cipitated chromium salts were washed with acetone, and the solvent was evaporated. A solution of the residue in 100 mL of ether was extracted with saturated sodium bicarbonate and saturated sodium chloride, dried ($MgSO_4$), and evaporated. The crude product was purified by flash chromatography on a 60-mm column with 1:4 ethyl acetate–hexane as eluant. The first product to be eluted from the column was evidently 1:2 mixture of recovered lactone and keto ester **21b** as a pale-yellow oil: yield, 1.30 g (26%); IR (film) ν_{max} 1770 (C=O), 1730 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70–2.26 (m, 10 H), 1.00 (d, J = 7 Hz, ~1.8 H, $CHCH_3$), 1.19 (d, J = 7 Hz, ~1.2 H, $CHCH_3$), 2.31–2.85 (m, 4 H), 3.64 (s, 3 H, $COOCH_3$). Keto ester **25** was eluted second and was obtained as a colorless viscous oil. MS (EI) indicated that **25** was contaminated with a small amount of **21b**: yield, 2.82 g (55%); IR (film) ν_{max} 1740 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.71–2.53 (m, 14 H), 0.90 (d, J = 6 Hz, ~1.2 H, $CHCH_3$), 0.95 (d, J = 6 Hz, ~1.8 H, $CHCH_3$), 3.64 (s, 3 H, $COOCH_3$); high-resolution mass spectrum calcd for $C_{14}H_{22}O_3$ m/e 238.1563 (M^+), found m/e 238.1564.

Methyl 2,3,3a,6,7,8,9,9a-Octahydro-4-methyl-1-oxo-1*H*-cyclopentacyclooctene-5-carboxylate (26). A refluxing solution of 4.6 mg (0.67 mmol) of lithium in 20 mL of anhydrous ammonia was stirred while 36 mg (0.15 mmol) of keto ester **22** in 2 mL of tetrahydrofuran was added over a 2-min period. After 5 min, excess lithium was destroyed with 0.05 mL of 3-hexyne. A 1-mL portion of 1:1 acetic acid-tetrahydrofuran solution was added, and the ammonia was evaporated. A solution of the residue in 30 mL of 1:1 ether–pentane was extracted with 25 mL of water and two 20-mL portions of saturated sodium chloride and was filtered through a pad of sodium sulfate. Evaporation of the solvent left 42 mg of isomeric keto esters as an oily yellow solid.

The crude product from the reduction was dissolved in 10 mL of a freshly prepared solution of 0.1 M sodium methoxide in methanol. The solution was heated at reflux for 19 h. At periodic intervals, 5-μL aliquots were removed and added to 20 μL of a 1:1 mixture of 5% hydrochloric acid–ether. The course of equilibration could be monitored by GLC analysis (column A; temperature program, 210 °C 3 min, 5 °C/min to 300 °C). After 19 h, only one peak was observed. The solution was cooled, diluted with 40 mL of saturated sodium chloride, and extracted with 30 mL of 1:1 ether–pentane. The organic layer was washed with 20 mL of saturated sodium chloride, filtered through a pad of sodium sulfate, and concentrated. Purification of the residue by preparative TLC, using 1:1 ether–hexane as eluant, gave 26 mg (72%) of keto ester **26** as a pale-yellow solid. An analytical sample was obtained by recrystallization from pentane: mp 72–73 °C; IR ($CHCl_3$) ν_{max} 1730 (C=O), 1709 (ester C=O) cm^{-1}; 220-MHz ^1H NMR ($CDCl_3$) δ 1.23–1.36 (m, 2 H, CH_2), 1.73–2.36 (m, 7 H, ring CH), 2.03 (s, ~3 H, $C=CCH_3$), 2.36–3.05 (m, 4 H, 3 allylic CH and ring CH), 3.59–3.91 (8-line m, 1 H, COCH), 3.74 (s, 3 H, $COOCH_3$); UV (hexane) λ_{max} 230 nm (ϵ 7380); high-resolution mass spectrum calcd for $C_{14}H_{20}O_3$ m/e 236.1407 (M^+), found m/e 236.1412.

Acknowledgment. This research was supported in part by grants from the National Science Foundation (No. 07513 and 11843).

Registry No. 1, 38127-47-8; **2**, 82430-72-6; (*E*)-**3**, 82430-73-7; **4**, 76379-96-9; (*E*)-**5**, 82430-74-8; **6**, 68965-63-9; **7**, 76379-97-0; (*E*)-**8**, 82430-75-9; (*E*)-**9**, 82430-76-0; **10**, 82430-77-1; **11a**, 82430-78-2; **11b**, 82430-79-3; **12a**, 82430-80-6; **12b**, 82430-81-7; **13**, 76379-98-1; **13** hydroxy acid sodium salt, 82430-90-8; **13** keto acid sodium salt, 82430-93-1; **14**, 82430-82-8; **15**, 82430-83-9; **17**, 76379-99-2; **17** hydroxy acid sodium salt, 82430-91-9; **17** keto acid sodium salt, 82430-94-2; **18**, 76380-00-2; **18** hydroxy acid sodium salt, 82430-92-0; **19**, 82430-84-0; **20a**, 76380-01-3; **20b**, 76380-02-4; **21a**, 82430-85-1; **21b**, 82430-86-2; **22**, 76380-03-5; **23**, 76380-06-8; **24**, 76380-04-6; **25**, 82430-87-3; **26**, 76380-05-7; cyclohexanone, 108-94-1; 4-bromo-1-butene, 5162-44-7; (*E*)-5-bromo-2-pentene, 7515-62-0; cyclopropyl methyl ketone, 765-43-5; cyclopropyl methyl carbinal, 765-42-4; 4-penten-1-ol, 821-09-0; 4-pentenal, 2100-17-6; 2-penten-4-yn-1-ol, 5557-88-0; 3,4-pentadien-1-ol, 24767-71-3; 3,4-pentadien-1-ol tosylate, 5557-87-9; 4,5-hexadienenitrile, 82430-88-4; 4-penten-1-yl trimethylsilyl ether, 14031-96-0; phenyl(tribromomethyl)mercury, 3294-60-8; 1,1-dibromo-2-[3-(trimethylsiloxy)propyl]cyclopropane, 82430-89-5; 4,5-hexadien-1-yl trimethylsilyl ether, 72038-66-5; 4,5-hexadien-1-ol, 40365-64-8; 4,5-hexadienal, 20521-51-1; (*E*)-2,5-dichloro-2-pentene, 5680-46-6; (*Z*)-2,5-dichloro-2-pentene, 5680-47-7; (*E*)-2-chloro-5-iodo-2-pentene, 70048-60-1; 3,4-pentadien-1-ol methanesulfonate, 82444-37-9; 5-bromo-1,2-pentadiene, 5558-05-4.

Structure of Physoperuvine

A. R. Pinder

Department of Chemistry, Clemson University, Clemson, South Carolina 29631

Received March 16, 1982

Evidence, chemical and spectroscopic in character, is presented that suggests that the structure 3-(methylamino)cycloheptanone (1) assigned to the alkaloid physoperuvine by earlier investigators may have to be revised.

The roots of *Physalis peruviana* (Solanaceae) contain the alkaloidal base physoperuvine as both the optically active (crystalline) and the racemic (liquid) variety, isolated by Ray and co-workers.[1,2] Chemical and spectroscopic investigations by these workers have led them to formulate the compound as 3-(methylamino)cycloheptanone (1, Chart I).

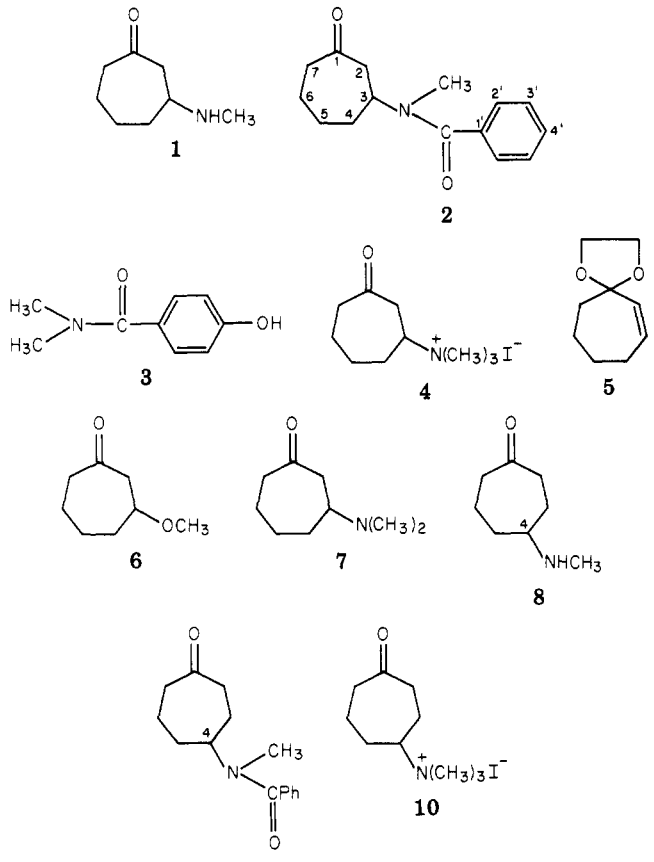
A critical examination of the chemical and spectroscopic observations detailed in these papers, coupled with our own studies in this area, force us to the conclusion that this formulation must be revised.

We are puzzled by a number of observations in these publications. For example, the carbonyl band in the IR spectrum of the alkaloid (at 1698 cm^{-1}) is described as weak.[1] We have synthesized several (methylamino)- and (dimethylamino)cycloalkanones, and in all cases we find the carbonyl band is very intense—the most intense band in the spectrum. There do not seem to be any structural features in 1 that would lead one to anticipate weak carbonyl absorption, and, indeed, synthetic 1 (see below) does exhibit a very intense absorption in the carbonyl region. Next, (+)-physoperuvine is described as a crystalline base of mp 153 °C.[1,2] "Chemical intuition" suggested to us that this melting point is unusually high for the structurally simple compound 3-(methylamino)cycloheptanone. Further, the mass spectral fragmentation diagram[1] will not lead to the ion formulated, and the ^{13}C NMR spectrum[2] of *N*-benzoylphysoperuvine (formulated as **2**) is not in agreement with that anticipated for **2**. For example, the chemical shift of the methyl group in **2** would be expected to be around δ 30–35 rather than 55.9. Cases for com-

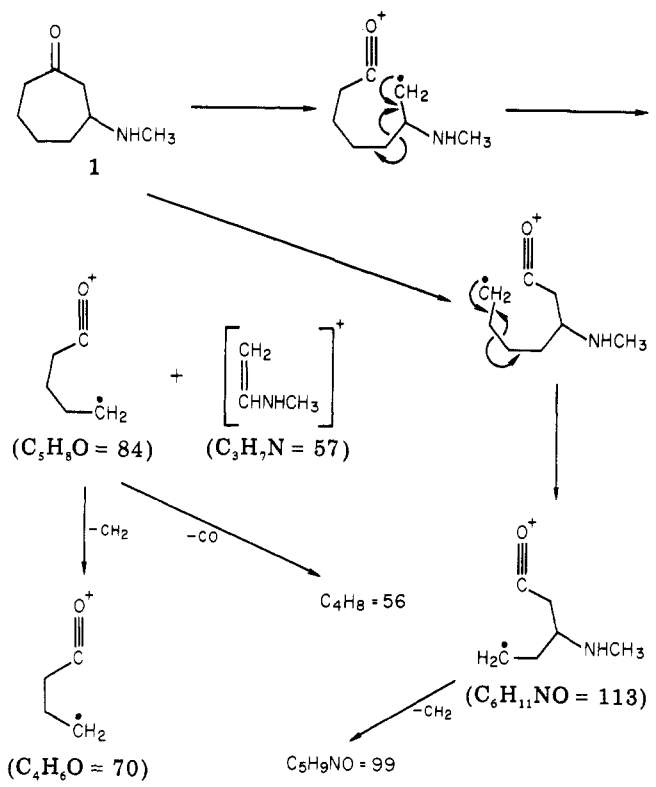
(1) Ray, A. B.; Sahai, M.; Sethi, P. D. *Chem. Ind. (London)* **1976**, 454.
(2) Sahai, M.; Ray, A. B. *J. Org. Chem.* **1980**, *45*, 3265.

0022-3263/82/1947-3607$01.25/0

Chart I



Scheme I



parison δ include *N,N*-dimethylacetamide (34.8, 39.9), *N,N*-dimethylformamide (31.15, 36.2), *N,N'*-dimethylurea (26.7), *N,N*-dimethyl-*p*-hydroxybenzamide (**3**) (37.3 and 1-methyl-2-pyrrolidone (29.2).[3]

It is also surprising that the *N*-benzoyl derivatives of (+)-physoperuvine and its racemic counterpart should have the same melting point, 136–137 °C. The same comment applies to the methiodide of (+)-physoperuvine, which is reported to have the same melting point (287–288 °C) as the synthetic racemic methiodide **4**.[2] Usually, optically active and racemic varieties of a compound yield crystalline derivatives of different melting points. A peculiar feature of *N,N*-dimethylphysoperuvinium chloride (formulated as **4** with Cl^- as anion) is the drastic conditions (KOH at 100 °C for 2 h) apparently necessary for it to suffer Hofmann degradation.[2] A consideration of structure **4** leads one to expect that very mild conditions would serve to bring about this reaction; in fact this proved to be the case for the iodide **4** (see below).

Finally, it is surprising that the authors did not attempt a synthesis of (±)-3-(methylamino)cycloheptanone (**1**) by the simple Michael addition of methylamine to 2-cycloheptenone, particularly as this was the route (using dimethylamine) they adopted for the synthesis of the analogous 3-dimethylamino compound.[2] It was this omission that was responsible for our interest in this work, and we describe here the results of our investigations on the synthesis of **1** and related compounds.

2-Cycloheptenone is known to be a rather labile compound. For reasons of steric strain the double bond shifts readily under the influence of basic and acidic catalysts into the 3,4-position.[4] Precautions had to be taken to prevent or minimize this rearrangment. The conjugated ketone was prepared from cycloheptanone as outlined by House and Lee,[5] but trouble was experienced with the methanolic sulfuric acid hydrolysis of the intermediate ketal **5**. The product contained appreciable amounts of 3-cycloheptenone and the methyl ether **6**. A more satisfactory hydrolysis was effected by 5% aqueous sulfuric acid in tetrahydrofuran as solvent.[6] The product was then found to be free of the unconjugated isomer on UV, IR, and NMR spectral evidence.

A preliminary model experiment using 2-cyclohexenone and methylamine showed that addition occurred readily and was noticeably exothermic. It was therefore desirable to conduct the desired addition at low temperature. Treatment of 2-cycloheptenone with methylamine at 0 °C afforded, in excellent yield, 3-(methylamino)cycloheptanone (**1**) as a clear, mobile, colorless liquid; GC analysis showed it to be >98% pure. It did not keep well, however, even at low temperature, and after a few days at 0 °C it had become yellow and had thickened considerably. Its IR spectrum (film) was normal with an intense carbonyl band and an NH band at 1695 and 3390 cm^{-1}, respectively. Its ^1H NMR spectrum (in $CDCl_3$) showed a very narrow doublet at δ 2.21 (3 H, J = 0.6 Hz, NCH_3), a complex set of multiplets centered around δ 2.40 ($CH-N$ and CH_2COCH_2), and an envelope centered at δ 1.60 (ring CH_2's). In D_2O the NCH_3 signal appeared as a sharp singlet at 2.27 ppm; there were no signals at 2.76 and 3.86 ppm.[2] The mass spectrum showed M^+ at m/e 141, as expected for $C_8H_{15}NO$. A comparison between this spectrum and that of physoperuvine[1,2] is summarized in Table I. Some of these peaks for the synthetic ketone may be

(3) Bruker ^{13}C Data Bank, Vol. 1, Bruker Physik, West Germany, 1976.

(4) Maclean, I.; Sneeden, R. P. A. *Tetrahedron* **1965**, *21*, 31.

(5) (a) House, H. O.; Lee, T. V. *J. Org. Chem.* **1979**, *44*, 2819 and references therein. (b) Garbisch, E. W., Jr. *J. Org. Chem.* **1965**, *30*, 2109.

(6) Compare: House, H. O.; Sieloff, R. F.; Lee, T. V.; deTar, M. B. *J. Org. Chem.* **1980**, *45*, 1800. I am indebted to Professor House for drawing my attention to this procedure and for correspondence about it.

Table I

peak, m/e	rel abundance, % physoperuvine	3-(methylamino)-cycloheptanone
141	36	13.9
113	24	1.4
99	?	71.5
98	39	3.7
84	39	94.7
83	?	30.7
70	100	100
68	?	14.2
57	85	44.9
56	?	19.9
55	?	14.7
42	?	16.9
41	?	12.4

explained by the fragmentations[7] shown in Scheme I. We conclude that, although there are certain resemblances in the mass spectra, the overall general spectroscopic comparison suggests that the natural base is not 1.

Treatment of 1 with benzoyl chloride in triethylamine yielded crystalline *N*-benzoyl-3-(methylamino)cycloheptanone (2), mp 89.5 °C. The reported value[1,2] for *N*-benzoylphysoperuvine is 136–137 °C (optically active or racemic). A mixture of the synthetic and racemic "natural" products[8] showed a depression (mixed mp 75–81 °C). The ^{1}H NMR spectrum of the synthetic amide (in $CDCl_3$) showed an envelope centered around δ 1.90 (ring CH_2's) and another around 2.51 (CH_2COCH_2), a sharp singlet at 2.83 (3 H, NCH_3), a broad multiplet at 4.80 (1 H, N–CH), and a singlet at 7.37 (5 H, ArH). These values are in agreement with those reported[1,2] for the benzoylated natural base with the exception that there is no signal at ca. δ 4.36 in the spectrum of the synthetic amide.

The ^{13}C NMR spectrum of the synthetic amide 2 was measured first in deuteriochloroform at ambient temperature. Not surprisingly, the N–CH_3 and N–CH carbons each showed two resonances, at δ 27.3 and 32.2 and 50.7 and 55.8 (Me_4Si = 0), respectively, in the proton-decoupled spectrum, corresponding to geometrical isomers resulting from the partial double-bond character of the OC–NH bond. In dimethyl-d_6 sulfoxide at 100 °C these pairs coalesced to give singlets at δ 30.7 and 53.6, respectively. These values are very different from the published values (δ 55.9 and 60.9, conditions not specified).[2] The correctness of our assignments was verified by the proton-coupled spectrum in $CDCl_3$ at ambient temperature: the NCH_3 signals above were both split into quartets and the NCH signals into doublets. The various spectral assignments are listed in Table II.

The preparation of the oxime of *N*-benzoylphysoperuvine has been described.[2] We have been unable, despite repeated efforts and use of forcing conditions, to prepare an oxime from *N*-benzoyl-3-(methylamino)cycloheptanone. At best there was only a partial oximation, and attempts to purify the derivative were unsuccessful.

The addition of dimethylamine to 2-cycloheptenone was next effected, again under mild, low-temperature conditions; it furnished 3-(dimethylamino)cycloheptanone (7) in excellent yield, shown to be pure by GC. Its spectral properties were as anticipated. Treatment with methyl iodide afforded the quaternary salt 4. The same salt was also obtained by reaction of (3-(methylamino)cycloheptanone (1) with methyl iodide. Its melting point, 184 °C dec, contrasts sharply with 287–288 °C reported for both the methiodide derived from (+)-physoperuvine and that derived from 7.[2,9] The synthetic methiodide is, of course, racemic, and therefore a melting point comparison of it with that from (+)-physoperuvine is almost certainly invalid; the methiodide derived from (±)-physoperuvine has not been described. The structure (4) assigned to our synthetic methiodide is confirmed by the observation that it undergoes Hoffman elimination to give 2-cycloheptenone and trimethylamine in quantitative yield under very mild conditions (aqueous $NaHCO_3$ at room temperature); this behavior would be expected on the basis of its formulation as 4.

Table II. ^{13}C Chemical Shift Assignments for Synthetic *N*-Benzoyl-3-(methylamino)cycloheptanone (2)[a]

carbon	25 °C in $CDCl_3$ proton decoupled	coupled	100 °C in Me_2SO-d_6, proton decoupled
1	211.4, 210.4	s, s	211.1
2	48.7, 47.5	t, t	48.6
3	55.8, 50.7	d, d	53.6
4	35.7, 34.4	t, t	34.9
5	24.2, 23.7	t, t	24.0
6	27.6, 26.9	t, t	27.5
7	43.8	t	44.3
N–CH_3	32.2, 27.3	q, ?[b]	30.7
amide C=O	171.0	s	
1′	136.3		
2′	126.9[c]		
3′	128.5[c]		
4′	129.6[c]		

[a] In ppm downfield from Me_4Si. [b] Overlaps with another signal; only part of quartet visible. [c] Assignments tentative, based on benzamide (Bruker Data Bank, spectrum no. 392).

Our observations suggest that physoperuvine is not identical with 3-(methylamino)cycloheptanone, but it is possible that the structure could be of a similar type. One candidate is 2-(methylamino)cycloheptanone, but this would seem to be ruled out by the formation of a tetradeuterio derivative by physoperuvine.[1,2] In any event we prepared a sample of this base by reaction between 2-bromocycloheptanone and methylamine. It proved to be very labile and difficult to purify and not the type of compound likely to be a natural product. The 4-isomer (8) seemed a more attractive possibility. We synthesized this compound from *p*-(methylamino)phenol by sequential reduction, oxidation, and ring expansion with diazomethane. It proved to be a crystalline solid, mp 75 °C, and formed a benzoyl derivative (9), mp 118 °C. The latter showed a small melting point depression (slight softening at 95–100 °C, collapsing at 108–111 °C) on admixture with authentic (±)-*N*-benzoylphysoperuvine. This result was not conclusive, and there is a possibility that the two amides are identical, in which case physoperuvine is 4-(methylamino)cycloheptanone (8). The synthetic base formed a methiodide (10), mp 250–251 °C dec, stable to aqueous bicarbonate at room temperature.

Apparently physoperuvine cannot be formulated as 2- or 3-(methylamino)cycloheptanone but might be the 4-isomer, although there are several discrepancies in melting points and mixed melting points that need to be explained. The structure of the base must be regarded as sub judice

(7) Pavia, D. L.; Lampman, G. M.; Kriz, G. S, Jr. "Introduction to Spectroscopy"; Saunders: Philadelphia, PA, 1979; p 263 et seq.

(8) We thank Dr. A. B. Ray for provision of an authentic sample of (±)-*N*-benzoylphysoperuvine.

(9) A recent private communication from Dr. Ray indicates that the melting point of his synthetic methiodide (4) should be corrected to 181 °C. A mixture of this compound and our methiodide had mp 183.5–184 °C. I thank Dr. Ray for a sample of his salt.

pending further studies, which we are now undertaking.

Experimental Section

Melting points and boiling points are uncorrected. UV and IR spectra were recorded on Perkin-Elmer 202 and 137 instruments, respectively. NMR spectra were measured on Varian 200-MHz, Bruker 180-MHz, and JEOL FX-90Q and FX-60Q instruments, and mass spectra on a Hewlett-Packard 5840A GC/MS spectrometer. GC was conducted on an F and M Model 810 gas chromatograph.

2-Cycloheptenone. The ketone was synthesized from cycloheptanone.[5,6] The final hydrolysis of the ethylene ketal **5** was conducted as follows. The ketal (13.3 g) in tetrahydrofuran (40 mL) was mixed with 5% aqueous H_2SO_4 (60 mL) and the mixture stirred at 25 °C for 20 min. Ether was added, and the whole was washed with aqueous sodium bicarbonate, dried (Na_2SO_4), and concentrated. The residue distilled at 108–110 °C (26 mmHg) and 117–120 °C (29 mmHg) (9.1 g, 96%); IR (film) 1652 cm^{-1}; UV λ_{max} (EtOH) 227 mm (ϵ 10 240);[5b] ^1H NMR ($CDCl_3$) δ 0.8–3.0 (8 H, m), 5.8–6.8 (2 H, =CH).

3-(Methylamino)cycloheptanone (1). 2-Cycloheptenone (2.2 g, 0.02 mol) was dissolved in ethanol (60.0 mL) and stirred at 0 °C during the gradual addition of methylamine (1.66 g of a 45% w/w solution in ethanol, 0.024 mol) during 20 min. The mixture was stirred at this temperature for a further hour, and then the ethanol and excess methylamine were removed on a rotary evaporator at 35–40 °C. The yellow, residual keto base distilled at 80–85 °C (bath, 0.01–0.02 mmHg; 2.0 g, 71%). GC (OV 101, 90 °C) showed the product to be essentially homogeneous; IR (film) 3390, 1695 cm^{-1}; 1H NMR ($CDCl_3$) δ 2.21 (s, 3 H, NCH_3), (D_2O) 2.27 (s, 3 H, NCH_3); mass spectrum, *m/e* 141 (14) (M^+), 112 (5), 99 (71.5), 84 (94.7), 83 (30.7), 71 (11), 70 (100), 68 (14.2), 57 (44.9), 56 (19.9), 55 (14.7), 42 (16.9), 41 (12.4). Anal. (Calcd for $C_9H_{15}NO$: C, 68.09; H, 10.64, N, 10.00. Found: C, 68.16; H, 10.50; N, 9.92.

***N*-Benzoyl-3-(methylamino)cycloheptanone (2).** The foregoing keto base (0.28 g) in a mixture of triethylamine (2 mL) and dry benzene (5 mL) was cooled in ice and agitated during the gradual addition of benzoyl chloride (0.29 g) in benzene (3 mL). The mixture was kept at 0 °C for 2 h and then mixed with ether, washed with dilute HCl and sodium bicarbonate, dried, and concentrated. The residual amide (0.3 g) crystallized from 1:1 benzene–petroleum (bp 60–80 °C), from which it separated in needles: mp 89.5 °C; ^1H NMR ($CDCl_3$) δ 1.90 (br), 2.51 (br), 2.83 (s, 3 H, NCH_3), 4.80 (br, 1 H, N–CH), 7.37 (s, 5 H, ArH); ^{13}C NMR, see Table I; mass spectrum, *m/e* 245 (14.4) (M^+), 160 (9.3), 140 (7.4), 136 (10.4), 105 (100), 77 (31.0). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.36; H, 7.84; N, 5.68. A mixture of this compound and (±)-*N*-benzoylphysoperuvine[8] (mp 136–137 °C) had a melting point of 75–81 °C. Attempts to make an oxime from this amide were only partially successful.

3-(Dimethylamino)cycloheptanone (7). Cycloheptenone (2.2 g, 0.02 mol) in absolute ethanol (6 mL) was stirred at 0 °C during the gradual addition (15–20 min) of 37.5% w/w ethanolic dimethylamine (2.88 g, 0.024 mol). The mixture was stirred for a further hour at 0 °C, then concentrated in vacuo at 35–40 °C. The residual keto base was distilled, bp 75–80 °C (bath, (0.03–0.04 mmHg; 2.66 g, 86%), with a single peak on GC (OV 101, 90 °C); IR (film) 1701, 1449, 1441 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.22 [s, $N(CH_3)_2$]; mass spectrum, *m/e* 155 (12.4) (M^+), 113 (14.9), 98 (63.5) 97 (18.9), 85 (10.1), 84 (100), 71 (56.3), 70 (18.7), 56 (14.7), 55 (12.4). Anal. Calcd for $C_9H_{17}NO$: C, 69.68; H, 10.97; N, 9.03. Found: C, 69.60; H, 10.95; N, 8.98.

3-(Dimethylamino)cycloheptanone Methiodide (4) (A). The above amino ketone (0.5 g) in dry acetone (50 mL) was cooled in ice and treated with methyl iodide (2–3 mL). After 12 h at 0 °C crystals that had separated were collected and recrystallized from methanol, from which the methiodide (0.8 g, 83%) separated in elongated prisms: mp 184 °C (dec); ^1H NMR (D_2O) δ 3.15 [s, 9 H, $N(CH_3)_3$], 3.83 (br, 1 H, *n*-CH). Anal. Calcd for $C_{10}H_{20}INO$: C, 40.40; H, 6.73; N, 4.71. Found: C, 40.27; H, 6.84; N, 4.91.

(B) 3-(Methylamino)cycloheptanone (1) (0.5 g) in dry acetone (150 mL) at 0 °C was similarly treated with methyl iodide (4 mL) in the presence of anhydrous potassium carbonate (5 g) and kept at this temperature overnight. The mixture was refluxed on the steam bath for 1.5 h and then filtered hot. The filtrate was evaporated to dryness and the residue crystallized from methanol to yield at methiodide, mp 184 °C, identical with that prepared as in **A**.

Hofmann Elimination of the Methiodide. The foregoing methiodide (2.76 g) in water (40 mL) was saturated with sodium bicarbonate and left at room temperature overnight. The mixture was subjected to continuous ether extraction for several hours and the extract dried (Na_2SO_4). The solvent was removed in vacuo and the residual liquid (1.02 g, 100%) identified as 2-cycloheptenone (IR, NMR). In a separate experiment trimethylamine was identified as its picrate, mp 216 °C.

4-(Methylamino)cycloheptanone (8). *p*-(Methylamino)-phenol sulfate was reduced catalytically[10] to 4-(methylamino)-cyclohexanol (mixture of cis and trans isomers), which was oxidized with chromic acid to 4-(methylamino)cyclohexanone.[11] This ketone 1.27 g) in methanol (5 mL) was cooled in ice, treated with powdered, anhydrous sodium carbonate, and stirred during the gradual addition (20 min) of *N*-nitrosomethylurethane (1.5 g). The mixture was stirred overnight at room temperature and then filtered, and the filtrate was freed of solvent in vacuo.[12] The residue distilled at 90–95 °C (bath, (0.1 mmHg; 1.0 g, 71%). The distillate solidified readily and crystallized from acetone in rhombs: mp 75 °C; ^1H NMR (D_2O) δ 1.69 (br, ring CH_2's, 2.37 (s, 3 H, NCH_3), 3.30 (m, 1 H, CHN); mass spectrum *m/e* 141 (64.8) (M^+), 113 (48.4), 112 (65.5):, 99 (64.1), 98 (100), 84 (27.6), 71 (22.0), 70 (92.7), 58 (24.2), 57 (56.9), 56 (16.7), 55 (22.2), 43 (10.0), 42 (26.7), 41 (19.7). Anal. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71; N, 9.92. Found: C, 67.91; H, 10.75; N, 9.87.

4-(Dimethylamino)cycloheptanone Methiodide (10). This salt was prepared from the foregoing secondary base exactly as described for the 3-isomer (see above). It separated from methanol in prisms, mp 250–251 °C (dec), with prior darkening and softening. Anal. Calcd for $C_{10}H_{20}INO$: C, 40.40; H, 6.73; N, 4.71. Found: C, 40.40, H, 6.78; N, 4.69. This salt was stable to sodium bicarbonate at room temperature.

***N*-Benzoyl-4-(methylamino)cycloheptanone (9).** The secondary base **8** was benzoylated exactly as outlined for the 3-isomer **1** (see above). The amide separated from 2:3 benzene–petroleum (bp 60–80 °C) in needles: mp 118 °C; ^1H NMR ($CDCl_3$) δ 1.61 (br), 1.98 (br), 2.55 (br), 2.88 (s, 3 H, NCH_3), 4.20 (br, 1 H, N–CH), 7.39 (s, 5 H, ArH); mass spectrum, *m/e* 245 (8.7) (M^+), 136 (36.5), 105 (100), 77 (36.1). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.37; H, 7.82; N, 5.67. A mixture of this amide and (±)-*N*-benzoylphysoperuvine[8] (mp 136–137 °C) softened at 95–100 °C and collapsed at 108–111 °C.

Acknowledgment. I am indebted to Dr. K. Kanamori, California Institute of Technology, for the ^{13}C NMR measurements and for helpful discussion of them. I thank also Dr. S. K. Gabriel (Milliken Research Corp., Spartanburg, SC) and J. N. Herron (this department) for NMR measurements. The JEOL FX-90Q NMR spectrometer was purchased with funds provided by the National Science Foundation. Some of the preliminary experimental work was performed by C. Knowles Zalesky.

Registry No. **1**, 60723-27-5; **2**, 82323-62-4; **4**, 82323-63-5; **5**, 1728-24-1; **7**, 82323-64-6; **8**, 82323-65-7; **9**, 82323-66-8; **10**, 82323-67-9; 2-cycloheptenone, 1121-66-0; methylamine, 74-89-5; dimethylamine, 124-40-3; 4-(dimethylamino)cycloheptanone, 82323-68-0.

(10) Heckel, H.; Adams, R. *J. Am. Chem. Soc.* **1925**, *47*, 1712.
(11) Russo, G.; Danieli, B. *Gazz. Chim. Ital.* **1965**, *95*, 438.
(12) Compare: Cook, J. W.; Raphael, R. A.; Scott, A. I. *J. Chem. Soc.* **1951**, 695. Pinder, A. R. *Ibid.* **1956**, 1577.