Aziridinyl Ketones. XVIII. The Rearrangement-Dehydrogenation of *cis*-1-Cyclohexyl-2-phenyl-3-aroylaziridines (1)

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The sequential nature of the unique rearrangement-dehydrogenation of *cis*-1-alkyl-2-aryl-3-aroylaziridines (**1a-d**) into 2-alkylamino-3-arylindenones (**2a-d**) when treated with a lithium amide has been established. Furthermore, a competitive degradation pathway has been discovered which leads to ω-aminoacetophenones and benzaldehyde, thereby accounting for the major product of this reaction. *trans*-1-Alkyl-2-aryl-3-aroylaziridines do not react with the lithium amides employed in these studies. Although 1-cyclohexyl-2-methyl-3-benzoylaziridine reacts with lithium amide to produce a 3-carbanion, neither a rearrangement-dehydrogenation to a 2-aminoindenone nor a more extensive degradation involving carbon-carbon bond cleavage is observed. Mechanistic pathways for these base catalyzed reactions are discussed.

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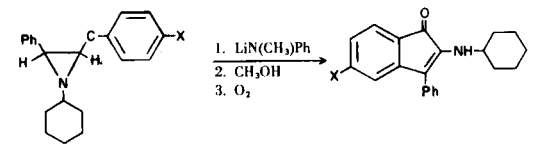
More than a decade has passed since the novel rearrangement-dehydrogenation (R-D) of *cis*-1-cyclohexyl-2-phenyl-3-benzoylaziridine (**1a**) into 2-cyclohexylamino-3-phenylindenone (**2a**) in the presence of lithium *N*-methylanilide or lithium diisopropylamide was first announced as a preliminary communication (2). More recently (3), a pathway for the R-D of **1a** into **2a** was suggested in a second communication. The scope of this reaction has now been extended to other *cis*-1-cyclohexyl-2-phenyl-3-aroylaziridines (**2**) and is discussed below. The corresponding *trans*-aziridine (**1a'**) is reduced to its *trans*-carbinol by the latter reagent, see reference (1), but does not undergo the R-D reaction with the former reagent. Also noteworthy is the fact that the 2-methyl analog **1e** fails to undergo the R-D reaction.

Scheme I

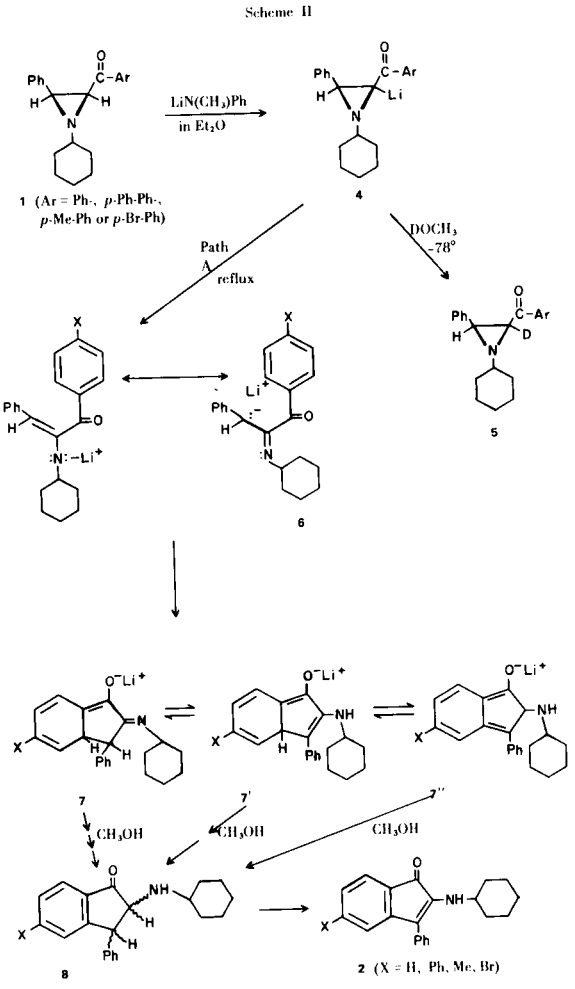


cis-Aroylaziridine (1)		Indenone (2)		
1	X	2	X	Yield (%)
a	H	a	H	20
b	Ph	b	Ph	14
c	CH_3	c	CH_3	29
d	Br	d	Br	22

The initial evidence for this reaction sequence came from the fact that only organic lithium compounds with substantial steric demand can effect the R-D of **1** into **2** (*e.g.*, only lithium *N*-methylanilide and lithium diisopropylamide have been found to cause this reaction). Previous investigations have shown that sodium bases effect eqimerization of aroylaziridines (4). Furthermore, phenyllithium, as well as various Grignard reagents, readily add to the carbonyl without affecting the aziridine ring (5,6). Hence, basic reagents, under mild conditions do not appear to cause destruction of the aziridine ring.

A reaction sequence for the transformation of aroylaziridines (**1**) into indenones (**2**) can now be put forth. Also a competing degradation pathway involving C-C bond scission accounts for the major product of the reaction, ω-cyclohexylaminoacetophenones (**3a-b**). In addition, the

Scheme II



inability of *trans*-1-cyclohexyl-2-phenyl-3-benozylaziridine (**1a'**) or *cis*-1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-aziridine (**1e**) to undergo the R-D reaction with either of the above bases has been investigated.

Results and Discussion.

Reported below is a viable mechanistic pathway whereby the transformation in Scheme I can best be rationalized.

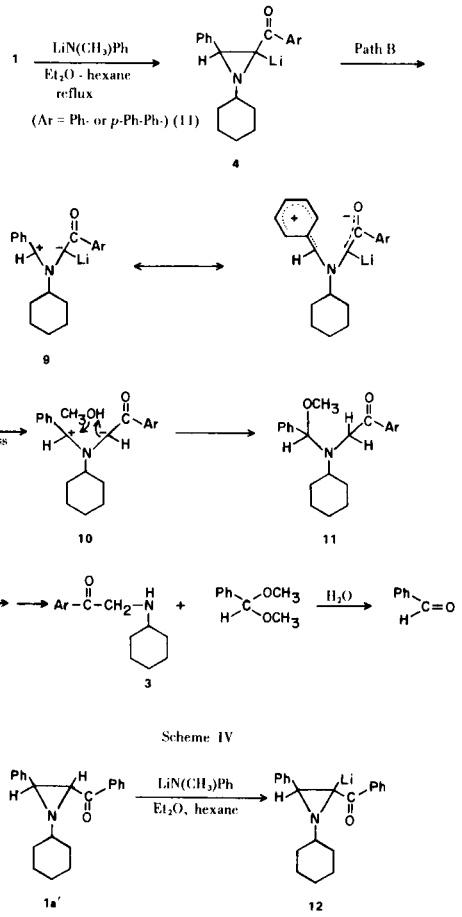
In our earlier publications (1,2) we reported that **1a** was converted into **2a** in 20% yield in the presence of lithium *N*-methylanilide. Our investigations have now found that the *p*-phenylbenzoyl (**1b**), *p*-toluyl (**1c**), and *p*-bromobenzoyl (**1d**) analogs also rearrange under identical conditions to their corresponding deeply purple colored 2-cyclohexylamino-3-phenyl-5-substituted-indenones: **2b**, **2c**, and **2d**. In all cases yields were below 30%. The structures of these compounds were established by elemental analysis, infrared, ultraviolet-visible, and ^{1}H nmr spectra.

The sequence of reactions shown in Scheme II best illustrates a plausible reaction pathway for the stereoselective rearrangement (*i.e.*, only the *cis* isomer rearranges) of **1** into **2**.

The first step in this pathway is thought to be the abstraction of the α-ring proton by the base to give *cis*-α-lithio-1-cyclohexyl-2-phenyl-3-benzoylaziridine (**5**). Intermediate **5** was detected by reacting **1a** with lithium *N*-methylanilide at low temperature (T = -78°) and then quenching the reaction with methanol-d_1. ^{1}H nmr revealed the α-proton peak to have diminished to 20% of its original height (see Experimental). Hence, based on this deuterium incorporation study, which is analogous to that of Eische and Galle in oxiranes (7), it appears reasonable to suggest that **5** is the first intermediate formed in the pathway.

Another important experiment was the transformation of **1a** into **2a** using azobenzene in lieu of oxygen as the hydrogen acceptor. This key experiment, for the first time, offers positive evidence that the immediate precursor of **2a** is 2,3-dihydro-2-cyclohexylamino-3-phenyl-indenone(**8**) (8). The evidence for this is two-fold. Visible spectroscopy studies show that azobenzene reacts to become hydrazobenzene upon addition to the reaction mixture and concomitantly the reaction mixture itself develops a purple color indicating the formation of the unsaturated indenone **2a** (see Experimental). Furthermore, since it is believed **7**, **7'**, and **7''** are in thermal equilibrium owing to the reversibility of their [1,3]suprafacial shifts, all paths, upon addition of methanol, lead to **8**. Since an equilibrium has been established, the most stable thermodynamic isomer wins out. The benzeniod 2,3-dihydro-intermediate **8** is expected to be more stable than any of its quinoid analogs (9). Use of the known

Scheme III



Scheme IV

hydrogen acceptor, azobenzene, specifies the timing of the loss of hydrogen (*i.e.*, it is lost after protonation by methanol and not before). Hence, intermediates such as **7**, **7'**, and **7''** cannot be ruled out in the mechanistic sequence of Scheme II. Unfortunately, however, all attempts to trap **6** *via* methylation have failed so that it is suspected that this particular intermediate enjoys only a transient existence.

In Scheme II a mechanistic sequence for the formation of **2a** has now been put forth; however, owing to the low yield of **2a** (*e.g.*, 20%), an investigation as to the fate of the remainder of the starting material **1a** was important. Recent laboratory work has revealed the major product of this reaction to be ω-cyclohexylaminoacetophenone (**3a**) and a possible pathway for its formation may now be put forth (see Scheme III) (10). Analogously, the major product of the reaction of **1b** with lithium *N*-methylanilide was **3b**. Here both **3a** and **3b** were identified on the basis of ^{1}H nmr, ir and independent synthesis. Finally, a trace amount of benzaldehyde was isolated in the work-up and the 2,4-DNP derivative gave the expected melting point of 237°, thereby accounting for the formation of the other degradation product.

Since the thermal process of ring cleavage of carboaziridines involves stereospecific conrotatory ring opening (12), the formation of an intermediate such as **9** in a refluxing ether-hexane mixture is not surprising. Furthermore, the presence of lithium *N*-methylanilide is thought to facilitate C-C bond scission by forming the immediate precursor of **9** (13). The ylid **9** is probably quite stable because of resonance and the nitrogen atmosphere, but upon addition of methanol it loses its carbon-lithium bond to become **10**, followed by a 1,3-dipolar addition of methanol to form the amide acetal **11**. This intermediate then fragments to form **3** as well as benzaldehyde acetal, which upon exposure to water becomes benzaldehyde. Hence, Path B, Scheme III, involves C-C bond scission and accounts for the major product of this reaction; *i.e.*, **3a** and **3b** are formed in 60% and 52% yields, respectively.

Attempts were made to effect a reaction between **1e** and lithium *N*-methylanilide; however, only starting material was recovered in 95% yield. No epimerization, R-D or ylid formation had occurred. Next an attempt was made to see if carbanion formation had occurred with **1e** by quenching the reaction mixture with methanol-d_1 instead of methanol. ^{1}H nmr revealed *cis*-α-deuterio-1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)aziridine had formed in ~60% yield. The obvious conclusion is that the *cis*-α-lithio carbanion of **1e** had formed, but subsequent cleavage of either the C-C or C_2-N bonds failed to occur in refluxing ether-hexane (9:1 mixture). In both instances, this may be attributed to the C_2 carbon's inability to sustain either a positive or negative charge owing to the C_2-methyl groups inability to act as an electron sink (14).

In marked contrast to the *cis* isomer (**1a**), *trans*-1-cyclohexyl-2-phenyl-3-benzoylaziridine (**1a'**), does not react with lithium *N*-methylanilide, while it reacts with lithium diisopropylamide to form *trans*-carbinols (1). Although the failure of the *trans*-carboaziridines to react with this base is surprising, the fact that up to 68.5% of the starting material is recovered gives credence to the argument that the intermediate **12** does not form (see Scheme IV), thereby preventing epimerization of **12** into **5**, deuterium exchange, or rearrangement of **1a** into indenone **2a**. The most probable factor preventing the reaction of this lithium base with **1a** is a steric interplay between the base and **1a**, thereby preventing the formation of **12**.

We intend to investigate this matter further by variations of size and strength of the base and by variations of the 1-alkyl-2-aryl-3-aroylaziridines.

Acknowledgement.

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EXPERIMENTAL

Infrared spectra were measured in either reagent grade carbon tetrachloride or deuteriochloroform on either a Perkin-Elmer Model 237 double beam recording spectrophotometer or a 621 grating spectrophotometer. The ^{1}H nmr were determined with a Varian A-60 high resolution spectrometer. Visible and ultraviolet spectra were obtained on a Carey Model 14 spectrophotometer. The mass spectra were determined by an AEI MS 50-76 spectrometer. Melting points were determined with an electrically heated melt-temp apparatus and are uncorrected. Elemental analysis were performed by Micro-Tech Laboratories, Skokie, Illinois.

The following 1-cyclohexyl-2-aryl-3-aroylaziridines were prepared by known procedures: **1a** and **1a'** (4), **1c** (15), **1d** (16) and **1e** (17).

The Reaction of *cis*-1-Cyclohexyl-2-phenyl-3-benzoylaziridine (**1a**) with Lithium *N*-Methylanilide. Synthesis of 2-Cyclohexylamino-3-phenylidenone (**2a**) and ω-Cyclohexylaminoacetophenone (**3a**).

Into a three-neck 250 ml. round bottom flask, under a nitrogen atmosphere, was added a solution of 11.0 mmoles of butyllithium in 7.0 ml. of *n*-hexane. Then 20 ml. of anhydrous ether was added dropwise, and with stirring, after which a solution of 4.32 ml. (40 mmoles) of *N*-methylaniline in 10 ml. of anhydrous ether was added. The mixture was then stirred for a ten minute period. A 2.0 g. (6.6 mmoles) amount of *cis*-1-cyclohexyl-2-phenyl-3-benzoylaziridine (**1a**) was next added and the mixture refluxed for three hours and then cooled. A 50 ml. quantity of methanol was added to the red colored solution and the mixture exposed to the air; a purple color developed within 15 minutes. After 12 hours, 50 ml. of *n*-hexane was added and the purple solution was extracted three times with 20 ml. portions of water. The organic phase was dried with magnesium sulfate, the solvents were evaporated, and the resulting purple oil chromatographed on alumina. Elution of the purple zone with a 9:1 petroleum ether (b.p. 30-60°)/benzene mixture afforded first **2a** and next an inseparable mixture of **3a** and *N*-methylaniline. Compound **2a** was recovered and recrystallized from methanol to give 0.39 g. (20% yield) of deep purple colored cystals, m.p. 119-120°; ^{1}H nmr (carbon tetrachloride, TMS): δ = 6.4-7.7 (m, 9H, aromatic), 2.7-3.3 (m, 1H, N-H) 0.94-2.10 ppm (m, 11H, cyclohexyl). Subsequent treatment of **2a** with deuterium oxide showed a peak to form at δ = 4.5 (indicative of DOH) and the peak at δ = 2.7-3.3 (m, 1H, N-H) had vanished. The ultraviolet-visible spectrum (methanol) had two general absorption regions with λ max at 265 (ε = 57,600) and 525 nm (ε = 13,500); ir (carbon tetrachloride): ν = 3370 (N-H) and 1720 (C=O) cm^{-1}; ms: m/e 303 (M$^+$). (Note: the substitution of lithium diisopropylamide for lithium *N*-methylanilide provided **2a** in 6.1% yield).

Anal. Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.60. Found: C, 83.09; H, 7.16; N, 4.62.

Since all attempts to separate **3a** and *N*-methylaniline were unsuccessful, the ratio of the integral of the cyclohexyl group of **3a** to the combined integral of the aromatic region of **3a** and *N*-methylaniline was employed to determine the amount of **3a** present in the mixture. From chromatography 1.65 g. oil was isolated and was determined to be 52% **3a** and 48% *N*-methylaniline (18). Hence, 0.86 g. of **3a** was calculated to be present (*e.g.* 60% yield). The ir (carbon tetrachloride) gave ν = 1705 cm^{-1}, indicative of the carbonyl group in **3a** as well as ν = 3325 cm^{-1}, indicative of a secondary amino group in both **3a** and *N*-methylaniline.

Independent Synthesis of ω-Cyclohexylaminoacetophenone (**3a**) and Its Hydrochloride Salt (**3a**).

This known compound (19) was obtained in 79% yield from the reaction of α-bromoacetophenone and two equivalents of cyclohexylamine in *n*-hexane solution and was isolated as its hydrochloride salt **3a'**, m.p. 250-252°, dec. (lit. m.p. 250-252°). Upon redissolving **3a'** in water and neutralizing with sodium bicarbonate, **3a** could be obtained by extracting with ether. The ether solution was next dried (magnesium sulfate) and vacuum stripped. After recrystallization from pentane and drying, white crystals were obtained, m.p. 85-89.5°; ^{1}H nmr (carbon tetrachloride, TMS): δ 7.20-8.16 (m, 5H, aromatic), 4.36 (d, 2H, CH_2), 4.15 (m, 1H, N-H), 0.90-2.11 ppm (m, 11H, cyclohexyl); treating with deuterium oxide gave ^{1}H nmr (carbon tetrachloride): δ = 7.20-8.16 (m, 5H, aromatic), 4.34 (s, 2H, CH_2), 4.72 (s, DOH), 0.90-2.11 ppm (m, 11H, cyclohexyl); ir (carbon tetrachloride): ν = 3325 (N-H) and 1705 (C=O) cm^{-1}.

Deuterium Exchange of cis-1-Cyclohexyl-2-phenyl-3-benzoylaziridine (**1a**) at Low Temperature.

Lithium *N*-methylanilide was prepared under a nitrogen atmosphere in the same manner and quantity as described above. The temperature of the solution was next lowered to -78° using a dry ice-acetone bath and then 2.0 g. of **1a** was added and the yellow solution was stirred for three hours at -78°. A 5.0 ml. amount of methanol-d_1 was added whereupon the solution became cloudy and milky white. This mixture was stirred for five more hours at this temperature and was then warmed to 0° and stirred for two more hours. Finally, the tan solution was allowed to warm to room temperature and was stirred overnight. The next day the solution was exposed to the air and no color change was observed. The tan mixture was next extracted with deuterium oxide (10.0 ml.) and dried with magnesium sulfate. The organic layer was next vacuum stripped to an oil which was examined by ^{1}H nmr. Although *N*-methylaniline was found to be present in the oil, the ^{1}H nmr revealed that the δ = 3.23 peak (20) had diminished to 20% of its original height relative to the constant area of the cyclohexyl group (δ = 0.84-2.04 (m, 11H)) (21).

The Reaction of **1a** with Lithium *N*-Methylanilide. Synthesis of **2a** and **3a** Using Azobenzene as the Proton Acceptor.

The lithium *N*-methylanilide base was prepared at room temperature in the exact quantity and manner as described above. Upon addition of 2.0 g. (6.6 mmoles) of **1a**, a red solution resulted which was then refluxed under a nitrogen atmopshere for twelve hours. The reaction mixture was then cooled to room temperature and 0.22 g. (1.2 mmoles) of azobenzene in 50 ml. of ultrapure methanol (distilled under nitrogen) was added (22). The mixture turned purple almost immediately and was stirred (still under a nitrogen atmosphere) for 12 hours. Next, 50 ml. of *n*-hexane was added. Just prior to the addition of *n*-hexane, however, visible spectra of varying concentrations of the reaction mixture were run to reveal λ max = 525 nm (in methanol) indicative of **2a**, but no general absorption was observed around λ max = 440 nm (indicating the absence of azobenzene). Also observed in the ultraviolet-visible spectrum was a peak of 390 nm, indicating the presence of *N*-methylaniline. After hexane addition, the reaction mixture was quenched by extracting it four times with aliquots of water. Aqueous and organic layers were then separated, and the organic layer was next dried with magnesium sulfate. Both the aqueous and purple organic solutions were left out in the air for 24 hours to allow for dehydrogenation of the hydrazobenzene (23). Following the exposure to the air, visible spectroscopy studies were made on the organic solution, giving λ max = 390, 440 and 525 nm, indicating that azobenzene had indeed returned (24). The organic solvents were then evaporated and a purple oil was obtained. Thin layer chromatography using petroleum ether (b.p. 30-60°) afforded three spots - one yellow, one orange and one purple. The mixture, a purple colored oil, was next chromatographed on alumina employing a 9:1 petroleum ether (b.p. 30-60°)/benzene mixture as the mobile phase. Consequently, two solids, one orange and one purple, and a yellow liquid were obtained (25). ^{1}H nmr and melting point studies revealed the orange solid to be azobenzene; the deep purple crystals had a m.p. of 119-120° and an ^{1}H nmr identical to that expected for **2a**; and the yellow spot was identified by ^{1}H nmr and ir to be an inseparable mixture of **3a** and *N*-methylaniline.

The Preparation of *cis*- and *trans*-1-Cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)aziridines (**1b**) and (**1b'**).

Following the literature procedure reported by Graff and Cromwell (26), **1b** was isolated in 44% yield. Upon recrystallization from a petroleum ether (b.p. 38-47°)/benzene mixture, **1b** had a m.p. of 144-146° (lit. m.p. 144-146°); ^{1}H nmr (deuteriochloroform): δ = 6.95-7.87 (m, 14H, aromatic), 3.17 (d, 2H, C_2-H and C_3-H), 0.84-2.04 ppm (m, 11H, cyclohexyl).

The *trans* isomer (**1b'**) was then isolated in 47% yield with m.p. 117-118° (lit. m.p. 117-118°); ^{1}H nmr (deuteriochloroform): δ = 7.04-8.06 (m, 14H, aromatic), 3.55 (t, 2H, C_2-H and C_3-H), 2.25-2.93 (m, 1H, N-CH), 0.84-2.04 ppm (m, 10H, cyclohexyl).

The Reaction of *cis*-1-Cyclohexyl-2-phenyl-3-(*p*-phenylbenzoyl)-aziridine (**1b**) with Lithium *N*-Methylanilide.

Into a three-neck 250 ml. round bottom flask, under a nitrogen atmosphere, was added a solution of 11 mmoles of butyllithium in 7.0 ml. of *n*-hexane. Then 20 ml. of anhydrous ether was added dropwise, with stirring, after which a solution of 4.32 ml. (40 mmoles) of distilled *N*-methylaniline in 10 ml. of anhydrous ether was added. The mixture was then stirred for five minutes. Next 2.50 g. (6.6 mmoles) of the *cis* aziridine **1b** was added to the reaction flask. The mixture turned dark green and was then refluxed under the nitrogen atmosphere for 12 hours. The green solution was then cooled to room temperature and 50 ml. of methanol was added followed by the addition of 50 ml. of *n*-hexane and exposure to the atmosphere (*i.e.*, O_2). The reaction mixture turned black and was (1) condensed down to a 8.78 g. oil and (2) taken down to a 5.45 g. oil by blowing nitrogen gas over it. The black oil was next chromatographed on alumina employing (1) a 9:1 benzene/petroleum ether (b.p. 38-47°) mixture for fractions #1-28; (2) a 9:1 petroleum ether (b.p. 38-47°)/methanol mixture for fractions #29-37; and (3) pure methanol for fractions #38-41 as the mobile phases wherein each fraction collected was 100 ml. in volume.

The first fraction collected was purple colored and weighed 0.02 g. (1.45% yield) with m.p. 121-122° and was identified as 2-cyclohexylamino-3,5-diphenylindenone (**2b**) with ir (carbon tetrachloride): ν 1720 (C=O) and ν 3370 (N-H) cm^{-1}; ^{1}H nmr (deuteriochloroform): δ = 7.0-7.7 (m, 13H, aromatic), 2.7-2.9 (m, 1H, N-H), 0.94-2.10 ppm (m, 11H, cyclohexyl).

Anal. Calcd. for $C_{27}H_{25}NO$: C, 85.45; H, 6.64; N, 3.69. Found: C, 85.43; H, 6.82; N, 3.52.

Fractions #2-7 afforded *N*-methylaniline which was identified in the routine fashion. No products were identified from fractions #8-28. Fraction #29 afforded a 0.29 g. oil and was shown by ^{1}H nmr to be a 8:1 mixture of *trans* **1b'** and *cis* **1b** aziridine, respectively. The ratio of isomers is based on the integral ratio of the *trans* δ = 3.55 (t) peak to that of the *cis* isomer's δ = 3.14 (d) peak. Hence, a total of 1.38 mmoles (21% yield) was present in the original mixture with 19% being the *trans* isomer **1b'** and 2% the original starting material **1b**.

Fractions #30-37 afforded a low melting solid, which upon recrystallization from chloroform had m.p. 149-154° and was suspected to be 0.45 g. fo 2-cyclohexylamino-*p*-phenylacetophenone (**3b**) in 42.3% yield (27); ir (carbon tetrachloride): ν = 1685 (C=O) and ν = 3420, 3310, 3065, and 3040 (all N-H) cm^{-1}; ^1H nmr (carbon tetrachloride, TMS) 7.20-8.16 (m, 9H, aromatic), 4.4 (d, 2H, CH_2), 4.15 (s, 1H, N-H), 0.80-2.25 ppm (m, 11H, cyclohexyl). Fractions #38-41 afforded an additional 0.1 g. of a solid identified by m.p. and ^1H nmr as **3b** to bring the total yield of ω-cyclohexylamino-*p*-phenylacetophenone (**3b**) up to 51.7%.

The Independent Synthesis of ω-Cyclohexylamino-*p*-phenylacetophenone (**3b**).

Following a procedure analogous to that of Mercer and Cromwell (19), 4.0 g. (14.5 mmoles) of α-bromo-*p*-phenylacetophenone (28) was placed in a 250 ml. two-neck round bottom flask equipped with stir bar and dropping funnel. To this flask was added 35 ml. benzene and 50 ml. anhydrous ether. Next, over a 15 minute period was added 2.88 g. (29.0 mmoles) of cyclohexylamine in 15 ml. benzene and 10 ml. anhydrous ether while keeping the temperature between 10° and 14° throughout the amine addition. The mixture was stirred at this temperature for an additional 1.5 hours. Then the reaction mixture, which first turned clear orange and then a brilliant yellow, was stirred at room temperature for an additional five hours. Cyclohexylamine hydrobromide was collected by filtration in 91.6% yield and the cloudy mother liquor was filtered again and vacuum stripped down to an oil. A 9:1 petroleum ether (b.p. 38-47°)/benzene mixture was added and the solution stored in the freezer for 24 hours. The next day 3.20 g. (75.3% yield) of a yellow solid was identified upon recrystallization from 9:1 petroleum ether (b.p. 83-47°)/benzene as **3b** m.p. 150-154°; ir (carbon tetrachloride): ν = 1685 (C=O) and ν = 3420, 3310, 3065 and 3040 (all N-H) cm^{-1}; ^1H nmr (carbon tetrachloride, TMS): δ = 7.20-8.16 (m, 9H, aromatic), 4.4 (d, 2H, CH_2), 4.15 (s, 1H, NH), 0.80-2.25 ppm (m, 11H, cyclohexyl); ^1H nmr (carbon tetrachloride, deuterium oxide, TMS): δ = 7.20-8.16 (m, 9H, aromatic), 4.4 (s, 2H, CH_2), 0.80-2.25 ppm (m, 11H, cyclohexyl) (29).

The Reaction of *cis*-1-Cyclohexyl-2-phenyl-3-*p*-toluylaziridine (**1c**) to Form 2-Cyclohexylamino-5-methyl-3-phenylindenone (**2c**).

Following the identical procedure used to transform **1a** into **2a**, **2c** was prepared from **1c** in 29% yield, m.p. 144-145°. The ultraviolet-visible spectrum (methanol) had two general absorption regions with λ max at 272 nm (ε = 48,000) and 550 nm (ε = 800); ir (carbon tetrachloride): ν = 1720 (C=O) cm^{-1} and ν = 3370 (N-H) cm^{-1}.

Anal. Calcd. for $C_{22}H_{23}NO$: C, 83.24; H, 7.30; N, 4.41. Found: C, 83.33; H, 7.26; N, 4.31.

The Reaction of *cis*-1-Cyclohexyl-2-phenyl-3-*p*-bromobenzoylaziridine (**1d**) to Form 5-Bromo-2-cyclohexylaminoacetophenone (**2d**).

Following the identical procedure used to transform **1a** into **2a**, **2d** was prepared from **1d** in 22% yield, m.p. 140-141°. The ultraviolet-visible spectrum (methanol) had two general absorption regions with λ max at 280 nm (ε = 52,400) and 560 nm (ε = 800); ir (carbon tetrachloride): ν = 1725 (C=O) cm^{-1} and ν = 3370 (N-H) cm^{-1}.

Anal. Calcd. for $C_{21}H_{20}BrNO$: C, 65.98; H, 5.27; Br, 20.90; N, 3.66. Found: C, 65.84; H, 5.30; Br, 20.64; N, 3.46.

Treatment of *cis*-1-Cyclohexyl-2-methyl-3-*p*-phenylbenzoylaziridine (**1e**) with Lithium *N*-Methylanilide.

Into a three-neck 250 ml. round bottom flask, under a nitrogen atmosphere, was added a solution of 11.0 mmoles of butyllithium in 7.0 ml. of *n*-hexane. Then 20 ml. of anhydrous ether was added dropwise, and with stirring, after which a solution of 4.32 ml. (40 mmoles) of *N*-methylaniline in 10 ml. of anhydrous ether was added. The reaction mixture was then stirred for a ten minute period. Then 2.09 g. (6.6 mmoles) of **1e** was added to the reaction vessel. The mixture remained yellow in color and was stirred overnight. After 12 hours refluxing the mixture was allowed to cool to room temperature. Still no color change was observed, however the reaction mixture did become cloudy-golden yellow. After 12 more hours *n*-hexane was added and air was bubbled in overnight. A ^1H nmr was run on the reaction mixture to reveal methanol, *N*-methylaniline and starting material **1e**. Next, all of the methanol was vacuum-stripped and the reaction mixture was dissolved in petroleum ether (b.p. 38-47°) whereupon yellow colored crystals precipitated from the organic layer. These crystals were recovered and found to weigh 0.9 g.; However, they were insoluble in every organic solvent tried and decomposed around 340°. Hence, they were assumed to be a salt of lithium. Next, the organic layer was condensed and found to weigh 2.6 g. (The ^1H nmr revealed the spectra to be that of **1e** and *N*-methylaniline superimposed on one another). The ratio of the cyclohexyl and C_1-methyl group to that of the phenyl region revealed the mixture to be 76.1% azirdine or 0.761 (2.6) = 1.98 g., or 94.6% of the aziridine **1e** can be accounted for (30).

Deuterium Exchange of *cis*-1-Cyclohexyl-2-phenyl-3-*p*-phenylbenzoylaziridine (**1e**).

Lithium *N*-methylanilide was prepared under a nitrogen atmosphere in the same quantity and manner as described above. Then, 2.09 g. (6.6 mmoles) of **1e** was added. The golden mixture was stirred and refluxed in a nitrogen atmosphere for 12 hours, 50 ml. of methanol-d_1 was added and no purple color was observed. Then, 50 ml. of *n*-hexane was added and the mixture was stirred for 12 hours, the solvent was stripped off and condensed to an oil. ^1H nmr revealed *cis*-α-deuterio-1-cyclohexyl-2-phenyl-3-*p*-phenylbenzoylaziridine had formed in ~60% yield (31,32).

Inertness of *trans*-1-Cyclohexyl-2-phenyl-3-benzoylaziridine (**1a'**) to Lithium *N*-Methylanilide.

A 1.40 g. (13.1 mmoles) solution of lithium *N*-methylanilide was prepared in the usual fashion. The yellow mixture was stirred for 10 minutes and then added to 2.0 g. (6.6 mmoles) of the *trans* aziridine (in the presence of air) which was dissolved in 20 ml. of anhydrous ether. After stirring the reaction mixture for ten minutes, 0.5 ml. (13.8 mmoles) of deuteriosulfuric acid was added dropwise followed by the addition of 5.0 ml. of deuterium oxide. After stirring, the ethereal layer was separated and dried with magnesium sulfate. Evaporation of the ether gave 1.37 g. (68.5% recovery) of **1a'** starting material, as revealed by ^1H nmr.

When the above experiment was repeated with the *cis* isomer **1a**, a wine colored solution resulted, which upon standing at room temperature exposed to air became purple colored. Using established procedures, violet crystals of **2a** were recovered in 20% yield, m.p. 118-120°. The infrared and ^1H nmr spectra of this compound were identical to that expected for **2a**.

REFERENCES AND NOTES

(1) For Part XVII see D. K. Wall, J. L. Imbach, A. E. Pohland, R. C. Badger, and N. H. Cromwell. *J. Heterocyclic Chem.*, 5, 77 (1968).

(2) A. E. Pohland, M. C. McMaster, R. C. Badger, N. H. Cromwell *J. Am. Chem. Soc.*, 87, 2510 (1965).

(3) P. Tarburton, D. K. Wall and N. H. Cromwell, *J. Heterocyclic Chem.*, 13, 411 (1976).

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(5) N. H. Cromwell, *J. Am. Chem. Soc.*, 69, 258 (1947).

(6) N. H. Cromwell, J. H. Anglin, Jr., F. W. Olsen, and N. G. Barker, *ibid.*, 73, 2803 (1951).

(7) J. J. Eische and J. E. Galle, *ibid.*, 98, 6448 (1976).

(8) The reduction of azobenzene to hydrazobenzene concurrent with the oxidation of **8** to **2a** is indicative of the intermediacy of **8**, *i.e.* for another example of this, see H. K. Leung, B. A. Phillips, and N. H. Cromwell, *J. Heterocyclic Chem.*, 13, 247 (1976).

(9) For a discussion of this phenomenon see Badger, "Aromatic Character", Cambridge University Press, London, 1969.

(10) This scheme is similar to the pathway proposed by P. B. Woller and N. H. Cromwell, *J. Heterocyclic Chem.* 5, 579 (1968) for a somewhat analogous thermally induced cleavage reaction of aziridinyl esters.

(11) Owing to the complicated procedure in obtaining the ω-cyclohexylacetophenones, only **3a** and **3b** were characterized and identified; similar products are thought to be obtained from the reaction of **1c** and **1d** but are not characterized here.

(12) P. B. Woller and N. H. Cromwell, *J. Org. Chem.*, 35, 888 (1970).

(13) In a refluxing 9:1 ether/hexane mixture (b.p. 40°) without base **1a** does not undergo C-C bond scission. In reference (10) it is suggested that T>65° is needed for this to occur.

(14) This is in sharp contrast to *cis*-1-cyclohexyl-2-phenyl-3-benzoylaziridine (**1a**) wherein the C_2-phenyl group is thought to support a positive charge (δ^+) in the case of ylid formation and support a negative charge (δ^-) in the case of indenone formation.

(15) N. H. Cromwell, N. G. Barker, R. A. Wankel, P. J. Vanderhorst, F. W. Olsen, and J. H. Anglin, Jr., *J. Am. Chem. Soc.*, 73, 1044 (1951).

(16) A. H. Pohland, R. D. Badger, and N. H. Cromwell, *Tetrahedron Letters*, 4369 (1965).

(17) N. H. Cromwell and R. J. Mohrbacher, *J. Am. Chem. Soc.*, 75, 6252 (1953).

(18) The ^{1}H nmr spectrum of **3a** is given below and the ^{1}H nmr spectrum of *N*-methylaniline is available in the Sadtler file.

(19) N. H. Cromwell and G. D. Mercer, *J. Am. Chem. Soc.*, 79, 3815 (1957).

(20) This peak is indicative of the α-proton in **1a**, see reference (3) for details.

(21) Here the ^{1}H nmr sample was treated with deuterium oxide in order that interference with the N-H peak of *N*-methylaniline could be avoided.

(22) Of course, 0.22 g. (1.2 mmoles) of azobenzene was used because only 0.39 g. (1.3 mmoles) of **2a** is obtained as the final product and this then allows all of azobenzene the opportunity to react.

(23) We had suspected that the reaction of azobenzene with hydrogen giving hydrazobenzene had occurred owing to the fact that no general absorption around 440 nm could be found.

(24) Upon exposure to the air for several hours the reaction of hydrazobenzene with oxygen giving azobenzene had taken place.

(25) The yellow liquid eluted last was found to be an inseparable mixture of **3a** and *N*-methylaniline.

(26) M. A. Graff and N. H. Cromwell, *J. Org. Chem.*, 17, 414 (1952).

(27) See experimental for the independent synthesis and identification of ω-cyclohexylamino-*p*-phenylacetophenone.

(28) For preparation of this compound from 4-acetylbiphenyl (Aldrich) see N. L. Drake and J. Bronitsky, *J. Am. Chem. Soc.*, 52, 3715 (1930).

(29) High resolution mass spectroscopy was used to identify **3b** and revealed an (M^+-1) ion at 292.1662 (9.21) and a (M^+-2) at 291.1630 (37.51) *vs.* 292.1690 and 291.1623 for the calculated values (see F. W. McLafferty, "Interpretation of Mass Spectra", W. A. Benjamin, Inc., Reading, Massachusetts, 1973, p. 17 and following).

(30) The ratio of the cyclohexy-C_1 methyl area to that of the phenyl region represents the % of **1e** in this mixture (both areas are representative of 14 H's in **1e**.).

(31) Deuterium exchange was assumed to have occurred as the α-ring proton at δ = 2.94 ppm was ~ 40% its original height as judged by the peak height of the 15 proton region from δ = 0.83-2.11 (includes β-ring proton, cyclohexyl and methyl groups) and is accurate to ± 10%.

(32) The *trans* isomer is assumed to be inert to deuterium exchange as **1a'** has been found unreactive to lithium *N*-methyl anilide.