Table III
Rates of Racemization of (+)-2,2-Diphenylcyclopropylnitrile with Sodium Methoxide

Solvent (v/v)	Nitrile concn, *M*	Base concn, *M*	*T*, °C[a]	k_2,[b] l. mol^{-1} sec^{-1} [c]
CH_3OH	0.011	0.95	75.7	$3.8 \pm 0.02 \times 10^{-7}$
CH_3OH[d]		0.97	92.59	$3.3 \pm 0.05 \times 10^{-6}$
50% CH_3OH–50% DMSO	0.017	0.48	50.0	$1.1 \pm 0.02 \times 10^{-6}$
40% CH_3OH–60% DMSO	0.012	0.078	50.0	$3.2 \pm 0.03 \times 10^{-6}$
25% CH_3OH–75% DMSO	0.013	0.078	50.0	$4.8 \pm 0.07 \times 10^{-5}$
25% CH_3OH–75% DMSO	0.019	0.077	75.7	$9.2 \pm 0.15 \times 10^{-4}$
15% CH_3OH–85% DMSO	0.014	0.11	50.0	$7.1 \pm 0.08 \times 10^{-4}$
10% CH_3OH–90% DMSO	0.012	0.028	50.0	$2.1 \pm 0.07 \times 10^{-3}$
10% CH_3OH–90% DMSO	0.027	0.087	30.0	$1.8 \pm 0.02 \times 10^{-4}$
5% CH_3OH–95% DMSO	0.016	0.073	30.0	$2.1 \pm 0.03 \times 10^{-3}$
5% CH_3OH–95% DMSO	0.015	0.021	50.0	$1.3 \pm 0.03 \times 10^{-2}$
1% CH_3OH–99% DMSO	0.016	0.016	30.0	$9.4 \pm 0.16 \times 10^{-2}$

[a] Temperatures are maintained within ±0.05° and checked against a calibrated thermometer. [b] $k_2 = k_0$. [c] The rate constants were calculated by the method of least squares. [d] Data from ref 1.

metallic sodium to anhydrous methanol in an atmosphere of purified nitrogen in a measuring flask. Solutions of the sodium methoxide in methanol–dimethyl sulfoxide mixtures were prepared using automatic burets to deliver the proper volume of methanol and DMSO.

For measurements conducted at 50° or below a jacketed 2-dm polarimeter tube thermostated by circulating water from a constant temperature bath was used. The reaction medium in a volumetric flask was equilibrated, the nitrile was added and the solution thoroughly mixed and transferred rapidly to the thermostated polarimeter tube, and readings were started immediately. A suitable time intervals readings were taken and recorded. The average of six readings each time was recorded which showed a maximum deviation of ±0.02°. A sealed ampoule technique was quite useful for rate measurements at temperatures above 50°. A "Bellingham and Stanley" model polarimeter was used in these measurements.

The rates were calculated by a simple graphic method and by using the equation for pseudo-first-order reactions

$$k_{obsd} = 2.303/t \log (a_0 - a_\infty)/(a_t - a_\infty)$$

where a_0 is the polarimetric reading at zero time, a_∞ is the reading at infinity reaction, and a_t is at time t. k_0, the bimolecular rate constant = k_{obsd}/base concentration.

Table III records the results of some typical kinetic runs that were mentioned in the text and used in the calculations of activation parameters.

Product Analysis. A 2-g sample of the nitrile was dissolved in methanol or a methanol–dimethyl sulfoxide mixture with a base concentration comparable to that used in kinetic runs. The solutions were sealed in tubes and placed in a bath at 50° for at least 10 half-lifes. The tubes were opened and the solvent was concentrated to a small volume. Addition of water precipitated quantitatively the racemic nitrile, which was washed and dried. The products, identified by melting point, mixture melting point, and ir spectra, were found to be identical in all respects with the racemic nitrile.

Acknowledgment. The authors are indebted to Professor H. M. Walborsky of the Florida State University for helpful discussions.

Registry No.—(+)-1, 51154-93-9.

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A Stable Iminoazetine from Diisobutene, Hydrogen Fluoride, and Hydrogen Cyanide. Its Thermal Dealkylation and Ring Expansion to an Imidazole

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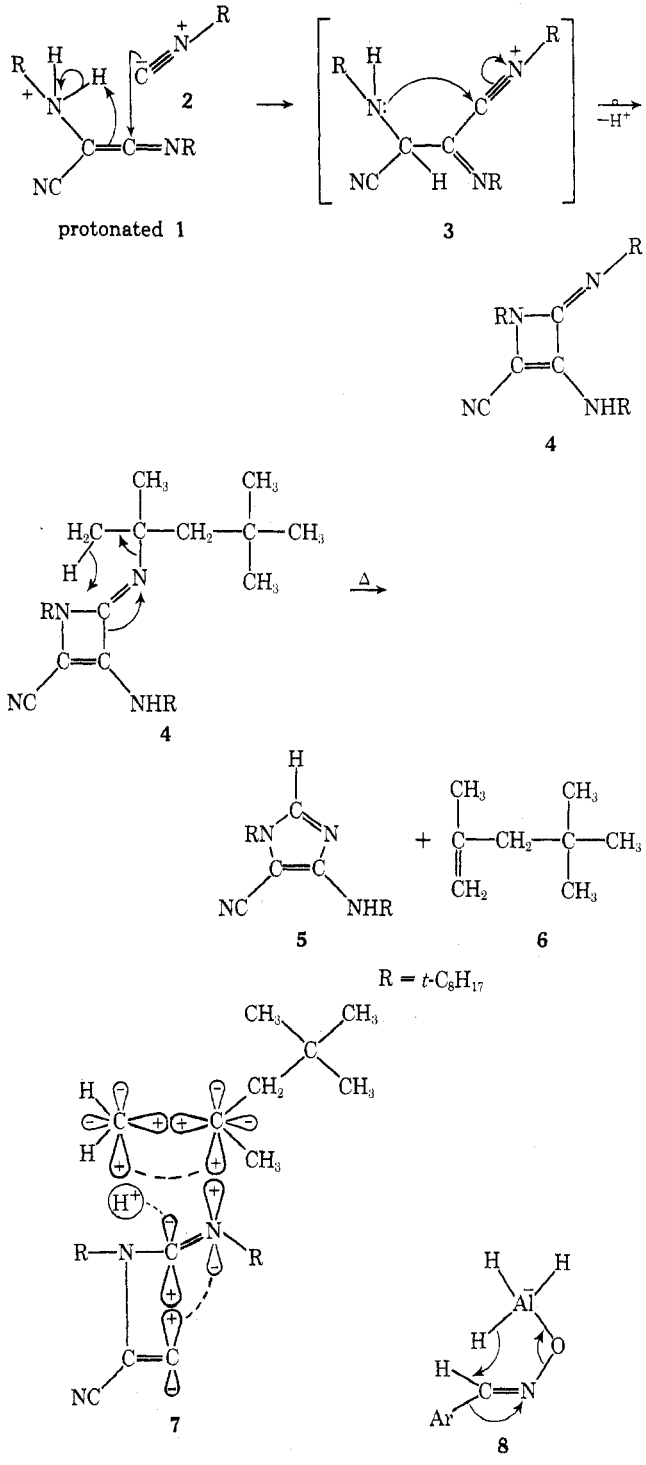
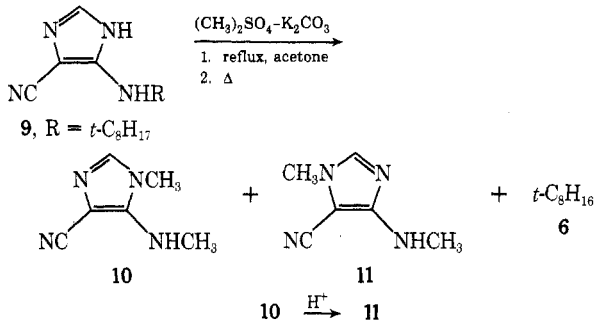
Under certain reaction and work-up conditions, the reaction of diisobutene with hydrogen fluoride and hydrogen cyanide yields a compound $C_{28}H_{52}N_4$ (**4**). Heating **4** in refluxing toluene causes expulsion of diisobutene to give a product $C_{20}H_{36}N_4$ (**5**). Spectral evidence and mechanistic considerations suggest that **4** is 1-*tert*-octyl-2-*tert*-octylimino-3-*tert*-octylamino-4-cyanoazetine and that **5** is 1-*tert*-octyl-4-*tert*-octylamino-5-cyanoimidazole. A symmetry-allowed [$_\sigma 2_s + {}_\sigma 2_a + {}_\sigma 2_a$] pericyclic mechanism is proposed.

A stable 2-imino-5-aminoazetine has apparently not been reported previously, but a few compounds have been described with the isomeric bis(imino)azetidine structure.[1]

Scheme I



Scheme II



However, 2-iminoazetines have recently been postulated as intermediates in the photochemical conversions of β-aminoacrylonitriles to imidazoles.[2] In the closely related photochemical conversion of diaminomaleonitrile to 4-amino-5-cyanoimidazole,[3] the proposed intermediate is 2-imino-3-amino-4-cyanoazetine, which is the analog of **4**, except for the *tert*-octyl substituents. In an earlier paper[4] it has been shown that the reaction of 2,4,4-trimethylpentene-2 (TMP) with hydrogen cyanide and hydrogen fluoride gives rise to several novel products. All of these, including the new iminoaminoazetine, have the general composition $(TMP)_n(HCN)_m$.

Results and Discussion

Under specific reaction and work-up conditions, the reaction of TMP with hydrogen cyanide and hydrogen fluoride gives rise to a previously unreported compound which is proposed to be 1-*tert*-octyl-2-*tert*-octylimino-3-*tert*-octylamino-4-cyanoazetine (**4**, Scheme I). This structure assignment is based on the following considerations. According to mass spectrum and elemental analysis, the composition of **4** is $C_{28}H_{52}N_4(TMP)_3(HCN)_4$. This formula implies the presence of three *tert*-octyl groups, each of which must be attached to a nitrogen atom according to the mechanistic considerations in ref 1. The nonequivalence of these three groups is evident from the nmr spectrum, which additionally shows a clear NH signal which disappears upon deuteration. The presence of an amino hydrogen is also confirmed by the ir spectrum. The ir and Raman spectra furthermore show a nitrile band, whose anomalously long wavelength (2150 cm^{-1}) is indicative of the presence of an enaminonitrile moiety.[4] Additional bands, shown in both ir and Raman spectra (1620, 1565 cm^{-1}), are consistent with a C=C-C=N moiety. The presence of such a conjugated system is confirmed by the uv spectrum. (See Experimental Section).

The formula of **4** is consistent with a product resulting from the addition of *tert*-octyl isocyanide (**2**, $C_9H_{17}N$) to *tert*-octylaminocyanoketen-*N*-*tert*-octylimine (**1**, $C_{19}H_{35}N_3$). Such a process seems reasonable because under the conditions described earlier[4] **2** is the basic building block and **1** is the most abundant product. Although the reaction of ketenimines with isonitriles under acidic conditions has apparently not been investigated, Deyrup, *et al.*,[1] report that, with acid catalysts, *N*-arylimines react with two molecules of *tert*-butyl isocyanide to give 2,3-bis(*tert*-butylimino)azetidines. These are related to 2-imino-3-aminoazetines by a tautomeric proton shift. A mechanism closely analogous to that suggested by Deyrup, *et al.*, can account for the formation of **4** (Scheme I). It is proposed that the immonium ion resulting from protonation of **1** on the imino nitrogen is attacked by the nucleophilic isocyanide carbon atom of **2** to give the nitrilium ion **3**. Intramolecular attack of the β-*tert*-octylamino group in **3** on the nitrilium carbon atom causes closure of the four-membered ring. Deprotonation gives a diiminoazetidine which rearranges to the aminoiminoazetine **4** through a 1,3 proton shift.

Compound **4** shows remarkable chemical inertness. This is possibly due to the steric crowding resulting from three bulky *tert*-octyl groups, attached to a rigid system. The iminoaminoazetine **4** resists catalytic hydrogenation at atmospheric pressure and room temperature. More severe conditions appear to cause degradation by a number of paths which are difficult to trace.

Compound **4** is quite stable to hydrolysis. It is unaffected by strong aqueous alkali, as is evident from the procedure used to separate **4** from the accompanying cyanoaminoimidazole **9** and from the diaminomaleonitrile **12**. (See Experimental Section.) At room temperature **4** also resists hydrolysis under acidic conditions.

Heating of **4** in the absence of a catalyst results in the loss of one *tert*-octyl group as 2,4,4-trimethylpentene-1 (**6**,

Table I
Spectra of 5 and 11

Uv max (MeOH), nm (ε × 10⁻³)		Ir (CHCl₃), cm⁻¹		Nmr (CDCl₃), δ, ppm	
5	11	5	11	5	11
284.0 (9.86)	275.5 (9.26)	3410 w	3435 m(NH)	7.08	7.12 (N=CH)
228.5 (5.05)	230.0 (4.53)	2180 s	2188 vs (C≡N)	3.88	4.12 (NH)
210.0 (~15.2)	210.0 (~15.2)	1565 vs	1585 vs (C=C-N=C)		

identified by glpc) and concomitant rearrangement to a new compound. Based on elemental analysis and spectral properties, this new compound is assigned the structure 1-*tert*-octyl-4-*tert*-octylamino-5-cyanoimidazole (**5**). The nmr spectrum exhibits resonances for two nonequivalent *tert*-octyl groups, one amino hydrogen, and a single-proton resonance at δ 7.08 in the region, characteristic for aromatic and heteroaromatic protons. This points to an imidazole moiety in **5**. For comparison, the heteroaromatic ring proton in the closely analogous 4-*tert*-octylamino-5-cyanoimidazole (**9**, Scheme II)[4] resonates at 7.12 ppm, and the corresponding signals for imidazole and 1-methylimidazole are located at 7.70 and 7.40 ppm.[5]

Convincing evidence for the proposed structure of **5** is provided by comparing its uv, ir, and Raman spectra with those of the model compound 1-methyl-4-methylamino-5-cyanoimidazole (**11**, Scheme II).[6] (See Table I.)

It is proposed that imidazole **5** is formed from azetine **4** by the concerted cyclic mechanism shown in Scheme I. This is a symmetry-allowed [$_{\sigma}2_s$ + $_{\sigma}2_a$ + $_{\sigma}2_a$] pericyclic process[7] (**7**, Scheme I). An essentially analogous mechanism has been suggested to explain the formation of secondary amines and the ring expansions which are common in the reduction of oximes by lithium aluminum hydride[8] (**8**, Scheme I).

Formation of **5** in high yield also occurs upon mild heating of a solution of **4** in acidic, aqueous tetrahydrofuran. It is suggested that the mechanism of the acid-catalyzed reaction—except for initial protonation of the imino nitrogen—resembles that proposed for the uncatalyzed thermal reaction.

Experimental Section

Materials. The 2,4,4-trimethylpentene-2 used was technical grade (95 mol % minimum) supplied by Phillips Petroleum Co. It was purified by treatment with $LiAlH_4$ in ether solution to reduce carbonyl-containing impurities followed by distillation through a spinning band column.

Hydrogen cyanide and hydrogen fluoride were obtained from Fumico, Inc., and The Matheson Co., respectively. 4-Cyano-5-*tert*-octylaminocyanoimidazole (**9**) was prepared according to ref 4.

1-*tert*-Octyl-2-*tert*-octylimino-3-*tert*-octylamino-4-cyanoazetine (4), Di-*tert*-octylaminomaleonitrile (12), and 4-Cyano-5-*tert*-octylaminoimidazole (9) from Hydrogen Cyanide, Hydrogen Fluoride, and 2,4,4-Trimethylpentene-2 (TMP). A polyethylene reactor with a polyethylene condenser and magnetic stirrer was charged with 150 g (1.34 mol) of TMP. The reactor was cooled to 0°, and the condenser was filled with ice. Then 54 g (78.4 ml, 2.00 mol) of hydrogen cyanide was introduced by distillation followed by 47.4 g (48 ml, 2.4 mol) of hydrogen fluoride. The reaction mixture was stirred at room temperature for 3 hr. Excess hydrogen cyanide and hydrogen fluoride were removed by sparging vigorously with nitrogen for 4 hr. Sparging was then stopped, the residue was rediluted with 100 ml of ether, and stirring at room temperature was continued for 16 hr. The ether solvent was then removed by sparging with nitrogen. Over an 8-min period, the yellow-brown residue was poured into a stirred, nitrogen-blanketed solution of 908 g of dipotassium hydrogen phosphate in 1000 ml of water which was kept at about 8° by means of an external ice bath. A 400-ml quantity of cold pentane was added, and, after stirring for an additional 30 sec, the aqueous layer was removed by means of a separatory funnel. The pentane layer contained suspended solids. It was filtered to yield a filtrate (A) and a precipitate. This precipitate was twice crystallized from hot benzene to yield a combined benzene mother liquor (B) and 17.8 g of straw-colored crystals of **4**, mp 163–163.5°. *Anal.* Calcd for $C_{26}H_{52}N_4$: C, 75.59; H, 11.81; N, 12.60. Found: C, 75.21; H, 11.69; N, 12.90. Mass spectrum (70 eV) *m/e* 444 (M^+); thermonam molecular weight 440; uv max (isooctane) 379, 264, 217 nm (ε × 10^{-3} 3.73, 8.21, 7.99); uv max (methanol) 360, 270, 210 nm (ε × 10^{-2} 1.02, 77.2, 75.5); ir (CCl_4) 3400 (broad, w, NH), 3180 (mw, overtone of 1620-cm^{-1} band), 2145 (s, C≡N), 1620 (vs), 1565 cm^{-1} (mw, sh) (both C=C-C=N); Raman (crystals) 2146 (vs, C≡N), 1615 (mw), 1568 cm^{-1} (m) (both C=C-C=N); nmr (CCl_4) δ 0.916 [C(CH_3)$_3$, 9 H], 0.983 [center of doublet, 2 C(CH_3)$_3$, 18 H], 1.677 [C(CH_3)$_2$, 6 H], 1.713 [2 C(CH_3)$_2$ + CH_2, total 14 H], 2.130 (CH_2, 2 H), 2.450 (CH_2, 2 H), 7.320 ppm (NH, 1 H). Additional yields of **4** were recovered from the original pentane filtrate (A) and from the combined benzene mother liquors (B) of **4** as follows.

The pentane filtrate was washed with two 200-ml portions of 30% aqueous KOH, dried ($MgSO_4$), filtered, and chilled at −5° for 12 hr. Filtration yielded a crystalline precipitate which according to ir spectra consisted of a mixture of **4** and di-*tert*-octylaminomaleonitrile (**12**). The two compounds could be separated owing to the different solubilities of their methanesulfonic acid salts. The precipitate was dissolved in 100 ml of ether and a solution of 3.5 g of methanesulfonic acid in 100 ml of ether was added. The ether solution was chilled at −5° for 12 hr and filtered to yield a filtrate (C) and a methanesulfonic acid salt of **12** (**12**·CH_3SO_3H) as a crystalline precipitate. This precipitate was dispersed in 100 ml of ether and stirred with a concentrated solution of potassium carbonate until all crystals had dissolved. The ether layer was separated and dried ($MgSO_4$), and the ether was removed *in vacuo*. The residue was recrystallized from hot hexane to yield 2.3 g of colorless crystals identified as **12** by ir spectrum and mixture melting point determination using for comparison an authentic sample of **12** prepared according to ref 4.

The original ether mother liquor of **12**·CH_3SO_3H (C) was also stirred with a concentrated solution of potassium carbonate. The ether layer was separated, dried ($MgCO_3$), and concentrated. After chilling at −5° for 5 hr, a crystalline precipitate (2.18 g) was obtained, which was identified as pure **4** by ir spectrum and mixture melting point determination.

Evaporation of the solvent from the combined benzene mother liquors (B) of the first batch of **4** yielded a crystalline residue which according to ir spectra consisted of a mixture of **4** and 4-cyano-5-*tert*-octylaminoimidazole (**9**). These two compounds could be separated because **9**, unlike **4**, is readily soluble in 1 *N* aqueous hydrochloric acid.[4] The precipitate was finely ground, vigorously stirred for 1 hr at room temperature with 100 ml of 1 *N* HCl, and filtered to yield an aqueous filtrate (D) and a precipitate (E). Neutralization of the filtrate D with a solution of potassium bicarbonate caused formation of a precipitate which was collected by filtration and crystallized from hot chloroform to yield 1.3 g of **9** identified by ir spectrum and mixture melting point determination.

The precipitate E was dispersed in 200 ml of ether and stirred with a concentrated aqueous solution of potassium carbonate until all solids had dissolved. The ether layer was separated, dried ($MgSO_4$), concentrated, and chilled (−5°, 7 hr) to yield upon filtration 2.5 g of crystals identified as **4** by ir spectrum and mixture melting point determination. The overall yield of **4** in this procedure is, therefore, 24.4 g (12.3% based on TMP).

3-*tert*-Octyl-4-*tert*-octylamino-5-cyanoimidazole (5) from 4. A toluene solution of 4.5 g of **4** was heated for 14 hr under a nitrogen blanket at reflux. The toluene was removed *in vacuo*, and the residue was dissolved in 50 ml of hot benzene. This solution was treated with Norit and after filtration was diluted with 75 ml of hexane. After chilling at −5° for 12 hr, a crystalline precipitate was obtained which was once recrystallized from a benzene–hexane mixture (1:3), 2.70 g of colorless crystals of **5**, mp 142–144°.

Anal. Calcd for $C_{20}H_{36}N_4$: C, 72.24; H, 10.91; N, 16.85. Found: C, 72.00; H, 11.09; N, 17.02. Mass spectrum (70 eV) *m/e* 332 (M^+); uv max (isooctane) 282, 225.7, 211.0 nm (ε × 10^{-3} 9.34; 5.33, 13.14); uv max (methanol) 284, 228.5, 210 nm (ε × 10^{-3} 9.86, 5.05, ~15.2); ir (CCl_4) 3410 (mw, NH), 3125 (vw, overtone of

1565-cm^{-1} band), 2180 (s, C≡N), 1565 cm^{-1} (vs, C=C-N=C); nmr (CCl_4) δ 0.861 [$C(CH_3)_3$, 9 H], 0.983 [$C(CH_3)_3$, 9 H], 1.417 [$C(CH_3)_2$, 6 H], 1.667 [$C(CH_3)_2$, 6 H], 1.760 (CH_2, 2 H), 1.959 (CH_2, 2 H), 3.884 (NH, 1 H, disappears upon deuteration), 7.084 ppm (N=CH, 1 H).

Attempted Acid-Catalyzed Hydrolysis of 4. Formation of 5. To a solution of 1.0 g of 4 in 15 ml of tetrahydrofuran was added 10 ml of water. The addition of 0.2 ml of methanesulfonic acid caused the yellow color to fade to colorless. After 24 hr at room temperature, one-quarter of this solution was treated with excess solid potassium carbonate. This resulted in formation of an aqueous layer and a yellow organic layer. The organic layer was separated, the solvent was removed *in vacuo*, and the residue was dissolved in hot hexane. The hexane solution was dried ($MgSO_4$), filtered, and cooled (−5°) to give 0.187 g of starting material (4), identified by mixture melting point determination and identity of infrared spectra.

The remaining three-quarters of the original solution was heated at reflux of tetrahydrofuran for 1 hr. The tetrahydrofuran was then removed *in vacuo*. This resulted in formation of an aqueous layer and an organic layer which solidified upon cooling. The crystals were collected by filtration and dissolved in hot hexane. The hexane solution was dried ($MgSO_4$), filtered, and cooled (−5°) to yield 0.55 g of colorless crystals, identified as **5** by mixture melting point determination and identity of infrared spectra.

1-Methyl-4-methylamino-5-cyanoimidazole (11). To a solution of 2.75 g (0.125 mol) of 4-cyano-5-*tert*-octylaminoimidazole (9) in 30 ml of acetone were added 3.15 g (2.37 ml, 0.025 mol) of dimethyl sulfate and 5 g of finely powdered potassium carbonate. The stirred mixture was heated at reflux for 2 hr. The acetone was removed *in vacuo*, and the residue was heated at 100° for an additional 2 hr. After cooling, 25 ml of concentrated ammonia was added to decompose excess dimethyl sulfate, and the mixture was heated at 60° for 30 min. Filtration yielded a solid residue, which was dissolved in 15 ml of chloroform. The chloroform solution was dried ($MgSO_4$), treated with Norit, and after filtration was chilled at −5° for 5 hr. The crystalline precipitate was redissolved in 50 ml of chloroform containing a trace of methanesulfonic acid. The solution was allowed to stand at room temperature for 12 hr. It was then concentrated to a 10-ml volume and chilled at −5° for 5 hr. Filtration yielded 0.62 g of **11** as colorless crystals, mp 162.0–163.7°. *Anal.* Calcd for $C_8H_8N_4$: C, 52.91; H, 5.93; N, 41.15. Found: C, 52.92; N, 5.91; N, 41.16. Mass spectrum (70 eV) *m/e* 136 (M^+); uv max (methanol) 275.5, 230 nm (ε × 10^{-3} 9.26, 4.53); ir ($CHCl_3$) 3435 (s, NH), 2188 (vs, C≡N), 1585 cm^{-1} (vs, C=C-N=C); Raman (crystals) 2188 (vs, C≡N), 1590 cm^{-1} (s, C=C-N=C); nmr ($CDCl_3$) δ 3.63 ($NHCH_3$, 3 H), 2.96 (NCH_3, 3 H), 4.12 ($NHCH_3$, 1 H, disappears upon deuteration), 7.12 ppm (N=CH, 1 H).

Registry No.—**4**, 51248-29-4; **5**, 51248-30-7; **9**, 30771-61-0; **11**, 15353-10-3; **12**, 30768-59-3; **12**·CH_3SO_3H, 51248-31-8; TMP, 107-40-4; HCN, 74-90-8; HF, 7664,39-3.

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(6) Compound **11** is prepared by treating 4-*tert*-octylamino-5-cyanoimidazole[4] (**9**) with 2 equiv of dimethyl sulfate and excess potassium carbonate in refluxing acetone, followed by thermolysis of the product (Scheme II). In this process, both the amino group and a ring nitrogen of **9** are methylated. Evidently, in the presence of potassium carbonate, Hofmann elimination of 2,4,4-trimethylpentene-1 (**6**) occurs, even though a quarternary ammonium salt is not involved. It appears that the *tert*-octyl substituent in the salt hinders approach of the base to the α NH but that β-elimination occurs readily. Generation of **6** is confirmed by glpc. The initial product appears to be a mixture of **11** and its isomer **10**, since the nmr spectrum shows three *N*-methyl resonances at 2.96, 3.03, and 3.63 ppm. Upon addition of a trace of methanesulfonic acid, the nmr spectrum simplifies to two resonances at 3.03 and 3.63 ppm. This suggests acid-catalyzed conversion of the less stable isomer **10** to the more stable **11**. The presence of the imidazole ring in **11** is evident from a resonance at 7.12 ppm. (See above.)
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Synthesis of Aryl-Substituted 1,3- and 1,4-Diazocine Derivatives

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The synthesis of aryl-substituted 1,3- and 1,4-diazocine derivatives was undertaken because their structural features suggested potential CNS activity. Reaction of methyl β-bromomethylcinnamate with *N,N'*-dimethylethylenediamine gave *N,N'*-dimethyl-2-phenylpiperazine-2-acetic acid methyl ester (**10a**), which was converted to 1,4-dimethyl-7-phenyl-1,2,3,4-tetrahydro-1,4-diazocin-5(8*H*)-one (**1a**). Catalytic and hydride reductions of **1a** led ultimately to the 6-phenylperhydro-1,4-diazocine **14.** The cis and trans isomers of 3-phenylproline, **34** and **33,** were prepared by a multistep synthesis starting from cinnamaldehyde and acetamidomalonate. Conversion of **33** to the methylthiohydantoin **36,** followed by desulfurization and quaternization with methyl iodide, gave the bicyclic intermediate **42,** which upon treatment with sodium hydride or lithium–ammonia underwent transannular ring opening to give 1,3-dimethyl-6-phenyl-1,2,3,7-tetrahydro-1,3-diazocin-4(8*H*)-one (**2**) and its perhydro analog **44,** respectively. On the other hand, reaction of **42** with sodium methylate or with sodium borohydride led to peripheral ring cleavage, giving *N*-methyl-3-phenylproline methyl ester (**46**) and the corresponding alcohol **45,** respectively.

Our interest in medium-ring heterocycles stems from an effort to develop structurally novel antipsychotic drugs. Tricyclic antipsychotic agents related to chlorpromazine have the following physicochemical parameters in common: a nearly flat aromatic ring system, substituted with an electronegative function, and a basic amine group separated by three carbon atoms from the aromatic ring system. In those compounds in which the aminoalkyl side chain is connected by a carbon–carbon double bond, only the cis isomers (side chain oriented toward the electronegative substituent) are active,[1] and this has led to the hypothesis[2] that for optimum activity the amine function should be in close proximity to the electronegative substituent. Therefore it was intriguing to incorporate these features in novel frameworks and to determine whether such nontricyclic structures would exhibit antipsychotic activity.

The diazocinone derivatives (**1** and **2**) are novel compounds which fulfill the above criteria; the aryl substituent serves as part of the aromatic ring system and the amide carbonyl as the electronegative substituent, with the basic ring nitrogen located appropriately in close proximity to the carbonyl group. We planned to synthesize **1** by cyclization of a linear precursor such as **3,** and **2** by transannular ring opening of a bicyclic precursor such as **4** (Scheme I).