Reactions of Amines. 19. Reactions of 1,3-Di-*tert*-butylaziridinone and 2-Bromo-*N*-*tert*-butyl-3,3-dimethylbutanamide with Selected Organometallic Reagents[1]

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Received April 27, 1976

1,3-Di-*tert*-butylaziridinone (**1c**) reacts with the phenyl bromide Grignard reagent to give *N*-*tert*-butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine (**4cz**) and with phenyllithium to give **4cz** plus 2-*tert*-butylamino-3,3-dimethyl-1-phenyl-1-butanone (**3cz**). α-Lactam **1c** reacts with an excess of the methyl halide Grignard reagents to give mixtures of 2-halo-*N*-*tert*-butyl-3,3-dimethylbutanamide (**2c**), *N,N'*,2,3-tetra-*tert*-butylbutanediamide (**7c**), *N*-*tert*-butyl-3,3-dimethylbutanamide (**8c**), *N*-*tert*-butyl-2,3,3-trimethylbutanamide (**9cw**), 3-*tert*-butylamino-4,4-dimethyl-2-pentanone (**3cw**), and *N*-*tert*-butyl-2-hydroxy-2,3,3-trimethylbutanimine (**4cw**). The choice of halide ion in the Grignard reagent appears to determine the relative amounts of the products, the combined yields of **2c** and **8c** decreasing and the yield of **4cw** increasing in the order iodide, bromide, chloride. Dimethylmagnesium reacts with **1c** to give largely **4cw**; and, depending on the conditions, methyllithium reacts to yield either **3cw** or **4cw**, or mixtures of these. The α-halo amide **2c** (X = Br) reacts with the Grignard reagents to give **4c**, **7c**, **8c**, and **9c** but little or no **3c**. The isomerization of **3c** to **4c** and vice versa is described. The solid-state structure of *N*-*tert*-butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine (**4cz**) has been determined by single-crystal x-ray diffraction and has been refined (anisotropically on C, O, and N; isotropically on H) by full-matrix least-squares techniques to R (unweighted) = 0.044 and r (weighted) = 0.048 using 1621 independent diffractometer-recorded reflections having $2\theta_{\mathrm{Mo}K\bar{\alpha}} < 55°$ and $I > 3\sigma(I)$. An intramolecular hydrogen bond is observed in the solid state between the hydroxyl oxygen atom and imine nitrogen atom.

A number of papers[3–8] have appeared in the past 5 years describing the reactions of organometallic reagents with the highly sterically stabilized α-lactams **1a–d**. Prior to the publication of these papers we had conducted an exploratory study[9] of the reactions of several α-lactams, including **1c**, with organomagnesium and organolithium reagents as a part of a more general study of the reactions of α-lactams. Inasmuch as our conclusions differed somewhat from those published, we have reexamined and extended our earlier observations. We report here our findings, which we hope will unify and clarify the previous reports which have appeared largely in the form of brief, somewhat contradictory, communications with a minimum of supporting data.

First, it should be noted that the reactions of the highly sterically stabilized α-lactams, such as **1a–d**, should be expected to be no more typical of the class of α-lactams than the reactions of di-*tert*-butyl ketone are typical of the class of ketones. Thus,the subset of reactions of **1a–d** with organometallic reagents appears to be somewhat more limited in scope than the set of all known reactions[9] of α-lactams with a given reagent. This will be demonstrated in later papers in this series.

Second, since we reported nearly 15 years ago[10] how easily α-lactams react with halide ion to give α-halo amides **2**, any conclusions drawn from observations of the reactions of α-lactams with reagents or solutions containing halide ion must take into consideration the possibility that **2** may be an intermediate in the observed reactions.

The first published report of a reaction between an α-lactam and an organometallic reagent was that of Sheehan and Nafissi-V.[3] Although subsequent investigators[4–9] have not been able to confirm either the observations or conclusions of Sheehan and Nafissi-V, the report apparently has stimulated others to examine the behavior of **1a–d** with organometallic reagents. Thus, in separate communications Talaty[6,7] and co-workers reported that **1a–d** react with *tert*-butyllithium at 25–30 °C to give products tentatively identified as α-hydroxy imines[6] (**4ay–dy**) and that **1b** and **1d** react with a variety of alkyllithiums at −78 °C to give the α-amino ketones **3b(x–z)** and **3d(x–z)**. However, Talaty et al.[4,7] reported also that **1d** reacted with the phenyl bromide Grignard reagent (at 0 °C followed by 3 h at room temperature) to give 78% of the α-halo amide **2d** (X = Br). This stands in contrast to a later report by Lengyel, Mark, and Troise[8] that **1b** reacted with the phenyl bromide Grignard reagent at 0 °C to give a 41.2% yield of the α-amino ketone **3bz**. Probably Talaty et al.[4] either used an insufficient amount of Grignard reagent or conditions that led to destruction of some of the reagent. Unless more than 1 equiv is used with most α-lactams, the halide **2** may be the major product. Even so, we believe that the product obtained by Lengyel, Mark, and Troise[8] was more probably the α-hydroxy imine **4bz** and **3bz** and that most of the conclusions of Talaty et al.[6,7] are correct.

In our experiments (Table I) when **1c** was treated with the phenyl bromide Grignard reagent in refluxing ether, the principal product was the α-hydroxy imine **4cz**. The structure of this compound was determined unequivocally by x-ray crystallography (vide infra). When **1c** was treated with excess phenyllithium at room temperature, a mixture of **3cz** and **4cz** in the ratio 2:1 was obtained. These two compounds form an isomeric pair of the type studied quite thoroughly by Stevens[11] and others. As Stevens[11,12] has carefully pointed out, the composition of a mixture of α-amino ketones and α-hydroxy imines of this type will depend on the environment from which they are isolated. The isolation of **4cz** rather than **3cz** in the reaction with the phenyl bromide Grignard reagent probably indicates that, under the conditions of the reaction, the complex **6cz** is more stable than **5cz** and that, in the reaction with excess phenyllithium, either the position of the equilibrium has changed (stabilization by the metallic ion being less significant) or some sort of kinetic control is being exercised.

Since the composition of a mixture of **3cz** and **4cz** will depend on the immediate past history of the pair,[11] it may not be profitable to label one or the other as the *thermally* more stable based on its isolation from the Grignard reaction. Thus, when **4cz** (or a mixture of **3cz** and **4cz**) was heated at 115 °C for 18–72 h, a quantitative conversion to **3cz** resulted, suggesting that in the melt **3cz** is the more stable. Furthermore, when **3cz** was treated with a large excess of the methyl

Table I. Approximate Analysis of Reaction Mixtures[a]

Substrate (S)	Reagent (R)	Mole ratio (S/R)	Temp,[b] °C	Time, h	2c	3cz	4cz	7c	8c	9cz	Other
1c	PhMgBr	1:1.2	RT	3			~100				
	PhLi	1:1.2	RT	8		22	35		Tr		43[c]
		1:2	RT	8		67	33				
2c	PhMgBr	1:1	RT	3	~100		Tr				
		1:2.5	RT	3	1.5	Tr?	55	17[d]	15	12	
		1:2.5	RT	3	6	Tr?	50	20[e]	14	10	
3cz	MeMgCl	1:1	RT	3		~100					
		1:2	RT	3		~100					
		1:31[f]	RT	3		9	50				41[g]
		1:40[f]	RT	3		<1	70				29[g]
4cz	None		~80	18			~100				
			~80	96		~100					
			80, 113	18, 18		~100					
			113	18		67	33				
			115	72		~100					

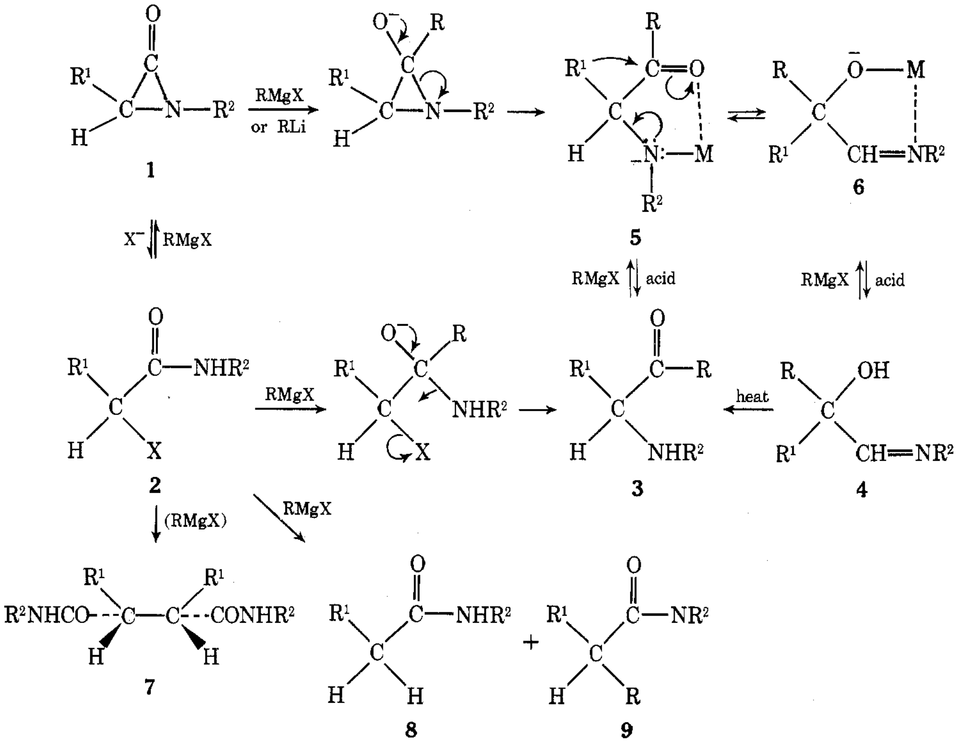
[a] Based on ^{1}H NMR analysis of crude reaction mixture; see Experimental Section. [b] RT = room temperature. [c] Recovered 1c. [d] Two substances in the ratio of ca. 12:5. [e] Two substances in the ratio of ca. 13:7. [f] In tetrahydrofuran. [g] Largely an unidentified product [^{1}H NMR δ ($CDCl_3$) 1.43 (9 H), 2.28 (2 H), 6.99 (1 H); δ (CCl_4) 1.42 (9 H), 2.23 (2 H), 6.85 (1 H)] plus traces of other products with ^{1}H NMR peaks at δ (CCl_4) 1.25, 1.00; δ ($CDCl_3$) 1.30, 1.26, 1.00.

chloride Grignard reagent, **3cz** was converted into a mixture of **4cz** and a frequently encountered by-product of undetermined structure, which appeared to be a cleavage product [^{1}H NMR peaks at δ 1.43 (*t*-Bu) and 1.36 but no peaks in the phenyl region]. This result would appear to support the role of the metal complex (**5** or **6**).

A simplified mechanism is given in the chart for the formation of **4** from **1** or **2**. Presumably, the transition state for the rearrangement step in the sequence **5** → **6** is similar to that proposed by Stevens[11] for the thermal rearrangement except that the hydrogen-bonded proton is replaced by the metallic ion (or complex). Possibly, other α-amino ketones could be isomerized to α-hydroxy imines using magnesium salts or complexes as intermediates.

The ^{1}H NMR spectra of **3cz** and **4cz** are quite different. In particular the spectrum of **4cz** shows the aldimine proton at δ 8.36 (CCl_4). Since the spectrum of the product assigned the structure **3bz** by Lengyel, Mark, and Troise[8] showed a 1 H singlet at δ 8.33 (CCl_4) and since their other spectral data (ir and ^{1}H NMR) are more in accord with those to be expected for **4bz** rather than **3bz** (based on our values for **3cz** and **4cz**), we conclude that their product was indeed **4bz**.

The reaction of the α-halo amide **2c** (X = Br) with the phenyl bromide Grignard reagent also gave **4cz** as the major product; however, the reaction was more complex than that with **1c**. In a careful analysis of the ^{1}H NMR spectrum of the crude reaction mixture (Table I) all of the peaks present could be accounted for on the basis that there were four products in addition to **4cz** and unreacted starting materials. Two of these could be regarded as "dimers" of **1c**. They were not



a, R¹ = 1-adamantyl; R² = *t*-Bu
b, R¹ = *t*-Bu; R² = 1-adamantyl
c, R¹ = R² = *t*-Bu
d, R¹ = R² = 1-adamantyl

w, R = Me
x, R = *i*-Pr
y, R = *t*-Bu
z, R = Ph

Table II. Approximate Analysis of Reaction Mixtures[a]

Substrate (S)	Reagent (R)	Mole ratio, S:R	Temp,[b] °C	Time, h	**2c**[c]	**3cw**	**4cw**	**7c**	**8c**	**9cw**	Other substances
1c	MeMgI	1:1	0, RT	3	37		6	6	21	6	24
		1:1	0, RT	3	40		10	7	23	10	10
		1:1	0, RT	3	30		3	4	40	6	20
		1:2.5	RT	3	Tr		18	3	67	13	
		1:1	0, RT	4	4		7	8	67	12	
		1:1	0, RT	3	Tr?		10	7	71	8	4
	MeMgBr	1:0.83	RT	3	~100						
		1:2.5	RT	3	61		22	3	9	4	
		1:1[d]	0, RT	3	42		58	?	?	?	
	MeMgCl	1:1[e]	0, RT	3	53		20		Tr?		27
		1:2.5[f]	RT	3	10		84				6
		1:2.5[e]	RT	3	>9		84				7
		1:2.5[e]	RT	3	>4		84		6		6
		1:6.25[e]	0, RT	3	4		87		Tr		10
		1:5[f]	0, RT	3	5		92		3		
	Me_2Mg	1:3	0, RT	20			~100				
	MeLi	1:1.5	0, RT	30			>95				<5
		1:2	RT	8	8	68	21				3
		1:2	0, −78[g]	2		>95					<5
		1:2	0, −78[g]	2		>95					<5
	$MgBr_2$	1:10	R, RT	3	~100						
2c (X = I)	MeMgI	1:1.67	0, RT	3	27			Tr?	55		18
2c (X = Br)	MeMgBr	1:2.5	RT	3	87		9		6		
		1:2.5	RT	3	20		8	10	51	11	
	MeMgCl	1:2.5[h]	RT	3	55/9		23	Tr?	13	Tr?	
		1:2.5[h]	RT	3	59/10		18	1	6	2	5[i]
		1:2.5[h]	RT	3	48/10		23	4.5	9	2.5	2.5[i]
		1:2.5	RT	3	66/10		13	5	2	4	
		1:2.5	RT	3	7/6		37	26	15	10	
		1:2.5	RT	3	3/6		21	24	5	36	4
		1:4[f,j]	RT	3	31/16		6	Tr	9	34	6
		1:2.5[f,j]	RT	3	32/17		7	Tr	7	30	7
4cw	None		114[k]	96			~100				
			150	19		9	91				
			150	69		52	48				[l]

[a] Based on ^1H NMR analysis of crude reaction mixture; see Experimental Section. [b] First temperature is that at which the reagent was added. The reaction was then allowed to warm up or cool down to the second temperature (RT = room temperature; R = reflux temperature). [c] Where two values are given the first is for **2c** (X = Br) and the second for **2c** (X = Cl). [d] In *n*-butyl ether. Traces of solvent made analysis for **7c**, **8c**, and **9c** infeasible. [e] Reagent in tetrahydrofuran diluted to final volume with ethyl ether. [f] In tetrahydrofuran. [g] Procedure A of ref 7 followed; yield of **3cw**, 87%. [h] Compound **2c** in solution, concentration 0.2 M. [i] Probably **1c**; ^1H NMR ($CDCl_3$) δ 2.74, 1.303, 1.002; (CCl_4) δ 2.61, 1.263, 0.987. See note 17. [j] Reagent concentration 0.02 M; anhydrous $FeCl_3$, 3.3×10^{-4} M. [k] In refluxing toluene. [l] Small amounts of other substances were formed, ^1H NMR δ (CCl_4) 1.43 and 1.18; the amounts could not be estimated from the ^1H NMR spectrum.

readily separated from each other by the usual techniques. Since there are several ways in which two units equivalent to **1c** might be linked together and since these could not be distinguished by simple spectral methods, selected crystals of one of the two products from the mixture were analyzed by x-ray crystallographic analysis and shown to be **7c**.[13] Presumably, based on its ^1H NMR spectrum, the other "dimer" was the epimer of **7c**, but this has not been established.

The other two products were the reduction product **8c** and the alkylation or cross-coupling product, *N*-*tert*-butyl-3,3-dimethyl-2-phenylbutanamide (**9cz**). Compounds **7c, 8c,** and **9cz** are the products to be expected from a coupling reaction of an alkyl halide (**2c**) and a Grignard reagent.[14] Traces of **3cz** appeared to be present, but the amounts were too small for certain identification. If compounds **7c**, **8c**, and **9cz** were present in the reaction mixtures resulting from the reaction of **1c** and the phenyl bromide Grignard reagent, the amounts were so small as to be difficult to identify. On the basis of this and the methyl halide Grignard reagent results described below we conclude that it is unlikely that **2c** is a *required* intermediate in the conversion of **1c** to **3cz** and **4cz**.

Although organolithium reagents appear to attack all α-lactams preferentially at the carbonyl group to give ketones (or their further addition products, tertiary alcohols), organomagnesium reagents generally attack at the α-carbon atom cleaving the 1–3 bond to give α-alkylation, α-substitution by halide ion, or reduction, depending on the reagent used and the conditions.[9] Thus, the products obtained by us and by Lengyel, Mark, and Troise[8] from the reaction of **1b** and **1c** with the phenyl bromide Grignard reagent are atypical. With these highly sterically stabilized α-lactams the phenyl bromide Grignard reagent appears to react (initially at least) in a manner similar to that of phenyllithium by addition to the carbonyl group. One explanation for the atypical behavior of the Grignard reagents is that the steric requirements of **1c** are such that formation of the required intermediate complex or transition state for attack at the α-carbon atom is inhibited but attack at the somewhat less hindered carbonyl carbon atom is allowed. If this reasoning is correct, the course of the reaction could be dependent on the size and reactivity of the specific organometallic species involved and the reactivity of the corresponding halide (if any) and might be altered by using a smaller reagent (such as the methyl halide Grignard reagent), by using a less nucleophilic halide, or by substituting a dialkylmagnesium for the Grignard reagent. To observe attack at the carbonyl carbon by the methyl halide Grignard reagent, **1c** would have to react with the reagent at a rate at least competitive with the rate of reaction with the magnesium halide (or halide ion) present. Therefore, we compared the reactions of **1c** with the Grignard reagents derived from methyl iodide, methyl bromide, and methyl chloride and with dimethylmagnesium (halide free) (see Table II).

The reaction of the methyl iodide Grignard reagent with **1c** was reported by Sheehan and Nafissi-V[3] to give the unique insertion product, *N-tert*-butyl-4,4-dimethylpentamide. Although our earlier experiments[9] had indicated that **2c** (X = I) was the major product,[15] we reran the reaction with the Grignard reagent prepared from magnesium from several commercial sources. Since α-lactam reactions are often dependent on reaction conditions, we tried low and high temperatures, normal and inverse addition, and various solvents. In no case did we obtain significant quantities of products besides **2c** (X = I) or the further reaction products of **2c**. Usually the **2c** (X = I) was accompanied by variable amounts of *N-tert*-butyl-3,3-dimethylbutanamide (**8c**) and small amounts of *N-tert*-butyl-2-hydroxy-2,3,3-trimethylbutanimine (**4cw**) and of *N-tert*-butyl-2,3,3-trimethylbutanamide (**9cw**). The amide **8c** appeared to result from the reduction of **2c** (X = I), and its yield was dependent to some extent on the amount of the excess methyl iodide Grignard reagent used [as shown by separate experiments carried out on **2c** (X = I)]. The origin of the hydroxy imine **4cw** was probably similar to that of **4cz** (vide supra). The α-alkylation product **9cw** may have formed by alkylation of **1c** or, more probably, by cross-coupling between **2c** and the Grignard reagent.[14] Under no set of experimental conditions have we been able to confirm the results and structural assignments of Sheehan and Nafissi-V.[3] As noted above, two other research groups[4,5] have independently reached the same conclusion.[16]

Like the methyl iodide Grignard reagent excess methyl bromide Grignard reagent reacted with **1c** to give a mixture of **2c** (X = Br), **4cw**, **7c**, **8c**, and **9cw** in which **2c** and **4cw** tended to predominate. The methyl chloride Grignard reagent reacted with **1c** to give principally **4cw** and only small amounts of **2c** (X = Cl) and **8c**, and excess dimethylmagnesium reacted with **1c** to give only **4cw**. Methyllithium reacted with **1c** to give mixtures of **3cw** and **4cw** ranging from approximately 0 to 100% of each product depending on conditions [plus a small amount of **2c** (X = Br) if lithium bromide was present]. Talaty's conditions[7] gave the highest yield of essentially pure **3cw**. Magnesium dibromide reacted readily with **1c** to give a nearly quantitative conversion to **2c** (X = Br). Thus, the α-alkylation product **9cw** was observed only in the experiments with the methyl iodide and methyl bromide Grignard reagents. If **9cw** was present in any of the other reactions of the methyl organometallic reagents with **1c** the amount was such that we could not detect it in the ^{1}H NMR spectra of the crude reaction mixtures.

In contrast to the behavior of **1c**, **2c** reacted with the methyl bromide and methyl chloride Grignard reagents to give widely varying yields of **4cw**, **7c**, **8c**, **9cw**, and (possibly) **1c**,[17] even when the conditions were apparently unchanged and the same batch of Grignard reagent was employed (Table II). For want of a better explanation, we attribute these variations to the presence of traces of transition metal ion impurities[14] which could have been introduced not only from the magnesium metal used in preparing the reagent but also from the solvents or apparatus. Those reactions that gave higher yields of **9cw** were visibly more vigorous. Although we have not carried out a systematic study of the effects of transition metal ions on the coupling reactions of **2c** with organometallic reagents, we did observe that 30–34% yields of **9cw** were obtained when catalytic amounts of ferric chloride were added to the reaction of **2c** (X = Br) with a large excess of the methyl chloride Grignard reagent.

The thermal isomerization of **4cw** to **3cw** proceeded much more slowly than that of **4cz** to **3cz** (Table II). After 69 h at 150 °C about half of the **4cw** had been converted to **3cw**. Small amounts of degradation or other isomerization products also formed, possibly including the alternative isomerization product, 2-(*N-tert*butylamino)-4,4-dimethylpentanone, formed by migration of the methyl rather than the *tert*-butyl group; however, migration of the *tert*-butyl group was clearly the preferred process as would be expected from the work of Stevens and others.[11]

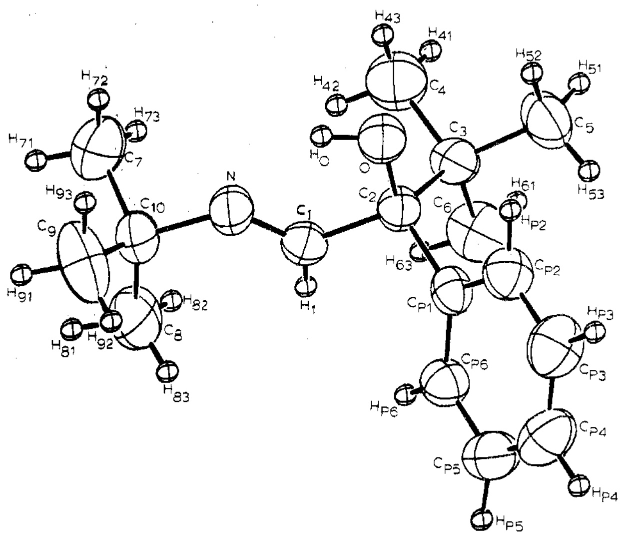


Figure 1. An ORTEP drawing showing the solid-state molecular structure of *N-tert*-butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine. All atoms except hydrogen are represented by a (50% probability) ellipsoid having the shape, orientation, and relative size consistent with the refined anisotropic thermal parameters listed in Table IV. Hydrogen atoms are represented by arbitrarily small spheres for purposes of clarity.

In summary it would appear that the variety of results obtained from the reaction of the highly sterically stabilized α-lactams with organometallic reagents can be attributed to variations in the choice of anion,[3,4] the amount of reagent,[4] the presence of impurities,[3,16] as well as the nature of the specific organometallic reagent.[18] When the competitive attack by magnesium halide (or halide ion) is suppressed, the characteristic reaction of highly sterically stabilized α-lactams with organomagnesium and organolithium reagents appears to be addition to the carbonyl group, followed in some instances by an amino ketone–hydroxy imine rearrangement.[11]

The labeling scheme used in the x-ray crystallographic analysis to designate the atoms of the *N-tert*-butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine molecule (**4cz**) is given in Figure 1. The final coordinates and anisotropic thermal parameters for all atoms except hydrogen are given in Tables III and IV, respectively.[19] The final least-squares refined positional and isotropic thermal parameters for the hydrogen atoms are given in Table V.[19] Covalent bond lengths are given in Table VI, and bond angles in Tables VII and VIII.

The crystallographic identification of the compound as a hydroxy-substituted imine was based primarily on the structural and thermal parameters for the $-N{=}C_1-C_2-O$ grouping and the successful location and refinement of the parameters for the hydrogen atoms. Relevant bond lengths involving these four atoms are shown in Figure 2. The lengths of 1.479 (3)[20] and 1.250 (3) Å for the $N-C_{10}$ and $N{=}C_1$ bonds correspond to values for carbon–nitrogen single and double bonds, respectively. The C_1-C_2 bond length of 1.525 (4) Å is essentially the value expected for an sp^2–sp^3 carbon–carbon single bond. Values of 1.430 (3) and 0.87 (3) Å for the C_2-O and $O-H_O$ bond lengths are typical x-ray values for single bonds from oxygen to carbon and hydrogen, respectively.[21]

Although the near (to within 0.03 Å) coplanarity of atoms C_{10}, N, C_1, H_1, and C_2 was anticipated from the presence of the $C_1{=}N$ double bond, the near (to within 0.11 Å) inclusion

Table VI. Bond Lengths in Crystalline *N-tert*-Butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine[a]

Type[b]	Bond length, Å	Type[b]	Bond length, Å	Type[b]	Bond length, Å
$O-C_2$	1.430 (3)	$C_{p1}-C_{p2}$	1.392 (4)	C_4-H_{41}	0.93 (3)
		$C_{p1}-C_{p6}$	1.391 (4)	C_4-H_{42}	0.98 (3)
$N-C_1$	1.250 (3)	$C_{p2}-C_{p3}$	1.378 (4)	C_4-H_{43}	0.98 (4)
		$C_{p3}-C_{p4}$	1.376 (5)	C_5-H_{51}	1.00 (3)
$N-C_{10}$	1.479 (3)	$C_{p4}-C_{p5}$	1.375 (5)	C_5-H_{52}	0.98 (4)
		$C_{p5}-C_{p6}$	1.386 (4)	C_5-H_{53}	0.99 (3)
C_1-C_2	1.525 (4)			C_6-H_{61}	0.98 (3)
C_2-C_{p1}	1.533 (4)	$O-H_O$	0.87 (3)	C_6-H_{62}	0.95 (3)
				C_6-H_{63}	0.98 (3)
C_2-C_3	1.569 (4)	C_1-H_1	0.98 (3)	C_7-H_{71}	0.94 (4)
C_3-C_4	1.525 (4)	$C_{p2}-H_{p2}$	0.95 (3)	C_7-H_{72}	1.02 (5)
C_3-C_5	1.537 (4)	$C_{p3}-H_{p3}$	0.96 (4)	C_7-H_{73}	1.03 (5)
C_3-C_6	1.526 (4)	$C_{p4}-H_{p4}$	0.92 (3)	C_8-H_{81}	0.96 (4)
$C_{10}-C_7$	1.531 (5)	$C_{p5}-H_{p5}$	0.96 (3)	C_8-H_{82}	1.04 (4)
$C_{10}-C_8$	1.515 (5)	$C_{p6}-H_{p6}$	0.97 (3)	C_8-H_{83}	0.96 (4)
$C_{10}-C_9$	1.516 (5)			C_9-H_{91}	0.95 (4)
				C_9-H_{92}	0.97 (4)
				C_9-H_{93}	1.05 (5)

[a] The number in parentheses following each entry is the estimated standard deviation in the last significant digit. [b] Atoms labeled in agreement with Figure 1. Each symbol for a hydrogen atom which is bonded to a carbon carries the same subscripts as the carbon atom to which it is bonded. In addition, methyl hydrogens carry a second (numerical) subscript to distinguish between hydrogens on the same carbon atom.

Table VII. Bond Angles for Nonhydrogen Atoms in Crystalline *N-tert*-Butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine[a]

Type[b]	Bond angle, deg	Type[b]	Bond angle, deg
C_1NC_{10}	122.4 (2)	OC_2C_3	108.0 (2)
NC_1C_2	119.1 (2)	$C_3C_2C_{p1}$	113.1 (2)
$C_2C_{p1}C_{p2}$	119.6 (2)	$C_2C_3C_4$	109.1 (2)
$C_2C_{p1}C_{p6}$	122.5 (2)	$C_2C_3C_5$	109.4 (2)
$C_{p2}C_{p1}C_{p6}$	117.9 (3)	$C_2C_3C_6$	111.6 (2)
$C_{p1}C_{p2}C_{p3}$	120.8 (3)	$C_4C_3C_5$	108.6 (3)
$C_{p2}C_{p3}C_{p4}$	120.6 (3)	$C_4C_3C_6$	109.6 (3)
$C_{p3}C_{p4}C_{p5}$	119.5 (3)	$C_5C_3C_6$	108.6 (3)
$C_{p4}C_{p5}C_{p6}$	120.1 (3)	$NC_{10}C_7$	104.7 (3)
$C_{p5}C_{p6}C_{p1}$	121.0 (3)	$NC_{10}C_8$	114.9 (3)
		$NC_{10}C_9$	105.4 (3)
C_1C_2O	107.6 (2)	$C_7C_{10}C_8$	110.2 (3)
$C_1C_2C_3$	110.1 (2)	$C_7C_{10}C_9$	110.4 (3)
$C_1C_2C_{p1}$	109.5 (2)	$C_8C_{10}C_9$	110.9 (3)
OC_2C_{p1}	108.5 (2)		

[a] The number in parentheses following each entry is the estimated standard deviation in the last significant digit. [b] Atoms labeled in agreement with Figure 1.

of atoms O and H_O in this five-atom mean plane was unexpected. However, with atoms C_2 and C_{10} occupying trans positions relative to the $C_1{=}N$ double bond, appropriate rotations about the C_1-C_2 and C_2-O single bonds can give the hydroxyl group a favorable orientation for forming an *intramolecular* hydrogen bond between atoms O and N. Atoms N, C_1, C_2, O, and H_O are coplanar to within 0.01 Å and form a five-membered ring which contains a $O-H_O\cdots N$ hydrogen bond. The 2.579 (3) Å $O\cdots N$ and 1.96 (3) Å $N\cdots H_O$ separations are shorter than their van der Waal's contact values[22] by 0.32 and 0.74 Å, respectively.

The six independent sp^2-sp^2 phenyl carbon–carbon bonds have an average length of 1.383 (4, 7, 9) Å[20] while the 24 independent C–H bonds average 0.98 (4, 2, 7) Å.[20] The 0.44 (4) Å elongation of the C_2-C_3 bond relative to the other six sp^3-sp^3 C–C single bonds which average 1.525 (5, 6, 12) Å[20] is presumably the result of steric crowding within the molecule. Crowding between the phenyl ring and the *tert*-butyl group attached to C_2 is reflected in a 3.6 (2)° opening of the $C_3-C_2-C_{p1}$ bond angle from the idealized tetrahedral value of 109.5°.

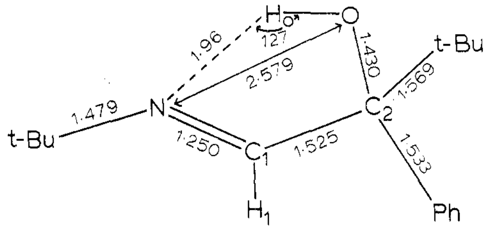


Figure 2. Diagram showing the primary structural features for the planar five-membered ring which contains the intramolecular hydrogen bond in the *N-tert*-butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine molecule.

Intramolecular (solid-state) crowding is also evidenced by short contacts involving the two hydrogen atoms of the phenyl group that are ortho to the $C_{p1}-C_2$ bond. Distances of 2.21 (4) and 2.35 (3) Å for the $H_{p6}\cdots H_1$ and $H_{p2}\cdots O$ contacts, respectively, are 0.19 and 0.25 Å shorter than the corresponding van der Waal's contact distances.[22]

Experimental Section

The methyl iodide Grignard reagent was prepared in the usual manner using oven-dried Vitro Clear-Seal glassware, flame-dried magnesium (Ventron, 99.9999%; or Research Organic/Inorganic Chemical Co., 99.95%) and a nitrogen atmosphere. Phenyl bromide Grignard reagent was prepared in the same manner using the 99.95% magnesium. Dimethylmagnesium was prepared from dimethylmercury (Ventron) according to the published procedure.[23] Commercial methyl bromide Grignard reagent (Ventron, 3.0 M in ether or 3 M in di-*n*-butyl ether), methyl chloride Grignard reagent (Ventron, 3.2 M in tetrahydrofuran), and methyllithium (Research Organic/Inorganic, 1.7 M in ether, halide free) were diluted with dry solvent before use. Phenyllithium was prepared in the usual manner from bromobenzene.

Analyses were by Micro-Tech Laboratories, Inc., Skokie, Ill. ^1H NMR spectra were determined using a Varian A-60D spectrometer, and ^{13}C NMR spectra using a Varian XL-100 spectrometer in the FT mode. Ir spectra were determined with a Perkin-Elmer 237 or 621 spectrometer. All melting and boiling points are uncorrected.

General Reaction Procedure. The following procedure was used for most of the experiments reported.

To the chosen quantity of a solution of the organometallic reagent a solution of 2.4 mmol of 1,3-di-*tert*-butylaziridinone[23] (**1c**) or a solution or suspension of 2.4 mmol of *N-tert*-butyl-2-bromo-3,3-dimethylbutanamide[24] (**2c**, X = Br) in anhydrous ether (or tetrahydrofuran) was added dropwise at the desired temperature under a nitrogen atmosphere. The volume of solvent was such that the concentration of organometallic reagent was 0.1–0.5 M (average, 0.3 M) after addition of the substrate. The concentration of α-lactam **1c** solution was 0.1–0.7 M (average 0.3 M) before addition; the concentration of the **2c** (X = Br) solution was 0.02–0.1 M (average 0.06 M) and of the **2c** (X = Br) suspension was 0.1–0.3 M (average 0.2 M). When addition was complete, the reaction mixture was stirred for an additional 3–30 h at room temperature or as specified in Tables I and II. Saturated aqueous ammonium chloride was added slowly with stirring. The layers were separated, the ethereal layer was washed with additional aqueous ammonium chloride, and the aqueous layers were extracted with ether. The combined ether layers were dried ($MgSO_4$), and the ether was evaporated. In general all crude reaction mixtures were soluble in $CDCl_3$ but some were only partially soluble in CCl_4 [the α-halo amides (**2c**) and the "dimer" **7c** being least soluble in the latter]. The ^1H NMR spectra of the soluble portion of all crude reaction mixtures were run in both solvents, as this procedure was found to facilitate analysis of the mixtures. Liquid residues were separated and purified by distillation under vacuum, and solid residues were separated and purified by extraction followed by repeated recrystallizations from appropriate solvents, or occasionally by column chromatography using a Florisil column and 0–15% solutions of ethyl acetate in Skellysolve B as eluent. The results of typical experiments

Table VIII. Bond Angles Involving Hydrogen Atoms in Crystalline *N*-*tert*-Butyl-2-hydroxy-3,3-dimethyl-2-phenylbutanimine[a]

Type[b]	Bond angle, deg	Type[b]	Bond angle, deg	Type[b]	Bond angle, deg
C_2OH_0	104 (2)	$C_3C_4H_{43}$	109 (2)	$C_{10}C_7H_{72}$	105 (3)
		$H_{41}C_4H_{42}$	112 (3)	$C_{10}C_7H_{73}$	110 (3)
NC_1H_1	125 (2)	$H_{41}C_4H_{43}$	109 (3)	$H_{71}C_7H_{72}$	108 (3)
$C_2C_1H_1$	116 (2)	$H_{42}C_4H_{43}$	107 (3)	$H_{71}C_7H_{73}$	110 (4)
$C_{p1}C_{p2}H_{p2}$	115 (2)	$C_3C_5H_{51}$	110 (2)	$H_{72}C_7H_{73}$	116 (4)
$C_{p3}C_{p2}H_{p2}$	124 (2)	$C_3C_5H_{52}$	109 (2)	$C_{10}C_8H_{81}$	109 (2)
$C_{p2}C_{p3}H_{p3}$	118 (2)	$C_3C_5H_{53}$	110 (2)	$C_{10}C_8H_{82}$	112 (2)
$C_{p4}C_{p3}H_{p3}$	121 (2)	$H_{51}C_5H_{52}$	106 (3)	$C_{10}C_8H_{83}$	111 (2)
$C_{p3}C_{p4}H_{p4}$	120 (2)	$H_{51}C_5H_{53}$	107 (3)	$H_{81}C_8H_{82}$	107 (3)
$C_{p5}C_{p4}H_{p4}$	121 (2)	$H_{52}C_5H_{53}$	116 (3)	$H_{81}C_8H_{83}$	114 (3)
$C_{p4}C_{p5}H_{p5}$	122 (2)	$C_3C_6H_{61}$	111 (2)	$H_{82}C_8H_{83}$	104 (3)
$C_{p6}C_{p5}H_{p5}$	118 (2)	$C_3C_6H_{62}$	113 (2)	$C_{10}C_9H_{91}$	106 (2)
$C_{p5}C_{p6}H_{p6}$	121 (2)	$C_3C_6H_{63}$	109 (2)	$C_{10}C_9H_{92}$	103 (3)
$C_{p1}C_{p6}H_{p6}$	119 (2)	$H_{61}C_6H_{62}$	103 (3)	$C_{10}C_9H_{93}$	107 (3)
		$H_{61}C_6H_{63}$	105 (3)	$H_{91}C_9H_{92}$	108 (4)
$C_3C_4H_{41}$	110 (2)	$H_{62}C_6H_{63}$	116 (3)	$H_{91}C_9H_{93}$	111 (4)
$C_3C_4H_{42}$	111 (2)	$C_{10}C_7H_{71}$	107 (2)	$H_{92}C_9H_{93}$	121 (4)

[a] The number in parentheses following each entry is the estimated standard deviation in the last significant digit. [b] Atoms labeled in agreement with Figure 1. Each symbol for a hydrogen atom which is bonded to a carbon carries the same subscripts as the carbon atom to which it is bonded. In addition, methyl hydrogens carry a second (numerical) subscript to distinguish between hydrogens on the same carbon atom.

Table IX. Properties of Reactants and Products[a]

				^{1}H NMR,[c] δ						Anal. calcd/found		
Registry no.	Compd	Mp, °C or bp, °C (Torr)	Ir,[b] cm^{-1}	Solvent	*t*-Bu-C	*t*-Bu-N	CH or CH_2	NH or OH[d]	Ph or Me	C	H	N
14387-89-4	**1c**	38 (0.4)[e]	1850	$CDCl_3$	1.002	1.303	2.73					
				CCl_4	0.987	1.265	2.62					
14387-96-3	**2c** (X = Br)	157–157.5[f,g]	3410;	$CDCl_3$	1.150	1.372	4.03	5.97				
			1665	CCl_4	1.122	1.340	3.96					
60294-83-9	**2c** (X = Cl)	130.5–132[f]	3410;	$CDCl_3$	1.11	1.37	3.99	6.08		58.38	9.80	6.81
			1665	CCl_4	1.08	1.34	3.90			58.00	9.75	6.65
30340-20-6	**2c** (X = I)	171.5–173[h,i]	3415;	$CDCl_3$	1.18	1.35	4.04	5.65				
			1666	CCl_4		1.34						
60294-84-0	**3cw**	49 (1.4)	3320;	$CDCl_3$	0.927	0.990	3.07	1.81	2.24	71.30	12.51	7.56
			1703	CCl_4	0.890	0.970	2.97	1.77	2.16	71.11	12.62	7.32
60294-85-1	**3cz**	98–99.5[j]	3324;	$CDCl_3$	0.880	1.007	4.04	2.11	[k]	77.68	10.19	5.66
			1671	CCl_4	0.867	1.015	3.97	2.09	[l]	77.59	10.12	5.49
60294-86-2	**4cw**	27 (0.4)	3350;	$CDCl_3$	0.937	1.208	7.74	4.77	1.198	71.30	12.51	7.56
			1665	CCl_4	0.895	1.202	7.71	4.33	1.110	71.35	12.77	7.37
60294-87-3	**4cz**	70–71[m]	3300;	$CDCl_3$	0.933	1.223	8.39	5.45	[n]	77.68	10.19	5.66
			1665	CCl_4	0.902	1.220	8.36	5.05	[o]	77.52	10.33	5.49
60319-04-2	**7c**	239–240[a,m,p]	3450,	$CDCl_3$	1.063	1.357	2.21	5.27		70.54	11.84	8.23
			1665	CCl_4	1.012	1.333	2.05			70.58	11.87	8.14
49633-54-7	**8c**	123.5–125.5[h]	3430;	$CDCl_3$	1.033	1.352	1.953	5.57		70.12	12.36	8.18
			1660	CCl_4	0.998	1.308	1.848	5.61		70.02	12.45	7.98
30340-21-7	**9cw**	138–140.5	3440;	$CDCl_3$	0.968	1.352	1.80[q]	5.21	1.073[r]			
			1670	CCl_4	0.928	1.308	1.82[q]	5.11	1.020[r]			
60294-88-4	**9cz**	147.5–149[s]	3450,	$CDCl_3$	1.022	1.303	2.90	5.30	7.32[t]	77.68	10.19	5.66
			1673	CCl_4	0.978	1.270	2.78	5.10	7.28[t]	77.51	10.22	5.58

[a] Satisfactory analytical data (±0.4%) for C, H, N were obtained for all new compounds in this table except **7c**, which was obtained as a mixture of diastereomers essentially free of other products (based on ^{1}H NMR analysis). The structure of **7c** was established by an x-ray crystallographic analysis (to be published elsewhere) of single crystals selected by hand from this mixture. The spectral and other data given in the table are for the mixture. [b] In $CHCl_3$. [c] See Experimental Section for procedures used. [d] Position variable; average valve is given. [e] Lit.[17] bp 38°C (0.4 Torr). [f] Recrystallized from petroleum ether (bp 30–60°C). [g] Lit.[17] mp 156–157 °C. [h] Purified by sublimation. [i] Lit.[4a] mp 168–170 °C. [j] Recrystallized from methanol. [k] Phenyl region similar in appearance to phenyl region of acetophenone with two clusters of peaks of 475–486 and 437–457 Hz at 60 MHz. [l] Phenyl region similar in appearance to that of acetophenone with two clusters of peaks at 470–485 and 443–456 Hz at 60 MHz. [m] Recrystallized from methanol–pentane. [n] Complex multiplet at 431–460 Hz at 60 MHz. [o] Complex multiplet at 427–455 Hz at 60 MHz. [p] An apparent diastereomer of **7c** (which was not isolated) showed the following NMR spectra: in $CDCl_3$, δ 1.078, 1.377, 2.17; in CCl_4, δ 1.325, 1.002, 2.03. [q] Quartet, *J* = 6.9 ± 0.1 Hz. [r] Doublet, *J* = 6.9 ± 0.1 Hz. [s] Lit.[4a] mp 147.5–148 °C. [t] Broad.

are summarized in Tables I and II, and the properties of the purified starting materials and products are given in Tables IX and X.

General Analytical Procedure. The ^{1}H NMR chemical shifts in the region 0–100 Hz (at 60 MHz) of purified reactants and products were determined as precisely as possible in both $CDCl_3$ and CCl_4 using Me_4Si and cyclohexane as internal standards (sweep width 100 Hz, sweep time 250 s). The values obtained are given in Table IX and are based on cyclohexane, δ 1.436 in both CCl_4[25] and $CDCl_3$.[26] For approximately 100 measurements (covering all compounds) the average deviation was ±0.1 Hz and the maximum deviation was ±0.3 Hz from the values given. Fortuitously there was little overlap of peaks in this region among the various reactants and products; therefore, identification of products was relatively easy.[27] Usually the entire crude reaction mixture was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR.

Table X. ^{13}C NMR Spectra[a] and Probable Assignments

Compd	C=O or C=N	α-C	$(CH_3)_3CN$	$(CH_3)_3CN$	$(CH_3)_3CC$	$(CH_3)_3CC$	CH_3-α-C	Phenyl C_1	Phenyl C_2	Phenyl C_3	Phenyl C_4
1c	161.07	54.17	55.99	27.78	31.31	27.14					
3cz	172.66	62.02	50.40	30.16	35.28	27.34		138.21	128.49	128.14	132.66
4cw	160.48	75.28	56.15	29.64	37.30	25.40	20.87				
4cz	159.13	77.94	56.55	29.64	38.77	25.56		142.62	126.31	127.14	127.06
8c	170.95	30.75	50.87	29.29	29.80	28.77					

[a] Determined in $CDCl_3$. The chemical shifts are given in parts per million downfield from internal Me_4Si.

The solvent was evaporated, and as much of the residue as possible was dissolved in CCl_4 and analyzed by ^1H NMR. The composition of the reaction mixtures was estimated on the basis of the machine integrals and, wherever possible, through use of a polar planimeter. Because of difficulties encountered due to overlap of the bases of some peaks, the results are considered to be no more accurate than ±10% (relative) for the larger percentages (<40%) and up to ±30% for the smaller values (<10%). The most approximate analysis was that of the **7c** diastereomers, which frequently gave broad peaks that overlapped those of **8c** sufficiently to make accurate analysis of **7c** difficult. In some experiments unidentifiable singlet peaks appeared in the 50-100-Hz region. These were summed and treated as if they were caused by *tert*-butyl groups (the most likely origin based on evaluation of the downfield portion of the spectrum) and are reported as "Other Substances". The results of the analyses are given in Tables I and II.

Isomerization of 4cw. A small amount of **4cw** (about 0.5 g) was heated under reflux in an oil bath held at 150 ± 2 °C. Periodically a sample of material was removed and analyzed by ^1H NMR spectroscopy. In one experiment a solution of **4cw** in a fivefold volume of toluene was heated under reflux and periodically analyzed in the same manner. The results are given in Table II.

Isomerization of 4cz. The first isomerization was unintentional and occurred when a reaction residue (from which most of the **7c** and much of the **4cz** had been removed by fractional extraction) was allowed to stand on the steam bath over the weekend, during which time the flask became filled with long, slender, needlelike crystals. ^1H NMR analysis of these indicated them to be essentially pure **3cz**. Since other materials were present in the residue, they could have had some effect on the rate of isomerization; therefore, 80–200-mg samples of purified **4cz** were heated at selected temperatures on the steam bath or in the oven in a lightly stoppered flask for 18–96 h. The contents of the flasks were analyzed by ^1H NMR. The results are given in Table I.

Isomerization of 3cz. The isomerization of **3cz** and the analysis of the resultant crude reaction mixture were conducted by the general reaction and analytical procedures described above for the reactions of **1c** and **2c** with organometallic reagents. The results are given in Table I.

Crystallographic Analysis of 4cz.[19] Single crystals (mp 70–71 °C) of $C_{16}H_{25}ON$, **4cz**, suitable for x-ray studies were obtained by crystallization from a methanol–pentane solution. They are monoclinic, space group $P2_1/c$-$C_{2h}{}^5$ (no. 14)[28] with $a = 13.938 \pm 0.002$ Å, $b = 6.141 \pm 0.001$ Å, $c = 18.793 \pm 0.002$ Å, $\beta = 104.42 \pm 0.01°$, and $Z = 4$ at 20 ± 1 °C [$d_{\text{calcd}} = 1.055$ g cm^{-3}, $d_{\text{measd}} = 1.044$ g cm^{-3}, μ_a (Mo $K\bar{\alpha}$)[29] = 0.07 mm^{-1}]. Intensity measurements were made on a Syntex $P\bar{1}$ Autodiffractometer for a nearly cube-shaped specimen (0.44 × 0.44 × 0.50 mm) which was sealed under nitrogen gas in a thin-walled glass capillary. A total of 3558 independent reflections having $2\theta_{\text{Mo}K\bar{\alpha}} < 55°$ (the equivalent of 1.0 limiting Cu $K\bar{\alpha}$ sphere) were collected using 1°-wide ω scans and graphite-monochromated Mo $K\bar{\alpha}$ radiation. A scanning rate of 2°/min was employed for the scan between ω settings 0.50° respectively above and below the calculated $K\bar{\alpha}$ doublet value ($\lambda_{K\bar{\alpha}} = 0.71069$ Å). Each 1° scan was divided into 19 equal (time) intervals and those 13 contiguous intervals which had the highest single accumulated count at their midpoint were used to calculate the net intensity from scanning. Background counts, each lasting for one-fourth the total time used for the net scan (13/19 of the total scan time), were measured at ω settings one degree above and below the calculated $K\bar{\alpha}$ doublet value for each reflection. The data were not corrected for absorption since the absorption of x-rays by a spherical crystal having the same volume as the crystal actually used would be virtually independent of scattering angle[30] ($\mu r = 0.02$) and deviations from this absorption occasioned by the use of the nearly cube-shaped specimen are practically negligible.

The 18 nonhydrogen atoms comprising the asymmetric unit appeared simultaneously on an E map which was calculated from a trial set of statistical direct methods (MULTAN) phases. All 25 chemically anticipated hydrogen atoms were located from a difference Fourier synthesis calculated from a full-matrix least-squares refined structural model [R(unweighted) = 0.102, r(weighted) = 0.112 for 1248 reflections having $2\theta_{\text{Mo}K\bar{\alpha}} < 43°$ and $I < 3\sigma(I)$] which incorporated unit weighting and anisotropic thermal parameters for all nonhydrogen atoms. All structure factor calculations employed the atomic form factors compiled by Cromer and Mann[31] and a least-squares refineable extinction correction[32] of the form $1/(1 + gI_c)^{1/2}$. The final cycles of empirically weighted full-matrix least-squares refinement which employed isotropic thermal parameters for hydrogen atoms and anisotropic thermal parameters for all others converged to values of 0.044 and 0.048 for R and r, respectively, for 1621 independent reflections having $2\theta_{\text{Mo}K\bar{\alpha}} < 55°$ and $I > 3\sigma(I)$.

Acknowledgments. This work was supported in part by Grants GP-4915 and GP-28261 from the National Science Foundation to H.E.B. and from the donors of the Petroleum Research Fund, administered by the American Chemical Society, to V.W.D. and by a generous grant of computation time from the University of Nebraska Computing Center.

Registry No.—**7c** diastereomer, 60294-89-5; PhBr, 108-86-1; PhLi, 591-51-5; MeCl, 74-87-3; MeI, 74-88-4; MeBr, 74-83-9; Me_2Mg, 2999-74-8; MeLi, 917-54-4; $MgBr_2$, 7789-48-2.

Supplementary Material Available. Tables III–V, a detailed description of the experimental conditions for the crystallographic study and a listing of observed and calculated structure factor amplitudes (15 pages). Ordering information is given on any current masthead page.

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(12) This point is best seen by careful examination of the Experimental Sections of the several papers by Stevens and co-workers listed in ref 11.

(13) Single crystals of dimer **7c** are monoclinic, space group $P2_1/n$ (an alternate setting of $P2_1/n$-$C_{2h}{}^5$), with $a = 13.479$ (1) Å, $b = 5.8751$ (7) Å, $c = 13.562$ (1) Å, $\beta = 102.488$ (8)°, and $Z = 2$ (dimers). The structure was solved using direct methods and the resulting structural parameters for the 32 crystallographically independent hydrogen and nonhydrogen atoms have been refined to convergence [$R = 0.039$ for 1668 independent, diffractometer-recorded (graphite-monochromated Mo $K\bar{\alpha}$ radiation with 1°-wide

ω scans) reflections having $2\theta_{\mathrm{MoK}\bar{\alpha}} < 55°$ and $I > 3\sigma(I)$] in cycles of empirically weighted least-squares refinement. Anisotropic thermal parameters were utilized for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. The estimated standard deviations for covalent bond lengths are 0.002–0.003 Å for bonds between two nonhydrogen atoms and 0.02–0.03 Å for bonds between a hydrogen and nonhydrogen atom. Full structural details will be published elsewhere.

(14) The coupling and cross-coupling reactions of alkyl halides and Grignard reagents (sometimes called Kharasch couplings) have been the subject of considerable study during the past 10 years. A recent review of much of this chemistry with leading references to other aspects is (a) H. Felkin and G. Swierczewski, *Tetrahedron,* **31,** 2735 (1975). Additional pertinent references are (b) Y. Ohbe and T. Matsuda, *Nippon Kagaku Zasshi,* **89,** 298 (1968) [*Chem. Abstr.,* **69,** 51309q (1968)]; (c) Y. Ohbe and T. Matsuda, *Bull. Chem. Soc. Jpn.,* **45,** 2947 (1972); (d) Y. Ohbe and T. Matsuda, *Tetrahedron,* **29,** 2989 (1973); (e) Y. Ohbe, M. Takagi, and T. Matsuda, *ibid.,* **30,** 2669 (1974); (f) M. Mori, S. Nishimura, and Y. Ban, *Tetrahedron Lett.,* 4951 (1973).

(15) Talaty et al.[4] reported that the ^{1}H NMR spectrum of their crude product showed the presence of two substances, **2c** (X = I) being by far the more abundant. The second product was not identified.

(16) The question remains as to the probable identity of the well-characterized Sheehan–Nafissi-V product. Our experimental observations lead us to conclude that the product may have been an impure sample of the reduction product **8c**, possibly contaminated with **9cw** and the diastereomers of the dimeric coupling product **7c**. The contaminants are required to explain the observed ^{1}H NMR spectrum, elemental analysis, and mass spectrum.

(17) The first preparation of an authentic α-lactam [H. E. Baumgarten, *J. Am. Chem. Soc.,* **84,** 4975 (1962)] involved the cyclization of an *N*-chloro amide with potassium *tert*-butoxide as base. The choice of base was deliberate, based on sound experimental analogies. Later the same base was used in the first successful preparation of an α-lactam through cyclization of an α-chloro amide [H. E. Baumgarten, J. J. Fuerholzer, R. D. Clark, and R. D. Thompson, *J. Am. Chem. Soc.,* **85,** 3303 (1963)]. Here, however, the choice of base was less critical and other bases could have been used (with the appropriate laboratory technique). Most other workers have elected to follow our lead in the choice of base. However, we have experimented with other bases. In fact, one can use (with care) powdered KOH (in THF) to prepare certain α-lactams by cyclization of α-halo amides, but this is *not* recommended. Various Grignard and organolithium reagents were among the bases studied for such cyclizations, and we were able to observe (using ir techniques) but not to prepare α-lactams using these bases. Thus, in two experiments with **2c** (X = Br) and the methyl chloride Grignard reagent (in dilute solution) we did observe the appropriate ^{1}H NMR peaks for **1c** in both $CDCl_3$ and CCl_4. The amount of this product (if it were **1c**) was such (2.5–5%) as to preclude the use of this base for preparative purposes; however, our observation does suggest that, in the devising of mechanistic pathways for the reactions of α-halo amides with bases, one should consider α-lactam-like intermediates. One example where such an intermediate is a reasonable alternative may be found in ref 14f.

(18) A referee has suggested that the results with the methyl halide Grignard reagents which show yields of **4cw** in the order I < Br < Cl (and the high yield of **4cw** with dimethylmagnesium) may be indicative of a single electron transfer mechanism. He suggests further that the effect of ferric chloride may also indicate a SET mechanism and wonders what the reaction with the *tert*-butyl chloride Grignard reaction might reveal. These reasonable suggestions are not new to us; however, we believe that any detailed mechanisms for these reactions will require evidence well beyond what is available to us since small changes in structure seem to have a substantial effect on heterolytic vs. SET mechanisms in the addition of organometallic reagents to the carbonyl group [cf. E. C. Ashby, J. Laemmle, and H. M. Neumann, *Acc. Chem. Res.,* **7,** 272 (1974); T. Holm and I. Crossland, *Acta Chem. Scand.,* **25,** 59 (1971)]. Furthermore, some metal-catalyzed Kharasch-type couplings go by SET mechanisms; others do not.[14] In 1967 we carried out a single experiment in which **1a** was treated with 2 equiv of the *tert*-butyl chloride Grignard reagent. The isolated and purified product in 72% yield was **2c** (X = Cl). Recent experiments on 1-*tert*-butyl-2-phenylaziridinone with this reagent have given similar results, a high yield of the α-chloro amide plus a complex mixture of other products that are still under investigation. In experiments in progress both **1a** and **2a** have reacted with the dimethyllithium cuprate to give high yields (73–83%) of **9cw** together with small amounts of **8c**, but no **4cw**. This reaction is generally regarded as not proceeding by an SET mechanism [cf. H. O. House, *Acc. Chem. Res.,* **9,** 59 (1976)]. On the other hand, some α-lactams *do* appear to react with organometallic reagents preferentially by a SET mechanism, especially 1-*tert*-butyl-3,3-diphenylaziridinone.[9]

(19) See paragraph at end of paper regarding supplementary material.

(20) The first number in parentheses following a given bond length or angle is the root mean square estimated standard deviation of an individual datum. The second and third numbers, when included, are the average and maximum deviations from the average value, respectively.

(21) "International Tables for X-Ray Crystallography", Vol. III, "Physical and Chemical Tables", Kynoch Press, Birmingham, England, 1968, p 276.

(22) L. Pauling, "The Nature of the Chemical Bond", 3d ed, Cornell University Press, Ithaca, N.Y., 1960, p 260.

(23) E. C. Ashby and R. C. Arnot, *J. Organomet. Chem.,* **14,** 1 (1968).

(24) J. C. Sheehan and J. H. Beeson, *J. Am. Chem. Soc.,* **89,** 362 (1967).

(25) G. W. Tiers, *J. Phys. Chem.,* **62,** 1151 (1958).

(26) P. Laszlo, *Prog. Nucl. Magn. Reson. Spectrosc.,* **3,** 241 (1967).

(27) With this procedure the detection of as little as 1% of any product with the possible exception under certain conditions of **7c** and **3cw** was possible.

(28) "International Tables for X-Ray Crystallography", Vol. I, "Symmetry Groups", Kynoch Press, Birmingham, England, 1969, p 99.

(29) Reference 21, p 166.

(30) "International Tables for X-Ray Crystallography", Vol. II, "Mathematical Tables", Kynoch Press, Birmingham, England, 1967, p 302.

(31) D. T. Cromer and J. B. Mann, *Acta Crystallogr., Sect. A,* **24,** 321 (1968).

(32) W. H. Zachariasen, *Acta Crystallogr.,* **23,** 558 (1967).

Reactions of Amines. 20. Syntheses of Racemic and Optically Active Alkylhydrazines and *N*-Acyl-*N*-alkyl- and *N*-Acyl-*N*-arylhydrazines[1,2]

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Received May 25, 1976

N-Acyl-*N*-alkyl- (**11**) and *N*-acyl-*N*-arylhydrazines (**5**) may be prepared by acylation of *N*-alkyl- (**9**) and *N*-aryl-*N*′-carbo-*tert*-butoxyhydrazines (**3**) followed by cleavage of the *N*′-carbo-*tert*-butoxy group. The intermediate **3** may be prepared by treatment of arylhydrazines with *tert*-butyl azidoformate (**2**). The intermediates **9** may be prepared by reduction of the corresponding ketone carbo-*tert*-butoxyhydrazones (**8**) or by the rearrangement [presumably via the diaziridinone (**17**)] of alkylureas (**15**). Cleavage of **9** prepared by the latter route has been used for the stereospecific synthesis of (*R*)-1-phenylethylhydrazine (**19a**) from (*R*)-1-phenylethylamine (**13a**) (via the urea **15a**).

Recently Moss and Powell[3] reported a new synthesis of hydrazines from alkyl diazotates that is sufficiently stereoselective to convert 1-phenylethylamine (**13a**) into 1-phenylethylhydrazine (**19a**) in 40% yield (as the oxalate) with a reported 54% net inversion of configuration. Like Moss and his coworkers, we have had a need for a simple, useful synthesis of optically active hydrazines but have found that most of the previously reported procedures[4,5] are deficient for our purpose in one respect or another. In addition we have required monosubstituted hydrazines with a *tert*-alkyl substituent and monosubstituted hydrazines acylated on the nonterminal nitrogen (i.e., *N*-aminoamides). This communication describes the procedures we are currently using for the synthesis of these several types of hydrazine derivatives. For this purpose the preparation of *N*-benzoyl-*N*-phenylhydrazine (**5**), several *N*-acyl-*N*-alkylhydrazines (**11**), racemic and optically active 1-phenylethylhydrazine (**19a**), *tert*-butylhydrazine (**22**), and related substances will be described.