methylene chloride, washed with water, and dried ($MgSO_4$) and the methylene chloride evaporated. The residual oil was chromatographed on 100/200 mesh silica gel, methylene chloride/ethanol (65/35) being used as eluent. The resultant 1,4-diketone (31% yield) was dissolved in absolute ethanol. An equivalent of aniline was added dropwise, and the solution was stirred overnight. Ethanol was evaporated in vacuo and replaced by methylene chloride and the organic layer washed with H_2O, dilute HCl, H_2O, dilute $NaHCO_3$, and H_2O and dried ($MgSO_4$). Distillation of the methylene chloride and crystallization of the residue from ethanol gave 0.25 g (87% based on 1,4-diketone) of yellow **8d**: mp 160–161 °C; NMR ($CDCl_3$) δ 8.09 (d, 2 H, J = 9.0 Hz), 7.2 (m, 13 H), 4.25 (q, 2 H, J = 7.0 Hz), 1.25 (t, 3 H, J = 7.0 Hz); IR ($CHCl_3$) 1700 cm^{-1} (C=O). Anal. Calcd for $C_{25}H_{20}N_2O_4$: C, 72.84; H, 4.89; N, 6.79. Found: C, 72.79; H, 4.95; N, 6.75.

Regiochemistry Assignments Based on NMR Data. In diethyl 2-(4-methylphenyl)-1,5-diphenylpyrrole-3,4-dicarboxylate (**8m**), prepared by the 1,3-dipolar addition of **4a** to diethyl acetylenedicarboxylate (**5**), there is no doubt that the ethoxycarbonyl groups are located at the 3- and 4-positions of the pyrrole ring. The 300-MHz FT Varian ^1H NMR spectrum of **8m** was taken, and it shows two overlapping triplets centered at δ 1.15 and 1.19, respectively, with J = 9.0 Hz. Each of the triplets shows additional poorly resolved splitting (J = 2.35 Hz). There are also two overlapping quartets centered at δ 4.19 and 4.21 J = 7.0 Hz), respectively. The overlapping of the quartets results in an apparent quintet centered at δ 4.20. The two outermost peaks are free of overlapping and have equal areas, as would be expected of compound **8m**. As previously noted for the methyl triplet, the individual peaks of the apparent quintet show poorly resolved splitting (J = 2.35 Hz).

Although a much more detailed analysis has been presented by Langridge,[28] we will simply point out here the obvious fact that, because of the presence of a 4-methylphenyl group at one of the α-positions of the pyrrole ring, the magnetic environments for the ethoxycarbonyl groups at the two β-positions are measurably different.

The 300-MHz ^1H NMR spectrum of the mixture of pyrroles (ratio of 95.4:4.6 by HPLC analysis) obtained by the 1,3-dipolar addition of **4a** to ethyl propiolate does not show two sets of triplets and two sets of quartets, separated by about 9–10 Hz, as would be expected if significant amounts of both regioisomers were present. However, a separation of 8 Hz is observed for the methyl triplets (with the outer peaks having nearly equal areas) when a mixture of equal amounts of authentic ethyl 2-(4-methylphenyl)-1,5-diphenylpyrrole-3-carboxylate (**8b**), obtained by the base-catalyzed addition of 2-(*N*-phenyl-4-methylbenzamido)-2-phenylacetonitrile (**2**) to ethyl acrylate, with the product of the 1,3-dipolar addition reaction. Therefore, the major (almost exclusive) product of the 1,3-dipolar addition reaction is **8a**.

The 300-MHz ^1H NMR spectrum of the mixture of regioisomers **8g** and **8h** (ratio of 98:2 by HPLC analysis), obtained by the dipolar addition of **4a** to **6**, does not show two sets of triplets and two sets of quartets, separated by about 9 Hz, as would be expected if significant amounts of both regioisomers were present. Exactly the same 300-MHz ^1H NMR spectrum was obtained for the authentic sample of ethyl 2-(4-methylphenyl)-1,4,5-triphenylpyrrole-3-carboxylate (**8g**) obtained by the base-catalyzed reaction of **3a** with ethyl cinnamate. Thus, it can be concluded that **8g** is the predominant regioisomer of the 1,3-dipolar addition reaction.

The 300-HMz ^1H NMR spectrum of the mixture of regioisomers **8c** and **8d** (ratio of 88.5:11.5 by HPLC analysis), obtained by the 1,3-dipolar addition of **4b** to **5**, shows a major triplet at δ 1.16 (J = 7.5 Hz) and a major quartet at δ 4.15 (J = 7.5 Hz). These overlap a minor triplet and quartet at δ 1.25 and 4.25, respectively. The 300-MHz ^1H NMR spectrum of authentic ethyl 2-(4-nitrophenyl)-1,5-diphenylpyrrole-3-carboxylate (**8d**), obtained by the modified Hantzsch reaction, shows a triplet at δ 1.25 (J = 7 Hz) and a quartet at δ 4.25 (J = 7 Hz). Thus, it can be concluded that the major regioisomer of the 1,3-dipolar addition reaction is **8c**.

The regiochemistry assignments of the remaining reaction mixtures were based initially on analogy with the proven cases discussed above. Thus, owing to the observation that, in reactions with ethyl propiolate (**5**), both **4a** (having an electron-donating *p*-methyl group) and **4b** (having an electron-withdrawing *p*-nitro group) gave predominantly **8a** and **8c** (with X = CO_2Et), then **4c** should also give predominantly **8e**. Corroboration for this assignment was obtained from the observed retention times of the major products in all three reactions in HPLC separations. In each case, the retention time of the major isomer was greater than that of the minor isomer. Similar methodology was used to make the regiochemistry assignments of the products of reactions of **4a** and **4c**, respectively, with ethyl phenylpropiolate (**6**).

(28) Landridge, D. C. H. Ph.D. Dissertation, University of Massachusetts, Amherst, MA, 1984.

Reactions of 1-*tert*-Butyl-3-phenylaziridinone and α-Bromo-*N*-*tert*-butylphenylacetamide with Benzyl-Grignard Reagents

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Received March 26, 1985

1-*tert*-Butyl-3-phenylaziridinone (**1**) reacts with benzyl halide Grignard reagents (Br and Cl) to give *N*-*tert*-butyl-2,3-diphenylpropanamide (**4**), *N*-*tert*-butyl-2-phenylacetamide (**3**), *N*-*tert*-butyl-2-*o*-tolyl-2-phenylacetamide (**5**), 1-(*tert*-butylamino)-1,3-diphenylpropan-2-one (**7**), *N*-benzyl-*N*-*tert*-butyl-2-phenylacetamide (**6**), and *N*-*tert*-butyl-2-halo-2-phenylacetamide (**2**, X = Br, Cl). The choice of solvent appears to determine the relative amounts of products **4** and **5**. The bromo amide **2** reacts with the Grignard reagent to give **3**, **4**, **5**, **6**, and **7** and may be involved to some extent in the reaction of **1** with benzyl-Grignard reagents. The formation of **5** represents a new type of "abnormal" product from a reaction of the benzyl-Grignard reagent; however, this product appears to fit well into the mechanistic pattern established for prior examples.

The reactions of benzyl-Grignard reagent with formaldehyde (and some other carbonyl compounds) have been known for many years to give "abnormal" of "rearrangement" products involving alkylation of the benzene ring as well as the expected addition product.[1-11] More recently it has been found that certain alkylating agents (*tert*-butyl chloride,[12-14] alkyl sulfates and tosy-

(1) Grignard, V. *Bull. Soc. Chim. Fr.* **1903**, *29*, 953.

(2) (a) Tiffeneau, M.; Delange, R. *C. R. Hebd. Seances Acad. Sci.* **1903**, *137*, 573. (b) Tiffeneau, M.; Delange, R. *J. Chem. Soc.* **1904**, *86*, 48.

(3) Schmidlin, J.; Garcia-Banus, A. *Chem. Ber.* **1912**, *45*, 3193.

(4) Mousseron, M.; Du, M. P. *Bull. Soc. Chim. Fr.* **1948**, *15*, 91.

0022-3263/85/1950-5507$01.50/0

Table I. Reactions of Aziridinone 1 and α-Bromo Amide 2 with Benzyl-Grignard Reagents

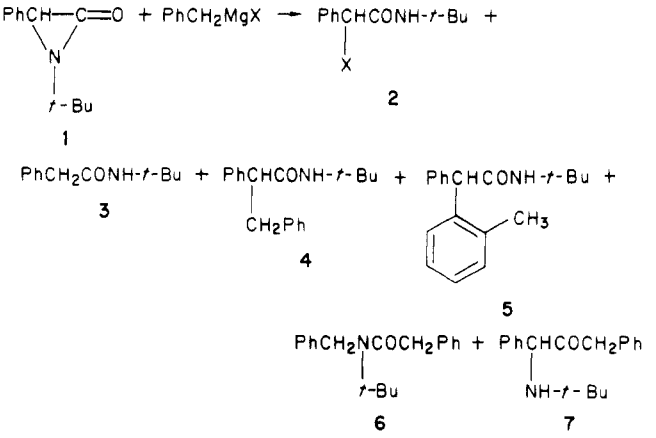
substrate (S)	reagent from (R)	molar ratio time, (R/S)[a]	time, h	yield,[b] % 2	3	4	5	6	7
1	$PhCH_2Br$[c]	3.1	3[d]	tr[e,f]	18	39	4	4	3
		3.1	3[g]	1[f]	22	32	7	2	2
		3.1	3[g]	2[f]	22	32	9	2	1
	$PhCH_2Br$[c,h]	3.1	3[d]	3[f]	24	13	15	12	3
	$PhCH_2Br$[i]	4.1	3[d]	4[f]	6	13	41	12	tr[e]
		3.1	3[g]	2[f]	7	15	37	10	tr[e]
2	$PhCH_2Br$[c]	4.1	6[d]		39	32	7	1	7
		5.0	6[g]		58	19	8	1	6
	$PhCH_2Br$[i]	5.0	6[d]		22	9	36	21	3
		5.0	6[g]		43	6	24	12	tr[e]
	$PhCH_2Br$[h,i]	5.0	6[d]		54	6	20	13	tr[e]
1	$PhCH_2Cl$[c]	3.1	3[d]	3[j]	13	31	11	4	5
		3.1	3[d]		11	70	10		8
		4.0	3[g]	2[j]	16	35	11	3	3
	$PhCH_2Cl$[i]	4.1	6[d]	5[j]	10	12	30	9	1
		4.0	6[g]	4[j]	10	15	34	8	tr[e]
	$PhCH_2Cl$[h,i]	4.0	6[d]	4[j]	7	15	43	10	tr[e]
2	$PhCH_2Cl$[c]	4.0	4[d]		30	41	11	4	2
		5.1	6[g]		45	20	9	4	4
	$PhCH_2Cl$[i]	5.0	6[d]		9	14	56	12	tr[e]
		5.0	6[g]		9	20	44	8	7

[a] Based on moles of benzyl halides (actual ratio about 75% of figure given). [b] Based on proton NMR analysis of crude reaction mixture (see Experimental Section). [c] In ether. [d] After substrate was added at 0 °C, the reaction mixture was allowed to warm up to room temperature. [e] Trace (<1%). [f] 2 (X = Br). [g] Reaction conducted in refluxing solvent. [h] 1.76×10^{-2} mmol of $FeCl_3$ in THF added. [i] In THF. [j] 2 (X = Cl).

lates,[15b] and chloromethyl methyl ether[15a]) also alkylate the ring in addition to forming coupling products. The several reactions observed and the interrelations between them probably are still not completely understood; however, the elegant research of Benkeser and his co-workers,[10,15] and more recently of Bernadon and Deberly,[11] have clarified the fundamental mechanisms as well as further demonstrated the complexity of the several reactions and equilibria involved. We have been studying the reactions of Grignard and other organometallic reagents with the aziridinones for some time[16] and have found that this carbonyl system often shows unusual reactions involving both addition and alkylation reactions; thus, it seemed appropriate to examine the reaction of this system with benzyl-Grignard reagents.

Because some aziridinones, particularly the well-studied, highly sterically stabilized aziridinones, and the 3,3-diarylaziridinones give other types of "abnormal" products with organometallic reagents, we have chosen to work with 1-*tert*-butyl-3-phenylaziridinone (**1**), which is easy to prepare, is moderately stable for short periods of time, and is probably as close to being a "typical" aziridinone as one can find without resorting to very labile compounds. As is our practice with the aziridinones,[16] we also studied the reactions of the precursor of **1**, 2-bromo-*N*-*tert*-butyl-2-phenylacetamide (**2**, X = Br).

Aziridinone **1** reacted with the benzyl-Grignard reagent to yield not only products like those reported previously[16] but also products of two new types not previously obtained from the reaction of aziridinones with organometallic reagents. In the former group were the expected products:



the 1,3-cleavage product, *N*-*tert*-butyl-2,3-diphenylpropanamide (**4**); the 1,2-cleavage product, 1-(*tert*-butylamino)-1,3-diphenyl-2-propanone (**7**); the reduction product, *N*-*tert*-butyl-2-phenylacetamide (**3**), and halide-derived 1,3-cleavage products, *N*-*tert*-butyl-2-halo-2-phenylacetamide (**2**, X = Br, Cl). The two new products were the 2,3-cleavage product, *N*-benzyl-*N*-*tert*-butyl-2-phenylacetamide (**6**) and the "abnormal" ortho-alkylation product, *N*-*tert*-butyl-2-phenyl-2-*o*-tolylacetamide (**5**). There were other unidentified products present (sometimes as much as 30% of reaction mixture). Usually the proton NMR spectrum of the crude reaction mixture had eight or more singlets (presumably *tert*-butyl groups) in the

(5) Johnson, J. R. *J. Am. Chem. Soc.* **1933**, *55*, 3029.
(6) (a) Young, W. G.; Siegel, S. *J. Am. Chem. Soc.* **1944**, *66*, 354. (b) Siegel, S.; Coburn, S. K.; Levering, D. R. *Ibid.* **1951**, *73*, 3163. (c) Siegel, S.; Boyer, W. M.; Jay, R. R. *Ibid.* **1951**, *73*, 3277.
(7) Partchamzad, I.; Guillemonat, A.; Traynard, J. C. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1968**, *266*, 717.
(8) Sjoholm, R. *Acta Chem. Scand., Ser. B* **1978**, *32*, 105.
(9) Kopecky, K. R.; Lau, M. P. *J. Org. Chem.* **1978**, *43*, 525.
(10) (a) Benkeser, R. A.; Trevillyan, A. E.; Mallan, J. M. *J. Organomet. Chem.* **1964**, *2*, 322. (b) Benkeser, R. A.; Johnson, T. E. *J. Am. Chem. Soc.* **1966**, *88*, 2220. (c) Benkeser, R. A.; DeTalva, W.; Darling, D. *J. Org. Chem.* **1979**, *44*, 25. (d) Benkeser, R. A.; Synder, D. C. *Ibid.* **1982**, *47*, 1243.
(11) Bernadon, C.; Deberly, A. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2631. (b) Bernadon, C.; Deberly, A. *J. Org. Chem.* **1982**, *47*, 463.
(12) Burtle, J. G.; Shriner, R. L. *J. Am. Chem. Soc.* **1947**, *69*, 2059.
(13) Berliner, E.; Berliner, F. *J. Am. Chem. Soc.* **1949**, *71*, 1195.
(14) Reuvers, A. J. M.; van Bekkum, H.; Wepster, B. M. *Tetrahedron* **1970**, *26*, 2683.
(15) (a) Benkeser, R. A.; DeTalvo, W. *J. Am. Chem. Soc.* **1967**, *89*, 2141. (b) Benkeser, R. A.; Johnson, T. E.; Tong, W. H. *J. Org. Chem.* **1968**, *33*, 2203.

(16) Background information and references on the various reactions of aziridinones with organometallic compounds may be found in he following paper along with some discussion of alternative reaction mechanisms that should be considered in all such reactions. Baumgarten, H. E.; McMahan, D. G.; Elia, V. J.; Gold, B. I.; Day, V. W.; Day, R. O. *J. Org. Chem.* **1976**, *41*, 3798.

region of δ 0.8–1.8. The complexity of the mixture made separation and identification of the individual components difficult. Thus, the selected results given in Table I were obtained by proton NMR analysis of the crude reaction mixtures. The identities of all products reported here were based on isolation and comparison with authentic samples. Since the molar ratio of Grignard reagent to substrate was at least 3:1 to insure the presence of excess Grignard reagent despite any complexation of the reagent with any intermediate or product,[17] those possible products related to the diols obtained in benzyl-Grignard reagent–formaldehyde reactions, which depend on an excess of carbonyl species,[10d] might not have formed.

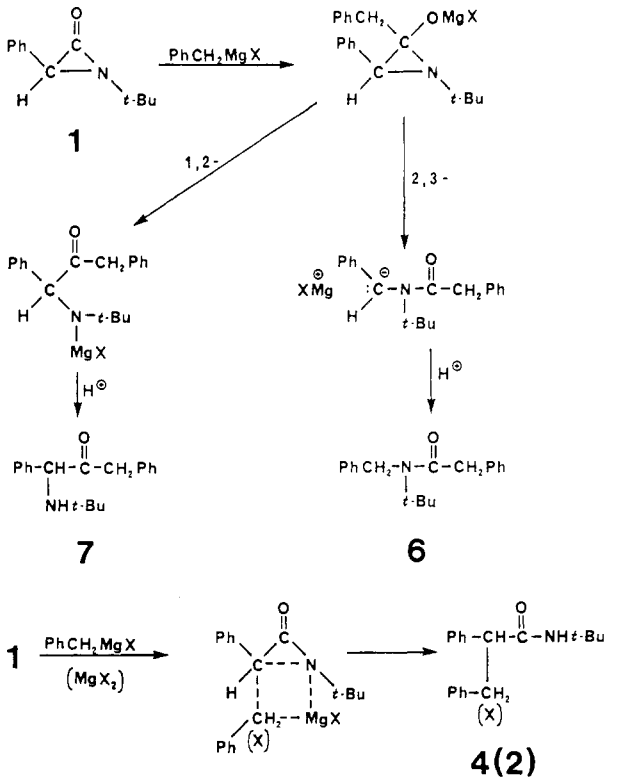
The choice of solvent seemed to play an important role in determining the amount of the ortho-alkylation product **5** relative to the other species present. When the reaction was conducted in THF, **5** was the predominant product; however, in the less basic, less coordinating solvent, diethyl ether, the α-alkylation product **4** was the principal product. The amount of the 2,3-cleavage product **6** was also greater in THF than in ether. The addition of ferric chloride also appeared to increase the amounts of both **5** and **6** relative to **3**, but the amount of **5** was more sensitive to the solvent than to the addition of ferric chloride.

When **1** was allowed to react with a solution of the benzyl chloride Grignard reagent which had been treated with dioxane to remove as much $MgCl_2$ as possible and to force the Schlenk equilibrium toward dibenzylmagnesium, the sole product was **4** in essentially quantitative yield.

Since para-alkylation has been observed in the reaction of benzyl-Grignard reagents with alkylating agents[12-15] and since we have observed para attack on a aryl substituent on the aziridinone ring by an organolithium reagent,[18,19] we synthesized the possible products **8** and **9** and looked for these among the reaction products. These substances either were not present or were present in amounts too small to be detected by our proton NMR analysis.

In general, the formation of reduced amide **3** in the reaction of **2** with Grignard reagents may be due to any of several possibilities. With *sec*-alkyl-Grignard reagents (such as isopropyl and cyclopentyl) **3** clearly arises from a β-hydrogen abstraction process as the corresponding alkene may be isolated in good yield from the reaction products.[18] This route is not possible for the benzyl-Grignard reagent. A second possibility is that the reduced amide **3** was formed as one of the coupling products from the further reaction of one of the primary reaction products, the halide **2**, with the benzyl-Grignard reagent.[20] A third possibility is that the formation of **3** was due to reduction of **1** by a small amount of magnesium hydride species present in the preparation of the benzyl-Grignard reagents from benzyl halides and magnesium. Such species have been shown to be present in some preparations of the methyl-Grignard reagent and to bring about reductions;[17a] however, whether such species can be found in benzyl-Grignard reagents apparently is not known. With diborane

Scheme I



the 3-ring (rather than the amide functionality) of **1** is reduced to form **3** in high yield.[18] A fourth possibility is that **3** arises from the reaction of solvent with a ring-opened radical formed in an SET (single electron transfer) (vide infra).

Any rationalization of the formation of the various "normal" and "abnormal" products obtained in this study must begin with the consideration of whether the reactions proceed by polar or by SET mechanisms.[17] Apparently the only persons who have attempted to distinguish between the two possibilities in a study of the "abnormal" reactions of benzyl-Grignard reagents were Reuvers, van Bekkum, and Wepster,[14] who concluded that the reaction of this reagent with *tert*-butyl bromide and chloride followed a polar route even though both ortho- and para-alkylation products were formed. However, dibenzylmagnesium has been shown to react with diaryl ketones by an SET route.[21] Probably, it is premature to rule out either possibility on the basis of the limited evidence available. In this paper the polar route will be discussed first as that is the route on which all of the previously published discussions of the "abnormal" reactions of benzyl Grignard reagent have been based. The polar mechanisms are shown in Schemes I and II.

Assuming a polar mechanism, the 1,3-cleavage product **4** and the α-halo amides **2** (X = Br, Cl) would be derived from the collapse of the four-centered complex formed between the benzyl-Grignard reagents or metal halides and **1** at the nitrogen atom (Scheme I). Based on the sole experiment that has tested the stereochemistry of 1,3-cleavages of aziridinones,[22] it seems likely that such attack takes place at the front face of the tetrahedral carbon rather than from the rear, opposite the N atom (possibly complexed to some magnesium species present). However, this conclusion is by no means certain, for **1** reacts not only

(17) (a) Ashby, E. C.; Weiseman, T. L.; Bowers, Jr., J. S.; Laemmle, J. T. *Tetrahedron Lett.* **1976**, 21. (b) Ashby, E. C. *Pure Appl. Chem.* **1980**, *52*, 545. (c) Ashby, E. C., Bowers, J.; Depriest, R. *Tetrahedron Lett.* **1980**, *21*, 3541. (d) Ashby, E. C.; Bowers, J. R., Jr.; *J. Am. Chem. Soc.* **1981**, *103*, 2242. (e) Ashby, E. C.; Goel, A. B. *Ibid.* **1981**, *103*, 4983.

(18) Baumgarten, H. E.; Elia, V. J.; Gold, B. I., Hagemeier, L. D., unpublished results.

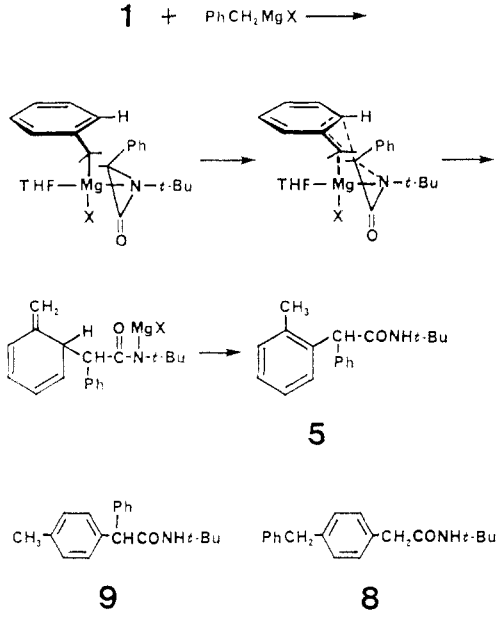
(19) Chiang, N.-C. Ph.D. Thesis, University of Nebraska—Lincoln, July 1980.

(20) The coupling and cross-coupling reactions of alkyl halides and Grignard reagents (sometimes called Kharasch couplings) have been the subject of considerable study. A review with leading references to other aspects is (a) Felkin, H.; Swierczewski, G. *Tetrahedron* **1975**, *31*, 2735. Other references may be found in note 14 of ref 16.

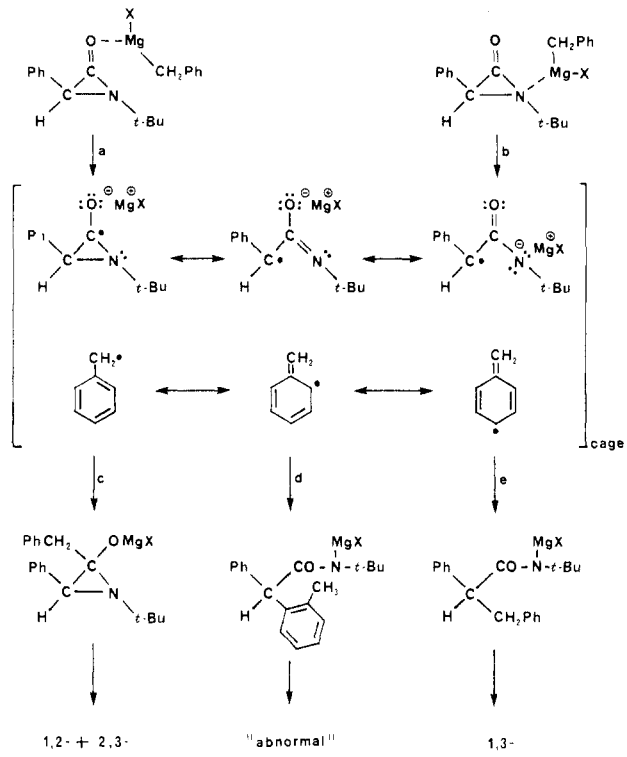
(21) Fauvarque, J. F.; Rouget, E. *C. R. Hebd. Seances Acad. Sci., Ser. C.* **1968**, *257*, 1355.

(22) Sarel, S.; Weissman, B. A.; Stein, Y. *Tetrahedron Lett.* 1971, 373.

Scheme II



Scheme III



with magnesium and zinc bromides to yield **2** (X = Br) in 50–55% yields at 0 °C[23] but also with tetraethylammonium chloride (in acetonitrile) to give **2** (X = Cl) in 67% yield.[24] Experiments to further test this presumed four-center, front-side attack in 1,3-cleavages are in progress.

The formation of the 1,2- and 2,3-cleavage products, **7** and **6**, by a polar route would involve acyl attack by the benzyl-Grignard reagent to form tetrahedral complexes with **1** at the carbonyl group followed by ring scission (Scheme I). Although reagents that react with aziridinones to give all three possible one-bond cleavage reactions are uncommon, we have found several such reagents and will be reporting these in subsequent papers.

Product **5**, the major product in THF, is clearly reminiscent of the "abnormal" reaction products of the benzyl-Grignard reagent; however, the formation of **5** must involve the α carbon atom rather than the carbonyl group of the aziridinone ring. Thus, the mechanism should resemble that for the reaction of benzyl-Grignard reagents with reactive alkylating agents[13-15] rather than that proposed recently by Benkeser[15d] for the formation of *o*-tolyl species from carbonyl compounds. Even so, many of the conclusions reached by Benkeser should be applicable here. One attractive polar mechanism involving a six-center transition state (in a chair-like conformation) is given in Scheme II. Details for the 1,3-hydride shift in the final stage of the reaction are not shown, as these have already been discussed in some detail by Benkeser.[15d]

If these reactions proceed, in whole or in part, by SET routes, the mechanisms shown in Schemes I and II may be modified as in Scheme III, which is a very much simplified outline of what might be a very complex set of reactions. For the ketone–Grignard reagent reaction Ashby[17] has shown that SET reactions are favored by stable radicals (radical anions and radical cations), good coordinating solvents (such as THF), and traces of transition-metal impurities in the magnesium used to prepare the reagent. The course of an SET reaction appears to depend on the stability of the radicals, steric factors, and the viscosity of the solvent. An SET reaction of an aziridinone would be expected to be more complex than that of a ketone, for electron transfer could involve either the carbonyl group as in path a or the 3-ring (or nitrogen atom) as in path b. Both the benzylic and aziridinone-derived radicals should be stabilized by resonance. Only three of the many possible resonance forms of the latter are shown, some of which might be better represented as a rapid rearrangement of MgX^+ from oxygen to nitrogen similar to the rearrangements in allylic Grignard reagents. After the SET step the product-determining step might involve a very rapid reaction in the radical anion–radical cation pair (not shown) or (given the possible stability of the radicals) a somewhat slower reaction of the dissociated radicals within the cage. The radicals could combine in various ways as shown in paths c, d, and e to give the intermediates necessary to form the products observed. Since **9** was not present in amounts detectable by our NMR analysis, the assumption would be that the reactions occurred too rapidly to permit reorientation of the partners and, thereby, attack at the para position of the benzyl radical.

We have no satisfactory rationalization of the effects of THF solvent or added ferric chloride. THF favors monomeric Grignard reagents, and both THF and ferric chloride favor SET reactions.[17] Therefore, we have considered, among others, the possibilities of an SET component in the ortho-alkylation reaction and a solvent effect in which the lesser steric demands of THF or of a monomeric benzyl Grignard reagent might stabilize the ortho-alkylation transition state. Since it appears that the dibenzylmagnesium prefers to give alkylation by simple 1,3-cleavage, a solvent-induced shift in the Schlenk

(23) Some years ago when we began to look at the reactions of aziridinones with Grignard reagents, we began by conducting the reactions at low temperatures, 0 to −70 °C, with RMgX to aziridinone ratios not much greater than 1:1. Under these conditions with **1** the major product with all Grignard reagents examined was **2** (in 51–63% isolated yield). A ratio of RMgX to aziridinone of 2:1 or greater was found to be best for survey experiments. However, this ratio should not be interpreted as indicating that an extra equivalent of RMgX is required for complexation with the *reactant* as Ashby[17] has shown that complex formation with the *product* may be cause of needed excesses of RMgX.

(24) Aziridinone **1** was the first authentic α-lactam. Before we learned to handle it properly, we had difficulty making KBr wafers from it for IR spectroscopy. At the high pressures then in vogue (1962), the pellet-making process converted **1** into **2** (X = Cl) (apparently quantitatively).

equilibrium is another possibility. However, interpretation of the experiment involving "dibenzylmagnesium" prepared by precipitation of $MgCl_2$ is clouded by the change of solvent to ether–dioxane. Ashby[17] has noted that the solvent-related interactions in Grignard additions and alkylations are still unresolved.

The α-bromo amide **2** (the precursor of **1**) also reacted with the benzyl-Grignard reagents to yield **3**, **4**, **5**, **6**, and **7**. The results were similar to those obtained from the reaction of the reagents with **1**, except that in most experiments the reduced amide **3** was the major product in both ether and THF and that the amounts of unidentified materials present were much smaller than with **1** (10% or less). Therefore, one cannot rule out the possibility that **2** may also be involved to some extent in the reaction of **1** with benzyl-Grignard reagents or that the reactions of **2** involved a prior ring closure to **1** brought about by the (basic) Grignard reagent.

In summary, the expected ring-cleavage products, **4**, **6**, and **7**, along with reduced amide **3**, α-halo amide **2** (Cl and Br), and the "abnormal" ortho-alkylation product **5** were obtained in the reaction of aziridinone **1** with the benzyl-Grignard reagent. The formation of **5** fits well into the family of mechanisms proposed by Benkeser and others to explain the formation of such products but may also be explained by an SET route.

Experimental Section

All melting and boiling points were uncorrected. The NMR spectra were determined with Varian A-60D or EM-390 spectrometers. IR spectra were determined with Perkin-Elmer 237 or Beckman Acculab 4 spectrometers. High-resolution mass spectra were run by the Midwest Center for Mass Spectrometry, University of Nebraska—Lincoln. Mallinckdrodt reagent grade anhydrous ether was used without further purification. Fisher reagent grade tetrahydrofuran was dried over $LiAlH_4$[25] and distilled under nitrogen. Microanalyses were by Galbraith Laboratories, Inc., Knoxville, TN.

Preparation of Grignard Reagents. The following typical procedure was used for the preparation of the benzyl-Grignard reagents. The reactions were carried out in oven-dried glassware under a nitrogen atmosphere. To a mixture of 0.18 g (7.5 mmol) of magnesium turnings in 5 mL of anhydrous ether was added 0.79 g (6.25 mmol) of benzyl chloride in 15 mL of ether. After the reaction was initiated, the addition was kept at such a rate as to maintain reflux. When the addition was complete and reflux ceased, the mixture was heated gently under reflux for 15 min and allowed to cool to room temperature. Enough ether was added to give the desired concentration (0.016–0.22 M, average value 0.12 M). The reagent was freshly prepared and was used in situ at the chosen temperature. The same procedure was used when THF was the solvent. Analysis of random preparations by Eastham's method[26] indicated an average yield of about 75–80%.

General Reaction Procedure. The following procedure was used for most of the experiments reported here. To the chosen quantity of the solution of the benzyl-Grignard reagent was added dropwise a solution of 2.5 mmol of 1-*tert*-butyl-3-phenylaziridinone (**1**) or 2-bromo-*N*-*tert*-butyl-2-phenylacetamide (**2**) in ether or THF at the desired temperature under nitrogen. The concentration of **1** was 0.075–0.28 M (average 0.18 M). Because of the limited solubility of **2**, its concentration was 0.01–0.02 M (average 0.015 M). In some experiments suspensions of **2** (0.1–0.2 M nominal concentration; average 0.15 M) were used with no significant differences in results. When the addition was complete, the mixture was stirred for an additional 3–6 h at room temerature or as specified in Table I. The mixture was hydrolyzed with saturated aqueous NH_4Cl. The ethereal layer was washed additional aqueous NH_4Cl, and the aqueous layers were extracted with ether. Evaporation of the dried ($MgSO_4$) solution left a residue that was completely soluble in $CDCl_3$. In some experiments the components were separated on a silica gel column using 10–30% solutions of ethyl acetate/pentane as eluant.

General Analytical Procedure. The chemical shifts of all highly purified starting materials and products (either isolated or synthesized) were determined in the region of 0–100 Hz (60 MHz) or 0–150 Hz (90 MHz) as precisely as possible (sweep width, 100–150 Hz; sweep times, 250 s). Cyclooctane (δ 1.54[27]) and Me_4Si were used as internal standards. The identities of the reaction products were determined by comparison of the *tert*-butyl groups of the authentic compounds referred to the cyclooctane as added standard. In most cases unidentified singlet peaks appeared in the 50–140-Hz region. For analytical purposes these were assumed to have been caused by *tert*-butyl groups. The composition of the crude reaction mixtures were determined through use of a polar planimeter and machine integrals. Because of the overlap of the bases of some peaks, the compositions were considered to be no more accurate than ±10% (relative) for the larger percentages (>40%) and up to ±25% for the smaller values (<15%). The results are summarized in Table I.

1-*tert*-Butyl-3-phenylaziridinone (1). A solution of 46.5 g (0.300 mol) of phenylacetyl chloride and 48.0 g (0.300 mole) of bromine in 250 mL of CCl_4 was heated under reflux for 8 h. The excess bromine and CCl_4 were removed by distillation under reduced pressure (about 15 torr). Distillation of the residue gave 70 g (99%) of α-bromophenylacetyl chloride, bp 110 °C (2.5 torr) (lit.[28] bp 125 °C (8 torr)). Addition of 23.4 g (0.100 mol) of the crude bromoacyl chloride to 14.6 g (0.200 mol) of *tert*-butylamine in 100 mL of CH_2Cl_2 at 0 °C gave 19.0 g (74%) of *N*-*tert*-butyl-2-bromo-2-phenylacetamide (**2**, X = Br), mp 128–130 °C (lit.[29] mp 128.5–130 °C): IR ($CHCl_3$) 3440 (NH), 1678 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.39 (s, 9 H, *t*-Bu), 5.31 (s, 1 H, CH), 7.30–7.47 (60 MHz, m, 5 H, Ph).

To a well-stirred solution of 6.75 g (0.025 mol) of **2** (X = Br) in 200 mL of cold (0 °C) ether was added a stirred suspension of 3.7 g of potassium *tert*-butoxide in 150 mL of anhydrous ether over a period of 1 h. The reaction mixture was filtered, and the filtrate was *rapidly* evaporated under reduced pressure to an oily residue. Recrystallization of the latter from dry pentane gave 2.6 g (55%) of **1**; mp 32–33 °C: IR ($CHCl_3$) 1850 cm^{-1}; NMR (CCl_4) δ 1.32 (s, 9 H, *t*-Bu), 3.67 (s, 1 H, CH), 7.19 (s, 5 H, Ph).

Reaction of 1 with Inorganic Halides. To a solution of 0.37 g of $MgBr_2$ in 5 mL of ether at 0 °C. The mixture was stirred for 1 h at 0 °C and then at room temperature overnight. Hydrolysis with 10 mL of saturated aqueous NH_4Cl solution, extraction of the product into ether, removal of solvent from the dried ($MgSO_4$) solution, and recrystallization from CH_2Cl_2–petroleum ether gave 0.25 g (55%) of 2-bromo-*N*-*tert*-butyl-2-phenylacetamide (**2**, X = Br), mp 128.5–130 °C.

Treatment of 0.25 g (1.37 mmol) of **1** with 0.31 g (1.37 mmol) of anhydrous $ZnBr_2$ dissolved in 20 mL of ether using the above procedure gave 0.22 g (60%) of **2** (X = Br).

Addition of 0.30 g (1.6 mmol) of **1** in 10 mL of dry acetonitrile to 0.35 g (2.1 mmol) of tetraethylammonium chloride in 10 mL of acetontrile gave a 67% yield of **2** (X = Cl), mp 125–127 C (lit.[30] mp 126.5–127.5 °C), IR and NMR spectra identical with those of an authentic sample.

***N*-*tert*-Butyl-2-phenylacetamide (3).** This substance was prepared by the reaction of phenylacetyl chloride with *tert*-butylamine in CH_2Cl_2 solution, mp 114–115 °C (lit.[31] mp 115–116°C); IR ($CHCl_3$) 3411 (NH), 1666 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.28 (s, 9 H, *t*-Bu), 3.47 (s, 2 H, CH_2), 7.28 (s, 5 H, Ph).

***N*-*tert*-Butyl-2,3-diphenylpropanamide (4).** In one reaction of **2** with the benzyl chloride Grignard reagent carried out as described above approximately 70% of **4** was present in the product, on the basis of NMR analysis. The material was isolated and purified by repeated recrystallized from CH_2Cl_2/petroleum

(25) See: "Organic Syntheses", Wiley: New York, Collect. Vol. 5, p 976 for precautions to be taken with THF.
(26) Eastham, J. F.; Watson, S. C. *J. Organomet. Chem.* **1967**, *9*, 165.
(27) Wiberg, K. B.; Nist, B. J. *J. Am. Chem. Soc.* **1961**, *83*, 1226.
(28) Truitt, P.; Mark, D.; Long, L.; Jeanes, J. *J. Chem. Soc.* **1948**, *70*, 4214.
(29) Coleman, G. H.; Peterson, R. L.; Goheen, G. E. *J. Am. Chem. Soc.* **1936**, *58*, 1874.
(30) Baumgarten, H. E.; Clark, R. D.; Fuerholzer, J. J.; Thompson, R. D. *J. Am. Chem. Soc.* **1963**, *85*, 3303.
(31) Ritter, J. J.; Minieri, P. P. *J. Am. Chem. Soc.* **1948**, *70*, 4045.

ether, giving a 42% purified yield of **4**: mp 187–188 °C; IR ($CHCl_3$) 3420 (NH), 1670 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.20 (s, 9 H, *t*-Bu), 2.87 and 3.40 (AB X, 3 H, CH_2CH), 5.08 (s, 1 H, NH), 7.12–7.23 (60-MHz, m, 10 H, Ar). Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.24; H, 8.19; N, 4.98.

***N*-*tert*-Butyl-2-phenyl-2-*o*-tolylacetamide (5).** Following the procedure of Staum,[32] phenyl-*o*-tolylcarbinol was synthesized by the addition of benzaldehyde to an ethereal solution of *o*-tolylmagnesium bromide followed by hydrolysis in 66% yield, mp 91–92.5 °C (lit.[28] mp 92 °C). The carbinol was converted in 86% yield to phenyl-*o*-tolylmethyl chloride by using a 15% excess of $SOCl_2$, bp 91 °C (0.02 torr) (lit.[28] mp 143–144 °C (0.5 torr)). Reaction of the chloro compound with sodium or cuprous cyanide in ethanol/water gave a 73% yield of crude 2-phenyl-2-*o*-tolylacetonitrile: IR ($CHCl_3$) 2220 cm^{-1}; NMR ($CDCl_3$) δ 2.27 (s, 3 H, CH_3), 5.50 (s, 1 H, CH), 7.07–7.50 (60 MHz, m, 9 H, Ar). Attempted hydrolysis of the crude nitrile with 50% aqueous H_2SO_4,[28] H_2SO_4, or 30% KOH plus H_2O_2 failed to give the desired acid. Hydrolysis with concentrated HCl gave only 5% (based on the chloride) crude *o*-tolylphenylacetic acid: IR ($CHCl_3$) 2610 (OH) and 1715 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 2.28 (s, 3 H, CH_3), 5.23 (s, 1 H, CH), 7.06–7.40 (60 MHz, m, 9 H, Ar), 10.00 (s, 1 H, COOh). The crude acid was converted to its acyl chloride with excess $SOCl_2$ as solvent and reactant. Addition of 2 equiv of *tert*-butylamine to the acyl chloride in CH_2Cl_2 gave **5** in 81% yield after recrystallization from hexane: mp 181–181.5 °C; IR ($CHCl_3$) 3400 (NH), 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.32 (s, 9 H, *t*-Bu), 2.25 (s, 3 H, CH_3), 4.97 (s, 1 H, CH), 5.25 (b, 1 H, NH), 7.08–7.33 (at 60 MHz, m, 9 H, Ar); mass spectrum, calcd for $C_{19}H_{23}NO$ 281.17795, found 281.178076. Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.12; H, 8.28; N, 4.85.

***N*-Benzyl-*N*-*tert*-butyl-2-phenylacetamide (6).** *N*-Benzylidene-*tert*-butylamine was prepared from *tert*-butylamine and benzaldehyde by the method of House,[33] 64% yield, bp 82 °C (6 torr) (lit.[29] bp 92 °C (8 torr)). The imine was hydrogenated (Pd/C) in methanol and distilled to give *N*-benzyl-*N*-*tert*-butylamine in 62% yield, bp 78 °C (6 torr) (lit.[29] bp 109–110 °C (25 torr)). The addition of phenylacetyl chloride to the amine in CH_2Cl_2 and recrystallization of the crude product from ethyl acetate/pentane gave the amide **6** in 78% yield: mp 65.5–67 °C; IR ($CHCl_3$) 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.97 (s, 9 H, *t*-Bu), 3.63 (s, 2 H, CH_2C=O), 4.57 (s, 2 H, $PhCH_2N$), 7.25–7.32 (at 60 MHz, m, 10, Ar); mass spectrum, calcd for $C_{19}H_{23}NO$ 281.17795, found 281.17795. Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.14; H, 8.24; N, 4.88.

1-(*tert*-Butylamino)-1,3-diphenyl-2-propanone (7). 1-Bromo-1,3-diphenyl-2-propanone was prepared in 69–80% yield following the procedure of Smith and Wilson:[34] mp 44–46°C (lit.[30] mp 45–47 °C). The reaction of this bromo ketone with *tert*-butylamine gave mixtures of **7** and the Favorski rearrangement product **4**.[35] The following procedure appeared to give the best ratio of ketone to amide. A solution of 2.9 g (0.01 mol) of the crude bromo ketone in 40 mL of THF was added dropwise to a solution of 1.46 g of freshly distilled *tert*-butylamine (0.02 mol) in 30 mL of THF under nitrogen. After the mixture had been stirred for 12 h at 25 °C, the *tert*-butylamine hydrobromide was filtered off, and the solvent was removed. The NMR spectrum of the crude product indicated it to consist of approximately 78% of **7**, 18% of **4**, and 4% of some other product. The crude product was extracted with 30 mL of petrolum ether (in which the amide was poorly soluble). The insoluble materials were filtered off, the solvent was removed gently in the rotary evaporator, and the residue was recrystallized from isopropyl alcohol (keeping the temperature below 60 °C). The yield of **7** was 70%: mp 70–72 °C; IR ($CHCl_3$) 3340 (NH), 1715 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 0.97 (s, 9 H, *t*-Bu), 2.43 (s, 1 H, NH), 3.67 (s, 2 H, CH_2), 6.8–7.3 (90 MHz, m, 10 H, Ar); mass spectrum, calcd for $C_{19}H_{23}NO$ 281.17795, found 281.17785. Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.88; H, 8.22; N, 4.84.

***N*-*tert*-Butyl-2-(*p*-benzylphenyl)acetamide (8).** *p*-Benzoylphenylacetic acid was prepared in 37% overall yield as described by Staum.[32] Hydrogenation (Pd/C) of the acid gave *p*-benzylphenylacetic acid in 32% yield. The crude acid was converted into the acyl chloride by using excess $SOCl_2$. Addition of the acyl chloride to *tert*-butylamine in CH_2Cl_2 and recrystallization of the product from ether/ethyl acetate gave a 43% yield of **8**: mp 132–133.5 °C; IR ($CHCl_3$) 3410 (NH), 1670 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.27 (s, 9 H, *t*-Bu), 3.42 (s, 2 H, CH_2C=O), 3.97 (s, 2 H, $ArCH_2Ar$); mass spectrum, calcd for $C_{19}H_{23}NO$ 281.17795, found 281.17771. Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.91; H, 8.19; N, 4.84.

***N*-*tert*-Butyl-2-phenyl-2-*p*-tolylacetamide (9).** Phenyl-*p*-tolylacetic acid was prepared by the $SnCl_4$-catalyzed Friedel–Crafts reaction of mandelic acid with toluene.[36] The acid was converted into the *N*-*tert*-butyl amide by successive treatment with $SOCl_2$ and *tert*-butylamine. The details are more pertinent to the chemistry of *N*-*tert*-butyl-3,3-diphenylaziridinone and will be published elsewhere. The properties of **9** are mp 175–177 °C; IR ($CHCl_3$) 3420 (NH), 1675 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.30 (s, 9 H, *t*-Bu), 2.28 (s, 3 H, CH_3), 4.72 (s, 2 H, CH_2), 7.05–7.18 (60 MHz, m, 9 H, Ar).

Reaction of 1 with Dibenzylmagnesium. Using syringe techniques 10 mL of dry dioxane was slowly added to a mixture of 20 mL of dry ether and 10 mL of freshly prepared 3 M benzyl-Grignard reagent in a sealed system under nitrogen.[37] The mixture was stirred at room temperature for 4 h and then allowed to settle. The clear solution above the settled precipitate of magnesium halide was carefully transferred to another flask (under nitrogen). To the latter was added 0.40 g (2.5 mmol) of **1** in 10 mL of ether slowly. The mixture was stirred for 1 h at room temperature, and 20 mL of saturated aqueous NH_4Cl was added. The ethereal layer was washed with water, dried, and evaporated. The residual oil was dissolved in CCl_4 and analyzed by NMR, which indicated that **4** was the only product in essentially 100% yield. Isolation of **4** by recrystallization from CH_2Cl_2–pentane afforded **4**, mp 187–188 °C.

Acknowledgment. Support for this work was provided by the National Science Foundation, the National Institues of Health, and the University of Nebraska—Lincoln Research Council.

Registry No. **1**, 27151-60-6; **2** (X = Br), 55341-86-1; **2** (X = Br, acid chloride), 19078-72-9; **2** (X = Cl), 65117-34-2; **3**, 6941-21-5; **4**, 98901-14-5; **5**, 98901-15-6; **5** (carboxylic acid), 92548-88-4; **5** (acid chloride), 92435-45-5; **6**, 98901-16-7; **7**, 98901-17-8; **8**, 98901-18-9; **8** (carboxylic acid), 35889-03-3; **8** (acid chloride), 98901-20-3; **9**, 98901-19-0; **9** (carboxylic acid), 1882-56-0; **9** (acid chloride), 98974-81-3; $PhCH_2Br$, 100-39-0; $PhCH_2Cl$, 100-44-7; *t*-$BuNH_2$, 75-64-9; $MgBr_2$, 7789-48-2; $ZnBr_2$, 7699-45-8; $Et_4N^+Cl^-$, 56-34-8; $PhCH_2COCl$, 103-80-0; *t*-$BuNHCH_2Ph$, 3378-72-1; $PhCHBrCOCH_2Ph$, 29417-77-4; PhCHO, 100-52-7; *o*-$BrC_6H_4CH_3$, 95-46-5; *o*-$H_3CC_6H_4CH(Ph)OH$, 5472-13-9; *o*-$H_3CC_6H_4CH(Ph)Cl$, 41870-52-4; *o*-$H_3CC_6H_4CH(Ph)CN$, 98901-21-4; PhCH=NBu-*t*, 6852-58-0; *p*-$PhCOC_6H_4CH_2CO_2H$, 26077-80-5; $PhCH(OH)CO_2H$, 90-64-2; $PHCH_3$, 108-88-3; Ph_2Mg, 6928-77-4.

(32) Staum, M. M. *U.S. At. Energy Comm.* **1961**, ORNL-3057; *Chem. Abstr.* **1962**, *56*, 2362g.

(33) House, H. O.; Liang, W. C.; Weeks, P. D. *J. Org. Chem.* **1974**, *39*, 3102.

(34) Smith, A. C. B.; Wilson, W. *J. Chem. Soc.* **1955**, 1342.

(35) Bordwell and Almy (Bordwell, F. G.; Almy, J. *J. Org. Chem.* **1973**, *38*, 571) reported that this bromo ketone gave mixtures of α-piperidino ketone and of Favorski rearrangement product on treatment with piperidine. They reported the best yields of amino ketone to be obtained in MeOH solution. We tried several solvents including MeOH and CH_2Cl_2, all of which gave largely the amino ketone. The procedure given here was the simplest and most reproducible.

(36) Bistrzychi, A.; Mauron, L. *Chem. Ber.* **1907**, *40*, 4063.

(37) Christensen, B. G.; Strachen, R. G.; Teenner, W. R.; Arison, R. H.; Hirschmann, R.; Chemerda, J. M. *J. Am. Chem. Soc.* **1960**, *82*, 3995. In another study we compared the reactions of derivatives of **1** with dimethylmagnesium prepared from dimethylmercury and by the dioxane precipitation technique. The results were essentially identical (Elia, V. J., Gold, B. I., unpublished results).