hydrogen bromide, then stirred at room temperature until the yellow color of the hydrobromide of **1d** had vanished. Evaporation of the solvent gave 0.48 g of 3-bromo-2-(α-*t*-butylaminobenzyl)-1-indanone hydrobromide (99%) as a poorly soluble white solid, recrystallized from chloroform: mp 183–184° (no trace of 3-bromo-2-benzal-1-indanone was found by tlc analysis of the reaction medium); ir peaks (Fluorolube) at ν 1680 (C=O, shift toward the low frequencies probably because of the existence of a hydrogen bond with $^+NH_2$), 1598 cm^{-1} (Ar); uv abosorption (chloroform) at 251, 296 mμ (ε 14,000, 3900), very different from the absorption expected of the indenone nucleus.[2]

Anal. Calcd for $C_{20}H_{23}Br_2NO$: C, 53.00; H, 5.14; Br, 35.30. N, 3.09. Found: C, 53.00; H, 5.31; Br, 35.75; N, 3.1.6

The elimination of the amino group of the preceding compound appears relatively difficult. A 40-mg sample of this compound was refluxed for 20 hr in 5 ml of methylene dichloride, with or without hydrogen bromide added, and found to decompose partly giving **1d** (or its salt) and traces of **2d** (tlc), but no 3-bromo-2-benzal-1-indanone was detected by tlc analysis.

A similar reaction from 0.15 g of **1a** in 20 ml of chloroform saturated with dry hydrogen bromide gave 0.21 g of 3-bromo-2-(α-isopropylaminobenzyl)-1-indanone hydrobromide (93%) as a poorly soluble white solid (and no 3-bromo-2-benzal-1-indanone as seen by tlc): mp 160° (chloroform); ir peaks (Fluorolube) at ν 1685 (C=O) and 1598 cm^{-1} (Ar); uv absorption (chloroform) at 253, 293 mμ (ε 16,200, 3000).

Anal. Calcd for $C_{19}H_{21}Br_2NO$: C, 52.00; H, 4.82; Br, 36.41; N, 3.19. Found: C, 51.79; H, 5.05; Br, 36.62; N, 3.25.

Registry No.—**1** (R_1, R_2 = pyrrolidino), 18559-82-5; **1c**, 18559-66-5; **1d**, 5387-51-9; **1e**, 18598-37-3; **1g**, 18559-68-7; **1h**, 18559-69-8; **2** (R_1, R_2 = pyrrolidino), 15982-88-4; **2c**, 18559-83-6; **2d**, 5387-52-0; **2e**, 18559-71-2; **2f**, 18559-72-3; **2g**, 18559-73-4; **2h**, 18559-74-5; **3**, 18559-75-6; **4**, 18559-76-7; **5**, 18559-77-8; **6**, 18559-78-9; 3-bromo-2-*p*-methylbenzal-1-indanone, 18559-79-0; 3-chloro-2-benzal-1-indanone, 15983-91-2; 3-bromo-2-(α-isopropylaminobenzyl)-1-indanone hydrobromide, 18559-81-4.

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