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New Bicyclic Enamines and Iminium Salts. II. Synthesis of 1,4-Dihydro-1,4-ethanoisoquinolinium Salts and 4,5-Dihydro-1*H*-1,4-methano-3-benzazepinium Salts by Reaction of Bridged Lactams with Organometallic Reagents[1]

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Structures of 1,4-dihydro-1,4-ethanoisoquinolinium salts **6**, earlier synthesized *via* reductive closure of 4-acyl-1-tetralone oximes, were confirmed, and a second, more versatile synthesis of those iminium salts and corresponding enamines **5** was found. Nickel-catalyzed reduction of oximino esters **1d** to amino esters **2**, thermal closure of *cis*-amino esters **2a** to bridged lactams **3**, and reaction of corresponding *N*-alkyl lactams **4** with alkyllithiums yields bridged enamines **5** protonated to give **6**. The synthesis was extended to preparation of 1,4-methanohydrobenzazepinium salts **9** *via* bridged enamines **8** from lactams **7**. Some comparisons of the two types of bridged enamines **5** and **8** are made, and certain alternative routes to lactams **3** and **4** are discussed.

Our first synthesis[2] of benzoisoquinuclideinium salts **6** and corresponding bridged enamines **5** involved palladium-catalyzed reduction of 4-acyl-1-tetralone oximes. That synthesis was limited in scope, owing to difficulties in obtaining required intermediates and the fact that by-products of reductive closure such as *trans*-amino ketones and further-reduced, bridged secondary amines usually accompanied the bridged imines. Bridged iminium salts **6** were at one time of a certain pharmacological interest;[3] hence we wished to enlarge the range of available 1,4-dihydro-1,4-ethanoisoquinolinium and related salts. This paper describes a route serving that purpose, of rather greater versatility than the first, proceeding through lactams, wherein the equivalent of a ketone group is now introduced after, rather than before, conversion of the 1-tetralone to a 1-aminotetralin.

The synthesis of requisite 1-tetralone-4-carboxylic acids **1b** as precursors of oximino esters **1d** is a matter of the very well precedented Michael addition of acrylonitrile or methyl acrylate to various phenylacetic esters and nitriles,[2,4-7] hydrolysis, either directly or *via* glutarimides, to α-arylglutaric acids, acid amides, or acid nitriles, and cyclization to tetralones, as outlined in Scheme I. A direct synthesis of α-phenylglutaric acid and anhydride, beginning with alkoxide-catalyzed monoaddition of methyl acrylate[5] to ethyl phenylacetate, was developed. The same technique worked well with some (R = methyl, aryl, and cyclohexyl) starting phenyl acetonitriles. Other compounds were cyanoethylated initially. Glutarimides, cyano esters, or dinitriles in which R = H or a small alkyl group are not especially difficult to hydrolyze completely to glutaric acids, but, when R = aryl or a hindering cycloalkyl or cycloalkylmethyl group, saponification requires drastic conditions and long periods of time. Cyclization of the glutaric acids or acid amides[7] with concentrated sulfuric acid gave tetralone acids and amides **1b** and **1a**, respectively. Contrary to one report,[8] it was found that at least some of the amides **1a** can be hydrolyzed to acids **1b** under strenuous acid conditions. Thus acids **1b** with a variety of R groups both known and novel were prepared.

Synthesis of **1b** (R = benzyl) was a special problem because all direct PPA or sulfuric acid cyclizations of α-benzyl-α-phenylglutaric acid and its derivatives led to a spiro diketone. A successful approach to the desired tetralonecarboxylic acid was found, consisting of reaction of benzyl homophthalic anhydride with acrylonitrile. In the presence of $KOCMe_3$ in THF, cyanoethylation and Dieckmann closure both occurred, giving a cyano keto acid which on acid hydrolysis af-

(1) Presented in part at the Gordon Research Conference on Heterocyclic Compounds, New Hampton, N. H., July 5, 1966.

(2) G. N. Walker and D. Alkalay, *J. Org. Chem.*, **32**, 2213 (1967), and references therein.

(3) (a) G. N. Walker, U. S. Patents 3,332,953 (1967) and 3,379,731 (1968); *Chem. Abstr.*, **68**, 59449 (1968), **69**, 96497 (1968). (b) G. N. Walker and K. Schenker, U. S. Patent 3,291,806 (1966). (c) G. N. Walker and R. B. Margerison, U. S. Patent 3,324,136 (1967). (d) W. E. Barrett and R. A. Rutledge, *Fed. Proc., Fed. Amer. Soc. Exp. Biol.*, **26**, 356 (1967).

(4) E. D. Bergman, D. Ginsburg, and R. Pappo, *Org. React.*, **10**, 179 (1959).

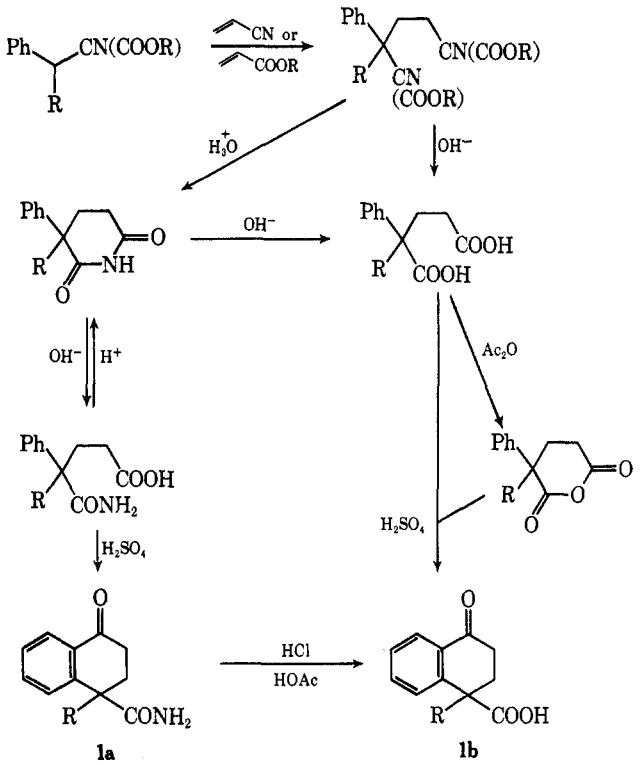
(5) L. A. Walter and R. H. Barry, U. S. Patent 2,524,643 (1950); *Chem. Abstr.*, **45**, 7154 (1951).

(6) C. F. Koelsch, *J. Org. Chem.*, **25**, 164 (1960).

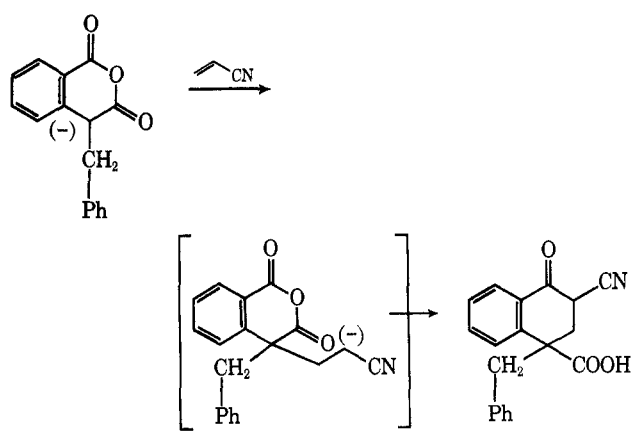
(7) K. Schenker, Belgian Patent 665,189 (1965); Netherlands Application 6,507,339; *Chem. Abstr.*, **65**, 696 (1966).

(8) W. Herz and G. Caple, *J. Org. Chem.*, **29**, 1691 (1964).

SCHEME I



forded **1b** (R = benzyl). This keto acid not only was employed as an additional intermediate in the principal series of 1,4-bridged compounds but also was converted *via* bromination of the corresponding amide[7] to the previously unreported bridged tetralone lactam corresponding to **7** (R = benzyl; R′ = H).



Esterification of the hindered acids **1b** with ethanol in the presence of both concentrated and fuming sulfuric acid conveniently afforded corresponding ethyl esters **1c**. These and certain amides **1a** were converted to corresponding oximes by standard procedures.

Palladium[2] was not suitable for hydrogenation of **1d** (R = Ph), as hydrogenolysis of the resulting amino group occurred. However, Raney nickel catalyzed hydrogenation of **1d** (R = Ph) (Scheme II) gave basic material which proved to be a mixture of both isomers **2a,b** of the amino ester. Each eventually was characterized as the hydrochloride. On standing, the crude **2a,b** (R = Ph) very slowly (weeks) deposited crystals of lactam **3** (R = Ph). This closure was accelerated by warming, and *cis*-**2a** was converted essentially completely to **3** after several days at 100°. Higher temperatures, used as a rule in isoquinuclidone closures not involving benzylamine moieties, seemed inadvisable here, since they promoted undue decomposition. The simple procedure of nickel reduction of oximino esters **1d**, followed by heating of crude amino ester **2** on a steam bath, was adopted for preparation of all the lactams **3** (Table I) from the various carbethoxytetralones. The neutral (and usually crystalline) lactams were in every case separated readily from remaining, oily *trans*-amino esters **2b**.

Another possible route to lactams **3** through hydrogenation of the oxime prepared from ketoamide **1a** (R = Ph) in the presence of nickel, gave an amino amide, but this product consisted almost entirely of the wrong (trans $NH_2/CONH_2$) isomer for lactam closure. The stereochemistry, which in fact may be owing to preferred adsorption of the polar $CONH_2$ group and its face of the molecule on the catalyst, was evident from the fact that hydrolysis of the aminoamide gave quantitatively the same amino acid as that obtained by hydrolysis of noncyclizing amino ester **2b** (R = Ph).

Ketoamide **1a** (R = Ph) and even the corresponding ketonitrile[8] could however be converted directly in one operation to lactam **3** (R = Ph) under the usual, high temperature conditions of the Leuckart reaction.[3c] Another proposed route to the bridged lactams was conversion (HBr) of the carbinol corresponding to **1a** to the bromotetralin carboxamide and internal displacement of bromo atom by amide moiety.[7] However, instead of a lactam, the bromoamide gave by HBr elimination the dihydronaphthalene amide, on treatment with sodium methoxide, sodium amide, or ammonia.

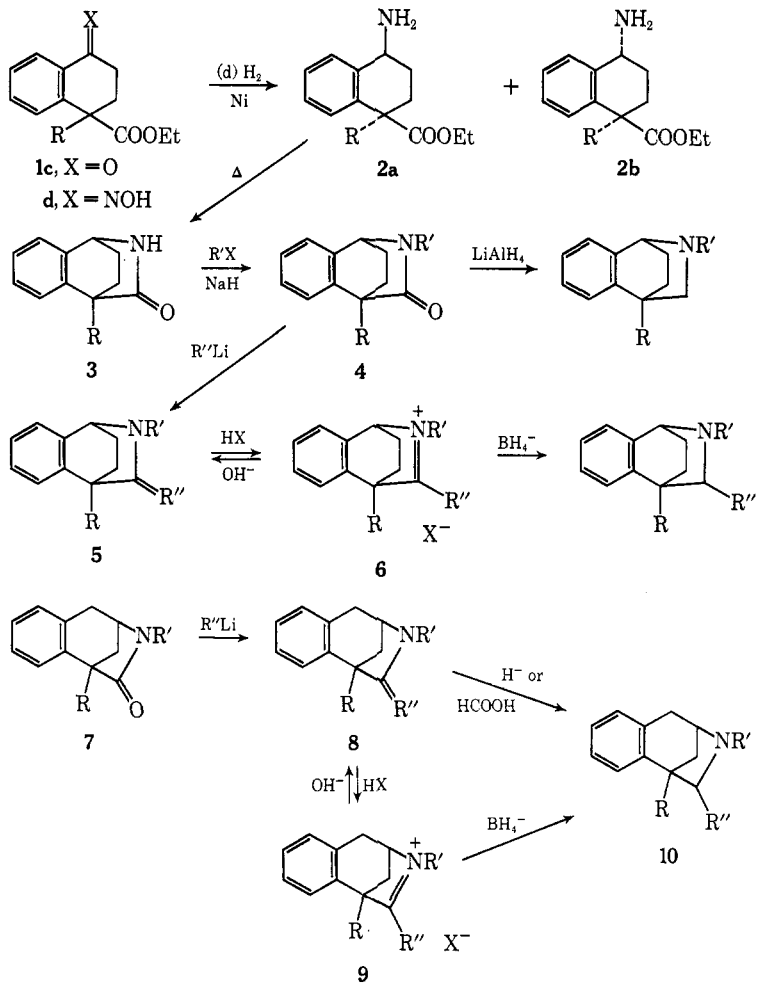
Alkylation of lactams **3** with methyl, benzyl, and other halides in the presence of NaH gave uniformly high yields of *N*-alkyl lactams **4**, also listed in Table I. Compound **4** (R = Ph; R′ = CH_3), key to the most thoroughly investigated members of the series, was identical with that lactam obtained earlier[2] by ozonolysis of enamine **5** (R = Ph; R′ = CH_3; R″ = CH_2), in turn obtained *via* the bridged imine, thus proving unequivocally the structures of the latter compounds.

Reactions of amides (particularly lactams) and nitriles with Grignard reagents[9] have sometimes been employed to synthesize imines or enamines. Except in compounds originating from lactams, there is often the disadvantage that imines, enamines, or iminium systems of common types can react further with the organometallic reagent, giving saturated amines.[10] On the other hand, conversion of phthalimidines to isoindoles, a type of enamine not susceptible to further attack by

(9) (a) R. Lukěs, *Collect. Czech. Chem. Commun.*, **2**, 531 (1930); **8**, 533 (1936); *Chem. Abstr.*, **25**, 102 (1931). (b) M. Montagne and G. Rousseau, *C. R. Acad. Sci.*, **196**, 1165 (1933). (c) L. C. Craig, *J. Amer. Chem. Soc.*, **55**, 295 (1933). (d) R. Adams and J. E. Mahan, *ibid.*, **64**, 2588 (1942). (e) J. H. Burckhalter and J. H. Short, *J. Org. Chem.*, **23**, 1278, 1281 (1958). (f) J. Knabe, *Arch. Pharm. (Weinheim)*, **298**, 257 (1965).

(10) M. Sommelet, *C. R. Acad. Sci.*, **183**, 302 (1926); H. Gilman and R. H. Kirby, *J. Amer. Chem. Soc.*, **55**, 1265 (1933), **63**, 2046 (1951); C. R. Hauser, R. M. Manyk, W. R. Brasen, and P. L. Bayless, *J. Org. Chem.*, **20**, 1119 (1955); C. R. Hauser and D. Lednicer, *ibid.*, **24**, 46 (1959); H. Boehme, H. Ellenberg, O. R. Herboth, and W. Lehners, *Ber.*, **92**, 1608 (1959); E. F. Godefroi and L. H. Simanyi, *J. Org. Chem.* **27**, 3882 (1962).

SCHEME II



carbanions, has been accomplished with alkyllithium reagents.[11]

Lactams **4**, especially those wherein R was an aryl or still more hindering group, reacted very sluggishly with excess methylmagnesium iodide; even at 100°, many hours were required to form an appreciable amount of basic product. Reaction with excess methyl-, ethyl-, or butyllithium, on the other hand, was complete in 0.5–1 hr in refluxing benzene when R was aryl or cycloalkyl and in 10–20 min at 30–50° when R was H or a small alkyl group. Moreover, under the appropriate conditions no appreciable tendency of these enamines to react further with even a large excess of the alkyllithium was observed. From **4** (R = Ph; R′ = CH_3) with CH_3MgI (low yield) and with CH_3Li (quantitatively), there was obtained enamine **5** (R = Ph; R′ = CH_3; R″ = CH_2), identical with that compound prepared earlier[2] (by action of bases on the iodomethane-quaternized, corresponding bridged imine), and converted by halogen acids to identical, corresponding iminium salts **6** (R = Ph; R′ = R″ = CH_3). The remaining *N*-alkyl lactams **4** were converted in uniformly high yields (70–90%) to corresponding enamines **5** with excess methyllithium, and thence to the varied, corresponding iminium salts **6**, listed in Table II. Two additional points of identity of products from the present method with those from the earlier route[2] were established, by synthesizing iminium salts **6** in which R = R″ = CH_3 and R′ = methyl and benzyl groups, identical with respective, earlier samples.

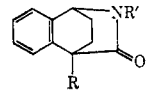
The new route *via* bridged lactams to compounds **6**, in summary, has three distinct advantages over the previous route through diketones,[2] namely (1) greater versatility in synthesis of intermediate tetralones, (2) ease of isolation of bicyclic lactams **3**, and (3) formation of enamines as virtually the only basic products in reaction of lactams **4** with alkyllithiums. Against these advantages one must set the fact that the present synthesis of **6** is longer, about eleven steps overall from available starting phenylacetic ester or nitrile.

Bridged lactams **7** (R = Ph and Et; R′ = CH_3, as well as other relatives), available[7] within our organization, were also found to react with excess methyllithium in benzene, giving bridged enamines **8** (2-methylene-1,4-methano-1,2,3,4-tetrahydro-3-benzazepines), which were converted by mineral acids in the same sense as **5** → **6** to the remaining title compounds, iminium salts **9**.

Enamines **8** appeared to be more readily oxidized by air and reduced by hydrides than were enamines **5**. This premise, founded on qualitative observations, was borne out by the fact that iminium formate **9** (R = Ph; R′ = R″ = CH_3; X = $HCOO^-$) on heating to

(11) G. Wittig and H. Streib, *Justus Liebigs Ann. Chem.*, **584**, 1 (1953); G. Wittig, G. Closs and F. Mindermann, *ibid.*, **594**, 89 (1955); W. Theilacker and H. Kalenda, *ibid.*, **584**, 87 (1953); W. Theilacker and W. Schmidt, *ibid.*, **597**, 95 (1955), and **605**, 43 (1957).

TABLE I
1,4-ETHANO-1,2,3,4-TETRAHYDRO-3-ISOQUINOLONES[a]



R	R′	Registry no.	Ir, C=O, λ_{max} (μ)	Mp, °C
C_6H_5	H	2997-32-2	5.97	268–270
C_6H_5	CH_3	2997-33-3	6.01	198–201
C_6H_5	$(CH_2)_2NMe_2$	27239-94-7	6.02	127–128
H	H	3118-16-9	5.98-6.10	200–201
H	CH_3	3118-05-6	6.00	133–135
CH_3	H	3118-20-5	5.98-6.06	165–166
CH_3	CH_3	2959-77-5	6.03	113–114
CH_3	$-CH_2C_6H_5$	27239-99-2	6.02	Oil
H	$-CH_2C_6H_5$	3036-51-9	6.02	86–87
Et	H	3118-03-4	6.0-6.02	164–165
Et	CH_3	2959-78-6	6.06	82–83
Et	$CH_2C_6H_5$	27240-03-5	6.05	85–88
c-C_5H_9	H	3195-56-0	5.98	157–158
c-C_5H_9	CH_3	2959-80-0	6.03	94–95
c-$C_6H_{11}CH_2$	H	3118-17-0	5.97	186–187
c-$C_6H_{11}CH_2$	CH_3	3118-06-7	5.97	71–73
p-PhF	H	3118-18-1	6.02	291–293
p-PhF	CH_3	3118-07-8	6.03	229–231
p-PhF	$CH_2C_6H_5$	27240-10-4	6.04	191–193
$-CH_2COOEt$	H	27240-11-5	5.98 (5.75)	123–124
$-CH_2COOEt$	CH_3	27240-12-6	5.99 (5.73)	Oil
$-(CH_2)_2COOEt$	H	3118-19-2	5.98 (3.13, 5.75)	123–124
$-(CH_2)_2COOEt$	CH_3	3118-08-9	6.02	Oil
$-CH_2C_6H_5$	H	3118-04-5	5.96	188–190
$CH_2C_6H_5$	CH_3	2959-79-7	6.01	126–128

[a] Satisfactory analyses (±0.4% for C, H, N) were obtained with all compounds listed in tables: Ed.

100° effervesced,[12] and there was isolated amine **10** (R = Ph; R′ = R″ = CH_3), the same as that obtained by $NaBH_4$ reduction of either **8** or **9**. The analogous 1,4-bridged iminium formate **6** (R = Ph; R′ = R″ = CH_3; X = $HCOO^-$) was not reduced under the same conditions, although **5** and **6** are in general reduced by hydrides to corresponding bridged amines.[2,3]

Experimental Section[13]

1-Amino-4-ethoxycarbonyl-4-phenyltetralin (2, R = Phenyl).—Hydrogenation of 24.4 g of 1-oximino-4-ethoxycarbonyl-4-phenyltetralin[2] in 200 ml of ethanol in the presence of 15 g (water and alcohol washed) of commercial Raney nickel, for 4 hr at 60°, resulted in absorption of 2.06 molar equiv of H_2 (13-lb pressure drop). Filtration and evaporation of the solvent gave (100%) a crude, isomeric mixture of amino esters. The material was soluble in dilute HCl.

From the solution of a sample of freshly prepared amine in dry ether with ethanolic HCl, there was precipitated a sample of **2a** (cis NH_2/COOEt) **hydrochloride.** Recrystallization (methanol–ether) gave colorless crystals: mp 187–189°; ir 5.81 μ; uv 265 nm (ε 430); soluble in dilute HCl.

Anal. Calcd for $C_{19}H_{21}NO_2 \cdot HCl$: C, 68.77; H, 6.68; N, 4.22. Found: C, 68.52; H, 6.65; N, 4.13.

From ether solution of mother liquors left after thermal closure to lactam (see following experiment) and maximal removal of that product, there was similarly obtained **2b** (trans NH_2/COOEt) **hydrochloride:** mp 246–248° (from ether); ir 5.77 μ.

Anal. Calcd for $C_{19}H_{21}NO_2 \cdot HCl$: C, 68.77; H, 6.68; N, 4.22. Found: C, 68.48; H, 6.68; N, 4.22.

Closure to Lactam 3 (R = C_6H_5).—Crude amino ester (29 g, mixture of isomers) from the preceding reduction was heated on a steam cone for 5 days; each day the crystalline lactam which had formed was collected and washed with ether, and the filtrate was evaporated and returned to the steam cone, until crystals no longer formed on heating the oil. There was accumulated a total of 10.8 g (44%) of crystals, in four crops: mp 268–270°, not raised on further recrystallization from ether or methanol; ir 3.16 and 5.97 μ; uv 257 nm (ε 390); insoluble in dilute acids.

Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.0; H, 6.18; N, 5.62.

The lactam was also isolated, in lower yield, from samples of crude amino ester which had been allowed to stand at room temperature several weeks.

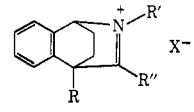
Other **4-substituted 1,2,3,4-tetrahydro-1,4-ethanoisoquinolin-3-ones**, listed in Table I, were prepared from the appropriate 4-carbethoxytetralone oximes by essentially the same two-step (reduction, 100° thermal closure) procedure, in yields of 20–40% and never exceeding 50%, except in the case of the 4-unsubstituted lactam (R = R′ = H) in which adsorption of R = H oximino ester with the carbethoxy group oriented away from surface of catalyst appeared to be particularly favored.

2-Methyl-4-phenyl-1,4-ethano-1,2,3,4-tetrahydro-3-isoquinolone (4, R = C_6H_5; R′ = CH_3).—A suspension of 7.1 g of **3** (R = C_6H_5) and 3.5 g of 56% NaH (oil) in 500 ml of toluene was refluxed and stirred 0.5 hr, cooled, treated with 30 ml of iodomethane, and stirred and refluxed 9 hr longer. The cooled, filtered, ether-diluted, twice water-washed, dried ($MgSO_4$), and evaporated organic solution gave on ether trituration 7.1 g of crystals: mp 198–201°, raised on recrystallization to mp 198.5–201.5°; ir 6.01 μ; uv 246 nm (ε 410). The sample was identical (ir, mixture melting point undepressed) with that obtained as described earlier[2] by ozonization of enamine **5** (R = C_6H_5; R′ = CH_3; R″ = H).

(12) Mechanism of the Leuckart reaction: P. L. deBenneville and J. H. MacCartney, *J. Amer. Chem. Soc.*, **72**, 3725 (1950); D. S. Noyce and F. S. Batchelor, *ibid.*, **74**, 4577 (1952); N. J. Leonard and R. R. Sauers, *ibid.*, **79**, 6210 (1957); A. G. Cook, W. C. Meyer, K. E. Ungrodt, and R. H. Mueller, *J. Org. Chem.*, **31**, 14 (1966).

(13) Calibrated melting points were obtained using a Thomas–Hoover silicone oil bath, infrared spectra (Nujol mulls, unless otherwise noted) were recorded with Perkin-Elmer double beam instrument, and ultraviolet spectra (methanol solutions, unless otherwise stated) were measured by Cary recording spectrophotometer. Hydrogenations were performed on the standard Parr shaker apparatus having a 4-l. reserve tank.

TABLE II
1,4-DIHYDRO-1,4-ETHANOISOQUINOLINIUM HALIDES



R	R′	R″	X⁻	Registry no.	Ir, C=O, λ_{max} (μ)	Mp, °C
H	CH_3	CH_3	Cl	2959-86-6	6.01	259–261[a]
H	CH_3	CH_3	I	3956-71-6	6.01	217.5–219.5
H	$CH_2C_6H_5$	CH_3	I	2959-90-2	6.08	169–170
C_6H_5	CH_3	Et	I	2997-37-7[c]	6.05	235–237 dec
			Cl	2997-36-6[d]	6.07	239–241 dec
C_6H_5	CH_3	*n*-Bu	Cl	2997-35-5	6.06	242–244[a]
Et	CH_3	CH_3	I	3063-67-0	6.06	*ca.* 140 dec
Et	$CH_2C_6H_5$	CH_3	I	27240-22-8	6.12	205–207
Cyclopentyl	CH_3	CH_3	I	3123-64-6[c]	6.09	213–216[b]
			Cl	2959-92-4[d]	6.08	243–244[b]
$c\text{-}C_6H_{11}CH_2$	CH_3	CH_3	Cl	3036-53-1	6.06	236–238.5
$p\text{-}FC_6H_5$	CH_3	CH_3	I	3022-26-2[e]	6.03	277–278
	$CH_2C_6H_5$	CH_3	I	27298-29-9[f]	6.13	246–247
$-CH_2C(OH)(CH_3)_2$	CH_3	CH_3	I	27240-27-3	6.10 (3.02)	200–201
$-(CH_2)_2C(OH)(CH_3)_2$	CH_3	CH_3	I	2959-87-7	6.10 (3.03)	188.5–190
$CH_2C_6H_5$	CH_3	CH_3	I	2959-91-3	6.09	239–240 dec

[a] Hemihydrate. [b] Monohydrate. [c] The iodide. [d] The chloride. [e] R′ = Me. [f] R′ = $CH_2C_6H_5$

The remaining *N*-alkyl lactams (R′ = methyl, benzyl, and $CH_2CH_2NMe_2$) of Table I were prepared by the same procedure, essentially quantitatively, with appropriate minor modification (extraction with HCl and reprecipitation with NaOH) in work-up procedure for the basic compound and use of ligroin (bp 39–53°) or hexane in recrystallizing the compounds of mp *ca.* 110° or below, and methanol or methanol–ether for others.

2-Methyl-3-methylene-4-phenyl-1,4-dihydro-1,4-ethanoisoquinoline (5, R = Phenyl; R′ = CH_3; R″ = CH_2) and Corresponding Iminium Salts (6, R″ = CH_3).—A solution of 5 g of 4-phenyl-*N*-methyl lactam from the preceding experiment in 750 ml of dry benzene was treated with 120 ml of methyllithium–ether solution (1.92 *M*) and refluxed 1 hr, during which time the solution became yellow and a heavy, white precipitate formed. The cooled mixture was treated with ice and water, and ether was added; the organic layer was washed twice with water and extracted with two portions (50 ml) of ice-cold, 18% hydrochloric acid. Gradual addition of cold 15–20% NaOH to the chilled, acid solution gave the enamine as colorless oil. In this instance, the enamine crystallized, after a short while. The collected, water-washed, air-dried crystals (5 g) had mp 168–172.5°. Recrystallization from ether gave a sample, mp 172–175°; mmp (with the same enamine) 171–175° prepared as described earlier (by action of base on methyliminium iodide from imine with iodomethane)[2] was undepressed, and ir (6.18, shoulder 6.21 μ) and uv (inflection 228 nm, ε 4670) were identical with those of the earlier sample.

The **iminium chloride sesquihydrate**, colorless crystals from ethanol–ether, mp 242–243°, and **iminium iodide monohydrate**, mp 245–247°, were prepared from the enamine using ethereal, ethanolic HCl and aqueous, ethanolic HI, respectively, and the samples of these salts were also respectively identical (mixture melting point, spectra) with those prepared *via* the earlier route[2] through 4-acetyl-4-phenyl-1-tetralone.

Two other enamines (2-methyl-3-alkylidene-4-aryl-1,4-ethano-1,2,3,4-tetrahydroisoquinolines), from reaction of 4-aryl-substituted 2-methyl-bridged lactams **4** with appropriate alkyllithium reagents according to the foregoing procedure, were obtained in crystalline form during the course of this work.

Compound 5 (R = phenyl; R′ = CH_3; R″ = $CHCH_3$) was crystallized from ether, mp 107–109°, ir 6.04 μ.

Anal. Calcd for $C_{20}H_{21}N$: C, 87.22; H, 7.69; N, 5.09. Found: C, 87.47; H, 7.86; N, 5.11.

Compound 5 (R = *p*-fluorophenyl; R′ = CH_3; R″ = CH_2) was crystallized from ether, mp 146–148°, ir 6.15 μ.

Anal. Calcd for $C_{19}H_{18}FN$: C, 81.69; H, 6.49; N, 5.02. Found: C, 81.72; H, 6.48; N, 4.92.

All remaining enamines **5** prepared were colorless or yellowish oils, most of then sensitive to air oxidation or apparent polymerization. The smaller the substituent R at position 4, the less stability they appeared to possess, judging from various qualitative observations made in the course of work-up and isolating individual compounds.

2-Benzyl-3,4-dimethyl-1,4-dihydro-1,4-ethanoisoquinolinium Bromide and Iodide (6, R = R″ = CH_3; R′ = $CH_2C_6H_5$; X = Br and I).—A solution of 1.2 g of crude lactam **4** (R = CH_3; R′ = $CH_2C_6H_5$) in 50 ml of benzene was treated with 15 ml of 1.92 *M* methyllithium–ether solution. After a 10-min reflux, the solution was allowed to stand overnight and then poured into ice and water. The basic fraction was isolated as in the preceding experiment. The crude enamine was a pale yellow, air-sensitive oil, and thus, after its extraction with ether, the ether solution was washed twice with water, dried (K_2CO_3), and concentrated *in vacuo* to a volume of 200 ml, and half of the solution was used to prepare each iminium salt.

A slight excess of saturated, ethanolic HBr solution precipitated the **bromide** initially as an oil, crystallizing after being washed (by decantation) with ether and rubbing with ether–ethanol, as 0.5 g of colorless crystals: mp 233–235° dec; mmp (with the same compound prepared as described earlier[2]) 234–236° dec (undepressed); and ir (6.08 μ) and uv (224–231 nm, ε 3450) identical.

Treatment of the remaining ether solution of enamine with a slight excess of a solution of 1.8 ml of concentrated HI in 5 ml of ethanol gave the iminium **iodide** (0.8 g), crystallizing in ethanol: mp 215–217° dec; ir 6.11 μ; uv 206–208 nm (ε 21,130) with inflection 220 mn (ε 17,290); also identical (mixture melting point, spectra) with an earlier sample.[2]

2,3,4-Trimethyl-1,4-dihydro-1,4-ethanoisoquinolinium Iodide (6, R = R′ = R″ = CH_3; X = I).—Reaction of 0.8 g of **4** (R = R′ = CH_3) in 50 ml of benzene with 15 ml of 1.92 *M* methyllithium–ether solution at 45° for 5 min and at room temperature overnight, followed by work-up as described in the preceding experiment to obtain enamine in a dried (K_2CO_3) ether solution, and treatment with 20% HI aqueous ethanolic solution gave 1 g of solvated crystals, mp *ca.* 179–184°. Recrystallization from acetone–ether and ethanol–ether and drying *in vacuo* gave colorless crystals, mp 213–215° dec; mixture melting point with an earlier sample of the same iodide[2] was undepressed and ir spectra (6.06 μ) of the two samples were identical.

The foregoing experiments suffice to indicate the general method (and its slight modifications) used in preparing the remaining iminium salts **6**, recrystallized as a rule from ethanol or ethanol–ether, listed in Table II, from the appropriate lactams **4**. An excess of the alkyllithium was invariably used, temperature and time of reaction being the critical factors rather than amount of reagent.

Compound 5 (R = Ph; R′ = CH_3; R″ = CH_2) was also prepared by heating a solution of 1.7 g of **4** (R = phenyl; R′ = CH_3) and CH_3MgI (prepared from 1.2 g of Mg) in 220 ml of dry

toluene at 100–110° for 16 hr. The chilled suspension was treated with dilute acid, and the aqueous layer chilled and made basic with K_2CO_3. The crude base, isolated in small amount (0.2 g) by extraction with ether, washing with water, drying (K_2CO_3), and evaporating the ether, was identified as the same enamine obtained by reaction of CH_3Li with the same lactam, by ir and by conversion to the iminium chloride sesquihydrate,[2] mp 239–241° dec, mixture melting point undepressed, and ir spectra identical.

From the neutral fraction of the above reaction, there was recovered 0.7 g of starting *N*-methyl-4-phenyl lactam.

2-Methyl-4-phenyl-1,4-ethano-1,2,3,4-tetrahydroisoquinoline.—Reduction of 3.9 g of lactam **4** (R = Ph; R′ = CH_3) with 12.5 g of lithium aluminum hydride in 1 l. of THF, stirring and refluxing 6 hr, or reduction of 2.1 g of the same lactam with 1.3 g of $LiAlH_2(OEt)_2$ in 250 ml of 1:1 THF–toluene for 3 hr (reflux), and the usual isolation of basic product gave in each case (crude yields 3.7 and 1.7 g, respectively) the same, partly crystalline, amine. Recrystallization of the separated crystals directly, from ether, afforded a sample of the **hemihydrate**, mp 205–215°.

Anal. Calcd for $C_{18}H_{19}N \cdot {}^1/_2H_2O$: C, 83.68; H, 7.80; N, 5.42. Found: C, 83.31; H, 7.62; N, 5.23.

Material which had been dissolved in dilute HCl and recovered by addition of cold NaOH solution was oily initially but crystallized in ether–ligroin giving colorless crystals of the amine, mp *ca.* 88–100°, changed on recrystallization to mp 86–88°.

Anal. Calcd for $C_{18}H_{19}N$: C, 86.70; H, 7.68; N, 5.62. Found: C, 86.00; H, 7.99; N, 5.91.

The corresponding **hydrochloride**, from ether–ethanol, had mp 272–275° dec and appeared, even after drying, to be slightly solvated.

Anal. Calcd for $C_{18}H_{19}N \cdot HCl$: C, 75.64; H, 7.05; N, 4.90. Found: C, 75.08; H, 7.15; N, 4.73.

The corresponding **methiodide**, prepared by a 15-min reflux of a sample of the crude base with iodomethane in ethanol and recrystallized from ether–ethanol, had mp 237–239° dec.

Anal. Calcd for $C_{19}H_{22}IN$: C, 58.32; H, 5.67; N, 3.58. Found: C, 58.04; H, 5.68; N, 3.55.

1-Phenyl-1,2,3,4-tetrahydro-4-oximinonaphthalene-1-carboxamide (**1a**, **R = Ph, Oxime**).—An ethanol solution of 5 g of ketoamide **1a** (R = Ph) together with hydroxylamine (prepared from 2.5 g of $H_2NOH \cdot HCl$ in 5 ml of water and a slight excess of cold NaOH solution) was refluxed 15 min, treated with a small amount of water, and chilled. The product was collected, washed with water, dried, and recrystallized from methanol: colorless crystals; mp 235–237°; ir 2.91, 3.23 and 5.98 μ.

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.74; N, 9.99. Found: C, 72.76; H, 5.93; N, 9.51.

4-Amino-1-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxamide.—Hydrogenation of 3.8 g of oximinoamide from the preceding experiment in 150 ml of ethanol with a teaspoon of washed Raney nickel at 60° until H_2 absorption ceased, filtration, evaporation, and ether trituration gave 3.0 g of colorless crystals, mp 169–171°, raised on recrystallization (ethyl acetate) to mp 170–172°. The compound was soluble in aqueous acids.

Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.82; H, 6.92; N, 10.58.

The aminoamide showed no sign of change on prolonged heating at 100° and lost NH_3 only when heated to 240–280°; from the glassy residue remaining after the latter treatment, no crystalline compounds could be isolated.

Hydrolysis of a sample of the aminoamide (concentrated HCl, 10-hr reflux) gave, after evaporation of excess reagent and recrystallization from water, the corresponding **amino acid hydrochloride**, as hygroscopic, colorless crystals, mp *ca.* 240° dec. Spectrally (ir 5.89 μ and very strong OH and NH bands) identical material was obtained by similar hydrolysis of crude amino ester **2b**, *i.e.*, the residual amine remaining after closure to lactam **3** (R = Ph).

4-Hydroxy-1-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxamide.—Portionwise, addition of 8 g of $NaBH_4$ to a suspension of 5 g of **1a**, R = Ph, in methanol, and 1 hr heating on a steam cone, followed by addition of water to the concentrated solution, gave crystals which were collected, washed with water, and dried. Recrystallization from ethanol–ethyl acetate gave a sample with mp 198.5–200° and ir 2.86, 2.99–3.10, and 6.02 μ, evidently one of the two possible isomers resulting in this reaction.

Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.62; H, 6.60; N, 5.27.

1-Phenyl-1,2-dihydronaphthalene-1-carboxamide.—Treatment of a dry benzene solution of crude, dry amide from the preceding experiment with anhydrous HBr, and isolation of **4-bromoamide** (by washing with $NaHCO_3$ solution and water, drying over $MgSO_4$ and evaporating) as a colorless, Beilstein-positive solid, mp *ca.* 145–150° dec, was followed by exploratory experiments along familiar lines using various bases. Several of these, notably treatment with $NaNH_2$ in toluene (2 hr at 100°), gave isolable amounts of colorless crystals: mp 172–173° (from ether); ir NH bands and 5.96 μ; uv 206, 261, and 264 nm (ϵ 25,210, 7960, and 7480, respectively).

Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.92; H, 6.23; N, 5.59.

1-Phenyl-2,3-dimethyl-1,4-methano-4,5-dihydro-1*H*-3-benzazepinium Chloride (**9**, **R = Ph**; **R′ = R″ = CH_3**; **X = Cl**).—A solution of 2.0 g of lactam **7** (R = Ph; R′ = CH_3)[7] in 100 ml of benzene was treated with 19 ml of 1.92 *M* methyllithium–ether, and the solution was refluxed for 1 hr, then chilled and poured over ice, and the ether-diluted, organic layer was washed twice with water and extracted with three 10-ml portions of 18% HCl. The chilled, aqueous solution was made basic by addition of NaOH solution, and the oily enamine extracted with ether. Evaporation of the water-washed and dried (K_2CO_3) ether solution *in vacuo* to 100 ml, followed by addition of just enough ethanolic HCl to cause complete precipitation of the salt, afforded 2.0 g of dense, pale yellow crystals, mp 148–152° dec, raised on further recrystallization (ethanol–ether) to mp 149.5–152° dec, which, after drying at room temperature, proved to be the **sesquihydrate**: ir 5.99 μ and an OH band indicating water of crystallization; uv 259 nm (ϵ 3960) and inflection 284 (2620).

Anal. Calcd for $C_{19}H_{20}ClN \cdot {}^3/_2H_2O$: C, 70.25; H· 7.14. N, 4.31. Found: C, 70.35; H, 6.98; N, 4.34.

In another experiment, 3 g of lactam and 35 ml of methyllithium (2 *M*) gave enamine which was converted by 10% aqueous, alcoholic HI to 3.8 g of the corresponding iminium **iodide**. Recrystallization from ethanol gave yellowish crystals: mp 265–267° dec; ir 6.02 μ; uv 211 and 258 nm (ϵ 28,700 and 3900, respectively) and inflection 289 (2250).

Anal. Calcd for $C_{19}H_{20}IN$: C, 58.62; H, 5.18; N, 3.60. Found: C, 58.77; H, 5.45; N, 3.61.

Iminium Salt 9 (**R = Et**; **R′ = R″ = CH_3**; **X = I**).—Reaction of 2.4 g of lactam **7** (R = Et; R′ = CH_3)[7] in 100 ml of benzene with 15 ml of 1.92 *M* methyllithium solution was conducted at 45° for 2 min, and the solution was let stand (air absent) overnight. Isolation of basic product as in the preceding experiment gave enamine as a yellow, quite air-sensitive oil. Immediate conversion to the iodide using a slight excess of *ca.* 10% aqueous, alcoholic HI afforded 3.4 g of yellow crystals, mp 249–251° dec. Recrystallization from methanol–ether gave a pure sample as colorless crystals: mp 253–254° dec; ir 6.01 μ; uv 216 and 255 nm (ϵ 19,500 and 2650) with inflection 280 (1800).

Anal. Calcd for $C_{15}H_{20}IN$: C, 52.79; H, 5.91; N, 4.11. Found: C, 52.78; H, 5.99; N, 4.08.

Additional, and more complex, examples of preparation of compounds **9** have been described elsewhere.[8b] However, all attempts to prepare ethylidene amines and salts **9** with R″ = Et, using ethyllithium, were unsuccessful.

Reductions of 9 (R = Ph; R′ = R″ = CH_3) and Corresponding Enamine 8.—A. Sodium borohydride was added in portions to a suspension of the iodide (3.2 g) in methanol (350 ml), and the resulting solution was warmed 1.9 hr on a steam cone, evaporating most of the solvent. The residue, treated with water, gave oily base, ether extract of which after washing (H_2O), drying ($MgSO_4$), and evaporation, gave 1.4 g of amine. Conversion to the corresponding **10** (R = Ph; R′ = R″ = CH_3) **hydrochloride** by addition of ethanolic HCl to an ether solution, and recrystallization from ethanol–ether afforded colorless crystals, mp 294–296° dec. The analytical sample, after drying *in vacuo*, had mp 300–301° dec; ir devoid of C=N band; uv 258 nm (ϵ 380).

Anal. Calcd for $C_{19}H_{21}N \cdot HCl$: C, 76.11; H, 7.40; N, 4.67. Found: C, 76.10; H, 7.59; N, 4.77.

B. Formic acid (2 ml, 98–100%) was added to 1 g of enamine **8** (R = Ph; R′ = CH_3; R″ = CH_2) (prepared directly from 1.1 g of lactam or regenerated from the corresponding iminium salt by treatment with NaOH solution and ether extraction). The iminium formate solution, heated at 100° for 0.5 hr, effervesced slowly. Treatment with water and dilute NaOH and isolation of the base as usual by ether extraction gave crude, yellowish oil. The amine was converted to the hydrochloride and re-

crystallized from ethanol–ether: colorless crystals, mp 295–297° dec; mixture melting point with hydrochloride sample from part A was undepressed; ir and uv spectra were identical; and analytical results on a dried sample were virtually the same as in part A.

Sodium borohydride reductions of other, more complex analogs of **9**,[3b] as well as compounds **5** and **6**,[2] to corresponding bridged amines, were reported previously.

α-Phenylglutaric Anhydride.—A. Methyl acrylate addition (86 g) during 5 min to a solution of 164 g of ethyl phenylacetate and dry sodium ethoxide (prepared from 4.6 g of sodium) in 1 l. of *tert*-BuOH and 1.5-hr standing, followed by treatment with ice and water and isolation of neutral product, gave 240 g of crude diester. B. Hydrolysis by 9 hr of reflux with 2300 ml of 15% KOH, followed by acidification of ether-washed, basic solution, gave 194 g of crude **α-phenylglutaric acid**. C. Conversion to the **anhydride**, by refluxing 1 hr with 200 ml of acetic anhydride, removal of excess reagent, and distillation *in vacuo* gave 107.6 g (56% overall): bp 170–180° (0.6 mm); mp 95–96°; ir 5.56 and 5.70 μ (lit.[14] mp 95–96°).

α-Methyl-α-phenylglutaric Acid.—A. Alkylation of 115 g of phenylacetonitrile in benzene (800 ml) in the presence of 43 g of $NaNH_2$ was carried out by adding 69 ml of iodomethane during 15 min to the stirred, ice-chilled suspension. After 6-hr stirring, during which time the mixture was allowed to warm gradually to room temperature, the neutral product was isolated as usual, by addition of water and evaporation of the water-washed, dried ($MgSO_4$) organic solution.

B. Methyl acrylate (93 ml) addition to the crude product of A (112 g) in 350 ml of *tert*-BuOH during 5 min, in the presence of 15 ml of 40% benzyltrimethylammonium methoxide solution, 3 hr of standing, addition of water, and isolation of the neutral product gave 148 g of crude cyano ester.

C. Hydrolysis of the crude oil from B by 14 hr of reflux and stirring with 2 l. of 30% KOH solution, until NH_3 was no longer evolved, and acidification of the ether-washed, basic solution, gave 161 g of crude diacid. A sample, recrystallized from ether, had mp 132–134°, ir 5.91 μ.

Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.61; H, 6.44.

The corresponding **anhydride** was prepared by 1.3-hr reflux of 41 g of diacid with 100 ml of acetic anhydride, followed by removal of excess reagent, distillation *in vacuo*, and recrystallization from ether: 18 g; bp 163–166° (1.45 mm); mp 81–82°; ir 5.55 and 5.68 μ.

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.60; H, 5.78.

α,α-Diphenylglutaric Acid.—This acid was obtained in four ways, as follows. A. Hydrolysis of α,α-diphenylglutaronitrile (98 g, mp 73–74°, prepared by cyanoethylation of diphenylacetonitrile in the presence of Triton B methoxide in tetrahydrofuran) with 545 g of potassium hydroxide in 660 ml of water, refluxing and stirring 4 days, and acidification of the ether-washed solution gave 91.5 g of diacid, mp 180–190°, after washing with water and air drying, suitable for use in cyclizations. A sample, recrystallized from ethyl acetate, had mp 199–200.5° (lit.[15] mp 193–195°), ir 5.80–5.84 μ.

B. Addition of methyl acrylate (72 g) to diphenylacetonitrile (250 g) in 1 l. of tetrahydrofuran in the presence of 40 ml of 40% Triton B methoxide, and hydrolysis of the resulting, crude cyano ester by refluxing 3 days with 3 l. of 30% potassium hydroxide solution, followed by filtration to remove 35 g of neutral material and acidification, gave 127 g of the diacid, mp 190°, suitable for further work.

C. Cyanoethylation of ethyl diphenylacetate (11.6 g) in the presence of dry sodium methoxide (prepared from 0.1 g of sodium) in 100 ml of tetrahydrofuran, using 2.7 g of acrylonitrile and warming at 65° for 1 hr, gave 4 g of crude cyano ester; hydrolysis with 200 ml of 20% potassium hydroxide solution and sufficient ethanol to dissolve the material (4-hr reflux) gave 3.9 g of diacid, mp 195–199°.

D. α,α-**Diphenylglutarimide** was obtained quantitatively by refluxing α,α-diphenylglutaronitrile for 4 hr with equal parts of concentrated hydrochloric and glacial acetic acids [mp 162.5–164° (lit.[15] mp 158–159°); ir 3.15, 3.24, 5.82, and 5.88 μ] and was hydrolyzed by prolonged reflux with 30% potassium hydroxide solution to give the diacid, melting point and spectra the same as in parts A and B.

α-Cyclopentyl-α-phenylglutarimide.—A. Cyanoethylation of 171.5 g of α-cyclopentylphenylacetonitrile[16] in 2 l. of *tert*-butyl alcohol in the presence of dry sodium methoxide (from 5.3 g of sodium) was carried out by adding 67 ml of acrylonitrile and, after the period of spontaneous reaction in which the temperature reached 43°, heating to 70° for 2 hr. The crude dinitrile, isolated as usual, did not crystallize and was used without purification in the next step.

B. Hydrolysis and imide formation were carried out by refluxing the crude product from A in 600 ml each of concentrated hydrochloric and glacial acetic acids for 6.5 hr. Removal of most of the acids *in vacuo*, and treatment of the residue with water gave an oil which was extracted with ether. The ether solution was washed with dilute sodium hydroxide solution and with seven portions of water and dried ($MgSO_4$). Upon evaporation to a smaller volume, the ether solution deposited 175 g of crystals: mp (after recrystallization from ether) 108.5–110°; ir 3.12 and 5.83–5.92 μ.

Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 75.06; H, 7.50; N, 5.24.

Corresponding Acid Amide.—After heating 175 g of glutarimide from the preceding experiment with 1300 ml of 30% potassium hydroxide solution for a week (90–100°), diluting with water, and acidifying, the crude products were extracted with ether. The water-washed and dried ($MgSO_4$) solution, on evaporation to a smaller volume and addition of a small amount of ethyl acetate, deposited 54.5 g of crystals: mp 157–160°, raised on recrystallization from ethanol–ether to mp 161–162°; ir 2.91, 5.89, and 6.09 μ.

Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.83; H, 7.85; N, 5.05.

The material remaining in the ether–ethyl acetate solution consisted mainly of the crude, **corresponding diacid** isolated as an oil (135 g) which still contained some of the acid amide. Further hydrolysis of this material with 1 l. of 30% KOH solution at 90–100° for 3 weeks finally removed nitrogen completely and afforded the diacid in suitable condition for further work, as a viscous oil, ir 5.88 μ (broad, unresolved doublet). The **corresponding anhydride**, ir 5.52 and 5.66 μ, was prepared by reaction of the diacid with acetic anhydride, but could not be induced to crystallize.

α-(Cyclohexylmethyl)-α-phenylglutarimide.—A. Alkylation of phenylacetonitrile (117 g) with cyclohexylmethyl bromide (194 g) in the presence of 43 g of sodium amide in 1.2 l. of toluene (refluxed and stirred 3.5 hr) gave 130 g of crude product,[16] an oil which still contained some phenylacetonitrile.

B. Methyl acrylate (60 ml) was added in portions to the crude product from A and 15 ml of 40% Triton B methoxide solution in 350 ml of *tert*-butyl alcohol, and after the exothermic period the solution was refluxed 1 hr. After isolation in the usual way, the crude material was converted without purification to the corresponding glutarimide.

C. Hydrolysis and imide formation. The crude material from part B (190 g), 600 ml of concentrated HCl, and 900 ml of glacial acetic acid were refluxed 3.5 hr. After removal of excess reagents *in vacuo* and treatment with water, the crude, partly crystalline material was collected and triturated with ether. The yield of α-cyclohexylmethyl-α-phenylglutarimide, mp 146–150°, was 48 g. Recrystallization from methanol raised the melting point to 150–151°, ir 3.11 and 5.81–5.89 μ.

Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.75; H, 8.12; N, 4.91. Found: C, 76.46; H, 8.22; N, 4.94.

The **corresponding acid amide** was obtained by 8 hr of reflux of 34.5 g of glutarimide with 600 ml of 30% KOH solution, followed by acidification: yield, 35.5 g of crystals; mp 210–215°, raised on recrystallization (methanol) to 225–226°; ir 2.89, 3.14, 5.88, and 6.10 μ.

Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.25; H, 8.31; N, 4.62. Found: C, 71.25; H, 8.21; N, 4.62.

α-Cyclohexyl-α-phenylglutaronitrile.—Acrylonitrile (1.9 g) in tetrahydrofuran (5 ml) was added slowly to a cooled (20–30°) solution of 7.9 g of α-cyclohexylphenylacetonitrile[16] in tetrahydrofuran (25 ml) in the presence of 1.1 ml of 40% Triton B solution. After standing 3 hr, the chilled, evaporated, and acidified solution was treated with water and the product isolated

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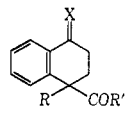
TABLE III
INTERMEDIATE TETRALONES AND DERIVATIVES[a]



R	R′	X	Registry no.	Mp, °C	Ir (μ) data
H	OEt	NOH	3118-23-8		5.82, 6.15
		=NNHCONH$_2$	3118-22-7	179–180	
CH$_3$	OH	O	3123-55-5	123–124	5.80, 5.87–5.92
C$_2$H$_5$	OEt	=DNP	20016-45-9	181–182	
C$_6$H$_5$	NH$_2$	O	2997-28-6	192–193	
	OEt	O	3389-98-8	89.5–91	
c-C$_5$H$_9$	NH$_2$	O	3123-63-5	110–112	5.95
					6.03
	OH	O	3123-62-4	113–115	5.85, 6.08
	OEt	=DNP	27240-37-5	167–169	
	OEt	NOH	3118-30-7	134–135	5.79
c-C$_6$H$_{11}$CH$_2$	NH$_2$	=DNP	3123-65-7	235–236	
	NH$_2$	NOH	3123-49-7	177–178	
	OH	O	3196-54-1	105–108	
	OEt	NOH	3118-24-9		5.77–5.84, 6.12
p-PhF	OH	O	3345-77-5	158–159	5.79, 6.05
	OEt	O	3118-11-4	112–113	5.80, 5.97
	OEt	NOH	3118-25-0	96–98	5.79
CH$_2$COOH	OH	=DNP	27249-17-8	238–240 dec	
CH$_2$COOEt	OEt	=DNP	27249-18-9	126–128	5.75, 6.13
CH$_2$CH$_2$COOEt	OEt	NOH	3195-61-7		5.76, 6.12
CH$_2$C$_6$H$_5$	OH	=DNP	3123-60-2	273–275 dec	
	OEt	=DNP	3118-29-4	165–167	
	OEt	NOH	3118-28-3	85–87	

[a] =DNP represents 2,4-dinitrophenylhydrazone.

(ether extraction) and triturated with ether to give 2.8 g of crystals: mp 92–96°, raised to 94.5–96° on recrystallization from ether; ir 4.43 μ.

Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 81.40; H, 8.04; N, 11.02.

Hydrolysis of this dinitrile (2.6 g) with 30% KOH solution (50 ml) at 100–120° for 15 hr did not lead to an acid amide but gave a corresponding **acid nitrile**, after acidification, isolation of the sodium bicarbonate-soluble fraction (1.7 g), and recrystallization from ethanol: mp 183–186°; ir 5.84 μ, *ca.* 4.4 μ (obscured by carboxyl bands), and no amide peak.

Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 74.76; H, 7.80; N, 5.16.

Cyclization of the dinitrile (1.3 g) with concentrated sulfuric acid (25 ml) at 25–30° for 22 hr followed by treatment with ice and isolation of the neutral product (ether extract washed with aqueous base and water) gave **4-cyclohexyl-1-tetralone-4-carboxamide** (0.4 g): recrystallized from ethanol, colorless crystals; mp 197–199°; ir 2.97, 3.18, and 5.99 μ (shoulders); uv 251 and 294 mμ (ε 9740 and 1690, respectively).

Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.08; H, 7.91; N, 5.28.

This tetralone amide resisted hydrolysis with acids or bases.

α-Phenyl-α-(*p*-fluorophenyl)glutaronitrile, Glutarimide, and Corresponding Glutaric Acid.—A. Phenyl *p*-fluorophenylacetonitrile was prepared following published procedures.[17] Phenylacetonitrile (236 g) was treated with bromine (334 g) at 72–110° over the course of 2 hr, as much HBr as possible being removed *in vacuo* from the crude bromonitrile, which was then condensed with 100 g of fluorobenzene in the presence of 294 g of anhydrous aluminum bromide at 45–50° (3 hr). After ice–HCl hydrolysis and isolation of neutral fraction, the product was distilled *in vacuo*, giving 289 g of oil, bp 148–156° (1.7–2.0 mm) [lit.[17] bp 192° (25 mm)].

B. Cyanoethylation of 289 g of product from part A with 78 g of acrylonitrile in 500 ml of *tert*-butyl alcohol and 41 ml of 40% Triton B methoxide solution during 2 hr with cooling, isolation of neutral product as an ether solution, filtration to remove 10 g of polymeric material, and evaporation gave 300 g of dark red oil which crystallized in the presence of ether–ligroin and afforded 129 g of the **dinitrile**: mp 73–77°, raised to 82–84° on recrystallization from ether (Norit); ir 4.42 μ.

Anal. Calcd for $C_{17}H_{13}FN_2$: C, 77.25; H, 4.96; N, 10.60. Found: C, 77.37; H, 4.91; N, 10.52.

C. Hydrolysis of 129 g of dinitrile with 500 ml of concentrated hydrochloric acid and 700 ml of glacial acetic acid (refluxed 5.5 hr), distillation of excess reagents *in vacuo*, and treatment with water gave 138 g of **glutarimide**, after collecting, washing with water, and air drying: mp 194–196°, raised to mp 197–199° on recrystallization from acetone–methanol; ir 3.14, 3.24, and doublet 5.84–5.91 μ.

Anal. Calcd for $C_{17}H_{14}FNO_2$: C, 72.07; H, 4.98; N, 4.95. Found: C, 71.92; H, 5.02; N, 4.86.

D. Hydrolysis of 138 g of glutarimide from part C by heating and stirring under reflux with a solution of 540 g of potassium hydroxide in 1 l. of water for 3 days gave after acidification a crude acid which was taken into ether; the ether solution was washed with water, dried ($MgSO_4$), and evaporated, yielding 117 g of **α-phenyl-α-(*p*-fluorophenyl)glutaric acid**, mp 174–178°. Recrystallization from ether gave material, mp 177–178°, ir 5.82–5.90 μ.

Anal. Calcd for $C_{17}H_{15}FO_4$: C, 67.54; H, 5.00. Found: C, 67.61; H, 5.12.

1-Tetralone-4-carboxylic Acids (1b) and -4-carboxamides (1a).—In general, the glutaric acid, anhydride, or acid amide was added, while stirring, to 30–40 parts (by weight) of concentrated H_2SO_4, if necessary cooling by means of a bath to prevent the temperature from rising above 60°. After standing overnight at room temperature, or for several days in the case of acid amides, the sulfuric acid solution was poured over 100 parts (by weight) of ice. The product was isolated by direct filtration if crystalline or extracted with ether, and the ether solution was washed well with water, as well as with dilute sodium carbonate or sodium hydroxide solution if the product were a neutral compound, dried ($MgSO_4$), and evaporated; the tetralones were characterized *per se*, or as suitable derivatives in the case of new compounds, prepared by standard methods and listed in Table III, and by hydrolysis of amides to corresponding acids as described in the following experiment.

Hydrolysis of 1-tetralone-4-carboxamides was carried out, *e.g.*, by refluxing 27 g of 4-cyclohexylmethyl-4-carboxamido-1-tetralone

(17) C. M. Robb and E. M. Schultz, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 347; H. Leditsche, H. Rolly, and H. Schmidt-Ruppin, U. S. Patent 2,843,594 (1958).

with 400 ml of concentrated hydrochloric acid and 200 ml of glacial acetic acid for 7 hr, followed by distillation of excess reagent *in vacuo*, treatment of the residue with water, subsequent filtration or extraction with ether, washing with water, drying ($MgSO_4$), and evaporation to give the crude keto acid which was then purified by recrystallization from ether or ether–ethanol.

Esterification of 1-Tetralone-4-carboxylic Acids.—The keto acid (30 g) was treated with 1 l. of absolute ethanol in which there was dissolved 75 ml of concentrated H_2SO_4 and 10 ml of 30% fuming H_2SO_4, and the solution was refluxed 18 hr. After removing most of the ethanol *in vacuo*, the chilled residue was poured over ice and the neutral product isolated by ether extraction, washing with successive portions of dilute NaOH solution and water, drying ($MgSO_4$), and evaporation. Characteristically the keto esters had ir 5.8 and 5.95 μ bands and uv λ_{max} ~295 mμ. If crystalline, the new compounds are listed in Table III.

Corresponding **oximino esters**, prepared by common procedure,[2,18] were also characterized by typical spectra, and some of them are listed in the table, together with miscellaneous data for various other derivatives of tetralones which were prepared. **Tetralone 1b** (R = CH_2CH_2COOH) was synthesized following Koelsch[6] and was esterified and converted to oxime by the usual procedure. **Tetralone 1c** (R = CH_2COOEt) was prepared starting from ethyl β-cyano-β-phenylpropionate[19] *via* cyanoethylation and hydrolysis by HCl and HOAc, 4-hr reflux, to 2-phenylbutane-1,2,4-tricarboxylic acid, mp 170–172° (from ether–ethyl acetate), ir 5.77–5.88 μ.

1-Cyclopentyl-1-phenyl-2-propanone.—Reaction of 170 g of α-cyclopentyl-α-phenyl acetonitrile[16] with methylmagnesium iodide (from 75 g of Mg) in toluene at 100° overnight, and HCl hydrolysis[20] gave 128 g of ketone, bp 110–127° (2.5 mm), ir 5.87 μ. The **2,4-dinitrophenylhydrazone**, yellow crystals from ethanol, had mp 116–118°.

Anal. Calcd for $C_{20}H_{22}N_4O_4$: C, 62.81; H, 5.80; N, 14.65. Found: C, 62.93; H, 5.84; N, 14.73.

Cyanoethylation of this ketone in THF (Triton B methoxide), tried several times, gave a maximum yield of 1% of **γ-cyclopentyl-γ-phenyl-δ-oxocapronitrile**, crystals from ether, mp 89–90°, ir 4.44 and 5.89 μ.

Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.70; H, 8.25; N, 5.72.

α-Benzyl-α-phenylglutaric Acid.—After addition of acrylonitrile or methyl acrylate to α-phenylhydrocinnamonitrile,[16] hydrolysis by prolonged boiling with 20% KOH solution gave the acid, mp 170–172°, ir 5.87 μ.

Anal. Calcd for $C_{18}N_{18}O_4$: C, 72.46; H, 6.08. Found: C, 72.32; H, 6.11.

Treatment with acetic anhydride afforded the corresponding **anhydride**: crystals from ether; mp 117–119°; ir 5.56 and 5.71 μ.

Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.31; H, 5.81.

Cyclization of either of these compounds with PPA (100°, 6 hr), or of the intermediate acid amide with concentrated sulfuric acid, gave the spiro diketone, **spiro[1-indanone-2,1′(4′)-tetralone]**: mp 131–133° from ether; ir 5.88 and 5.97 μ.

Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.41; H, 5.37.

The corresponding **2,4-dinitrophenylhydrazone**, red crystals from ethyl acetate, had mp 270–271°.

Anal. Calcd for $C_{24}H_{18}O_5N_4$: C, 65.15; H, 4.10; N, 12.66. Found: C, 64.55; H, 4.48; N, 12.50.

2-Cyano-4-benzyl-1-tetralone-4-carboxylic Acid.—A stirred solution of 35 g of benzyl homophthalic anhydride[21] (mp 116–118°, prepared from dimethyl homophthalate by $NaOCH_3$ condensation with benzaldehyde, hydrogenation over Pd, NaOH hydrolysis, and treatment with acetic anhydride) in 300 ml of THF was treated with 19 g of $KOCMe_3$ with cooling, then 32 ml of acrylonitrile during 10 min (spontaneous temperature rise from 17–29°), and stirred 1 hr. The initially bright yellow color of the solution faded almost completely. The solution was refluxed gently 0.5 hr; a salt separated. After chilling, treatment with ice and HCl, and addition of water, the oil was extracted with ether. The water-washed and dried ($MgSO_4$) solution on evaporation gave yellow oil, crystallizing partly and giving on trituration with ether 14.5 g of crystals: mp 191–193° from ether; ir 4.44, 5.85, and 5.92 μ; uv 204, 230, and 295 nm (ϵ 26,380, 13,150, 7300); $FeCl_3$ test, weak green; soluble in aqueous NaOH.

Anal. Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59. Found: C, 74.68; H, 5.02; N, 4.50.

Hydrolysis and decarboxylation of the cyano keto acid (9.9 g) with acetic acid (70 ml) and concentrated HCl (270 ml) and refluxing 4 hr (initial, voluminous precipitate, redissolving on further boiling) gave **4-benzyl-1-tetralone-4-carboxylic acid**, listed, together with its derivatives prepared by usual methods, in Table III.

4-Benzyl-1-tetralone-4-carboxamide.—The acid from preceding hydrolysis (45 g) reacted in mildly exothermic manner with oxalyl chloride (200 ml) in the presence of pyridine (0.5 ml). After warming to 45° for 0.7 hr, removal of excess reagent *in vacuo* gave a residue which was treated with excess concentrated NH_4OH. The ether-extracted, washed, and dried ($MgSO_4$) product crystallized in ether (yield, 20.1 g) and was recrystallized from methanol: mp 159–161°; ir 2.92, 3.15, 6.02, and 6.13–6.26 μ; uv 206, 249, and 293 nm (ϵ 31,000, 9760, 1670).

Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.39; H, 6.13; N, 5.01. Found: C, 77.60; H, 6.14; N, 4.91.

1-Benzyl-1,4-methano-1,2,4,5-tetrahydro-3*H*-3-benzazepin-2,5-dione.—Bromine (3.6 g), added to a solution of the preceding ketoamide (6 g) in glacial HOAc (60 ml), was absorbed smoothly at 40–50°. After 0.5 hr the crude bromoamide was isolated by removal of the solvent *in vacuo*. A solution of the material in ether was filtered, concentrated, and added to a solution of sodium (1.4 g) in methanol (100 ml), and a slightly exothermic reaction occurred. After standing overnight, the solution was concentrated *in vacuo* and treated with water, and the product was extracted with ethyl acetate. The washed (aqueous $NaHCO_3$, water) and dried ($MgSO_4$) organic layer on evaporation gave red oil, crystallizing slowly and partly in the presence of methanol. Trituration with ethanol and recrystallization from the same solvent gave 0.5 g of colorless crystals: mp 201.5–203°; ir 3.01, 5.85, and 5.98 μ; uv 208, 230, 256, and 294 nm (ϵ 30,030, 9540, 6400, 1980).[7]

Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.81; H, 5.61; N, 5.09.

In attempting to characterize the intermediate bromoamide, an ether solution of some of the material was washed with aqueous $NaHCO_3$ and water, dried, and allowed to stand with methanol. There was isolated a sample of what appeared to be **2-methoxy-4-benzyl-1-tetralone-4-carboxamide**: mp 225–226° dec (from methanol); ir 2.90, 2.98, and doublet 5.83–5.93 μ; uv 208, 229, 258–264, and 294 nm (ϵ 33,600, 9560, 7000, 2200).

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.76; H, 6.19; N, 4.53. Found: C, 73.72; H, 6.14; N, 4.55.

α-(3,4-Dimethoxyphenyl)-α-phenylacetamide.—Condensation of 117 g of veratrole and 76 g of mandelonitrile with 425 ml of 74% sulfuric acid[22] at 70° for 1 hr, hydrolysis with ice, extraction with ether, and evaporation of washed and dried ether solution gave 36.5 g of crystals: mp 144–147° from ethanol–ether; ir 2.97, 3.15, and 6.07 μ.

Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 71.20; H, 6.48; N, 5.10.

The corresponding **acid**, from HCl–HOAc hydrolysis, had mp 96–98°, ir 5.91 μ.

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.38; H, 5.86.

The corresponding **nitrile**, prepared by dehydration of the amide (38 g) with P_2O_5 (165 g) in toluene (2 l., refluxed 3 hr), was an oil, ir 4.44 μ.

α-(3,4-Dimethoxyphenyl)-α-phenylglutaronitrile.—Addition of acrylonitrile (10.3 g) to the foregoing nitrile (33.5 g) in THF (50 ml) in the presence of $NaOCH_3$ (from 0.8 g Na) gave 27.4 g of dinitrile: crystals from ether–methanol; mp 138.5–140°; ir 4.43 μ.

Anal. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.39; H, 6.05; N, 8.93.

Hydrolysis with 45% KOH solution (20-hr reflux) gave quantitatively the corresponding **diacid**, an oil. Reflux for 1 hr with acetic anhydride converted the acid to the corresponding **anhydride**: crystals from ether–ethyl acetate; mp 123–124°; ir 5.53 and 5.66 μ.

(18) G. N. Walker, D. Alkalay, and R. T. Smith, *J. Org. Chem.*, **30**, 2973 (1965).

(19) C. F. H. Allen and H. B. Johnson, *Org. Syn.*, **30**, 83 (1950).

(20) C. R. Hauser, *et al.*, *J. Org. Chem.*, **15**, 359 (1950); *J. Amer. Chem. Soc.*, **70**, 426 (1948); G. Vasiliu, *et al.*, *Chem. Abstr.*, **34**, 4058 (1940).

(21) W. Dieckmann, *Chem. Ber.*, **47**, 1428 (1914); E. Müller, *Justus Liebigs Ann. Chem.*, **491**, 251 (1931).

(22) A. Müller and M. Vajda, *J. Org. Chem.*, **17**, 800 (1952).

Anal. Calcd for $C_{19}H_{18}O_6$: C, 69.92; H, 5.56. Found: C, 69.80; H, 5.65.

4-Phenyl-6,7-dimethoxy-1-tetralone-4-carboxylic Acid.—Anhydride from the preceding experiment (13 g) was treated with 130 ml BF_3–HOAc. After standing overnight and hydrolysis with 800 ml of 15% NaOAc solution, acidification with HCl and extraction with ether afforded 13 g of crude keto acid as yellow oil.

The **2,4-dinitrophenylhydrazone** was recrystallized from ethanol–ethyl acetate, red crystals, mp 166–169°.

Two-day reflux of 13.5 g of the keto acid with a solution of 35 ml of concentrated sulfuric acid and 5 ml of oleum in 1 l. of ethanol provided the corresponding **ethyl ester**: crystals (11.1 g) from ethanol; mp 147–149°; ir 5.78 and 5.96 μ; uv 237, 277, and 312 nm (ϵ 23,190, 11,100, 7020).

Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 70.80; H, 6.30.

The **oxime** was prepared from the ethyl ester as usual: crystals from pentane–ether: mp 148–149°; ir 3.12 and 5.77 μ; uv 212, 269, 303 nm (ϵ 28,760, 15,750, 6270).

Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.08; H, 6.13; N, 3.84.

1,4-Ethano-4-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydro-3-isoquinolone.—Hydrogenation (50 psi) of 9.0 g of oximino ester from the preceding experiment in 300 ml of ethanol in the presence of 10 g of Raney nickel for 1.5 hr (4.0-lb pressure drop), filtration, and evaporation gave an oily mixture of amino esters, which was heated (neat) on a steam cone for 2.5 days. On cooling, the material solidified. Trituration with ether gave 1.1 g of the lactam: mp 230–234°, raised on further recrystallization (methanol) to mp 236–237°; ir 3.12 and 5.98 μ; uv 241, 285 nm (ϵ 3980, 3810); insoluble in acids.

Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.76; H, 6.19; N, 4.53. Found: C, 73.32; H, 6.32; N, 4.62.

Ether solution of the remaining material with pentane gave crystals of **1-amino-4-ethoxycarbonyl-4-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene**, evidently the trans-amino ester (1.9 g): acid-soluble; mp 139–141° after recrystallization from methanol–ether; ir 5.78 μ and NH_2 bands. The corresponding **hydrochloride**, recrystallized from ethanol–ether, had mp 244–245°.

Anal. Calcd for $C_{21}H_{26}NO_4Cl$: C, 64.36; H, 6.69; N, 3.57. Found: C, 64.34; H, 6.88; N, 3.69.

The ***N*-methyl lactam**, from NaH–iodomethane alkylation as usual of the lactam, (quantitatively), had mp 200–202° (from methanol–ether), ir 5.99 μ.

Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.42; H, 6.76; N, 4.42.

1,4-Dihydro-1,4-ethano-2,3-dimethyl-4-phenyl-6,7-dimethoxyisoquinolinium Chloride.—A solution of 0.6 g of *N*-methyl lactam from the preceding experiment in 100 ml of benzene and 25 ml of 1.92 *M* methyllithium–ether was heated under reflux 50 min. After treatment with ice and addition of ether, the basic product was isolated from the water-washed, organic layer by extraction with cold 18% hydrochloric acid, addition of 20% NaOH solution at 0°, and extraction with ether. The water-washed and dried (K_2CO_3) ether solution (100 ml), treated with a slight excess of 5% ethanolic HCl, gave the iminium chloride (0.3 g) as yellow crystals, mp *ca.* 200°. After recrystallization from ethanol–ether and drying *in vacuo*, the salt was obtained in the form of the **monohydrate**: mp 210–213° dec; ir 6.01–6.03 μ and broad OH (H_2O) band; uv 231 and 283 nm (ϵ 7620 and 2830).

Anal. Calcd for $C_{21}H_{24}NO_2Cl \cdot H_2O$: C, 67.10; H, 6.97; N, 3.73. Found: C, 67.32; H, 7.16; N, 3.51.

The salt, like other compounds of Table II, was readily soluble in water. The corresponding base (enamine) discolored and became gradually less ether-soluble on standing exposed to air, and satisfactory spectra could not be obtained.

Registry No.—**1a** (R = Ph) oxime, 27249-23-6; **2a** (R = Ph) HCl, 17772-08-6; **2b** (R = Ph) HCl, 17772-09-7; **5** (R = Ph; R′ = Me; R″ = CH_2), 2997-34-4; **5** (R = Ph; R′ = Me; R″ = $CHCH_3$), 2997-39-9; **5** (R = *p*-fluorophenyl; R′ = Me; R″ = CH_2), 2959-81-1; **6** (R = Ph; R′ = Me = R″) Cl, 3196-50-7; **6** (R = Ph; R′ = Me = R″) I, 2997-13-9; **6** (R = R″ = Me; R′ = CH_2Ph) Br, 2959-89-9; **6** (R = R″ = Me; R′ = CH_2Ph) I, 3123-56-6; **6** (R = R′ = R″ = Me) I, 2959-88-8; **9** (R = Ph; R′ = R″ = Me) Cl, 13695-65-3; **9** (R = Ph; R = R″ = Me) I, 13695-66-4; **9** (R = Et; R′ = R″ = Me) I, 13695-68-6; **10** (R = Ph; R′ = R″ = Me) HCl, 13695-67-5; 2-methyl-4-phenyl-1,4-ethane-1,2,3,4-tetrahydroisoquinoline, 14577-66-3, 14657-45-5 (HCl), 4909-86-8 (methiodide); 4-amino-1-phenyl-1,2,3,4-tetrahydronaphthalene-1-cuboxamide, 27249-39-4, 27249-40-7 (amino acid HCl); 4-hydroxy-1-phenyl-1,2,3,4-tetrahydronaphthalene-1-carboxamide, 27249-41-8; 1-phenyl-1,2-dihydronaphthalene-1-carboxamide, 27249-42-9; α-methyl-α-phenylglutaric acid, 3123-54-4; 2897-84-9 (anhydride); α-cyclopentyl-α-phenylglutarimide, 2897-90-7, 3123-61-3 (acid amide); α-(cyclohexylmethyl)-α-phenylglutarimide, 2959-97-9, 3123-48-6 (acid amide); α-cyclohexyl-α-phenylglutaronitrile, 20881-44-1, 27249-49-6 (acid nitrile); 4-cyclohexyl-1-tetralone-4-carboxamide, 27249-50-9; α-phenyl-α-(*p*-fluorophenyl)glutaronitrile, 2897-80-5, 2897-81-6 (glutarimide), 3123-51-1 (glutaric acid); 2-phenylbutane-1,2,4-tricarboxylic acid, 27249-54-3; 1-cyclopentyl-1-phenyl-2-propanone, 27249-55-4, 27249-56-5 (2,4-DNP); γ-cyclopentyl-γ-phenyl-δ-oxocapronitrile, 27249-57-6; α-benzyl-α-phenylglutaric acid, 27272-80-6, 14701-87-2 (anhydride); spiro[1-indanone-2,1′(4′)-tetralone], 27272-82-8, 12505-71-4 (2,4-DNP); 2-cyano-4-benzyl-1-tetralone-4-carboxylic acid, 3123-59-9; 4-benzyl-1-tetralone-4-carboxamide, 27272-84-0; 1-benzyl-1,4-methano-1,2,4,5-tetrahydro-3*H*-3-benzazepin-2,5-dione, 27272-85-1; 2-methoxy-4-benzyl-1-tetratone-4-carboxamide, 27272-86-2; α-(3,4-dimethoxyphenyl)-α-phenylacetamide, 2959-98-0, 17777-02-5 (acid); α-(3,4-dimethoxyphenyl)-α-phenylglutaronitrile, 2960-00-1, 2897-73-6 (anhydride); 4-phenyl-6,7-dimethoxy-1-tetralone-4-carboxylic acid, 2897-72-5 (2,4-DNP), 2897-71-4 (ethyl ester), 2897-74-7 (oxime); 1,4-ethano-4-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydro-3-isoquinolone, 2897-75-8; 1-amino-4-ethoxycarbonyl-4-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene, 27272-94-2, 27272-95-3 (HCl), 2897-77-0 (*N*-methyl lactam); 1,4-dihydro-1,4-ethano-2,3-dimethyl-4-phenyl-6,7-dimethoxyisoquinolinium chloride, 3123-50-0.

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