M, were prepared in carbon tetrachloride (reagent grade); 5-ml aliquots were transferred to constricted Pyrex tubes (previously washed in an alkaline soap solution, thoroughly rinsed, and dried), degassed, sealed, and placed in the thermostat. The rate of reaction was followed by iodometric analysis for peroxide.[20] An aliquot of 4.0 ml of reaction solution was placed in a 125-ml glass-stoppered erlenmeyer flask. The carbon tetrachloride was removed by a gentle stream of purified nitrogen gas. (Control experiments showed that peroxylactone was not lost by this procedure.) Acetone (15 ml of reagent grade) was added and the solution was degassed by powdered Dry Ice. Sodium iodide (1 g) and 10% aqueous hydrochloric acid (3 ml) were added and the flask was stoppered. After 10 min in the dark, 25 ml of distilled water was added, and the liberated iodine was titrated with 0.01 N thiosulfate solution to the disappearance of the iodine color. Frequent blank determinations were made but were always 0. Analysis by a number of the previously published methods for analysis of peroxides gave less satisfactory results. Scatter in the kinetic data observed in early runs was eliminated (and the over-all rate somewhat reduced) by the inclusion of pyridine, at *ca.* 0.02 M.

The rate of disappearance of peroxylactone was unaffected by oxygen, glass wool, or added azobisisobutyronitrile. The kinetic data are summarized in Table II.

Control Experiments. A. α-Methylstyrene Oxide.—Subjection of the epoxide to vpc analysis affords a single peak. Retention times of epoxide and α-phenylpropionaldehyde differ only slightly (61.8 and 60.8) on the columns used for product analyses. The hot wire of the vpc detector rearranges the epoxide to the aldehyde.

A solution of the epoxide, 0.0496 M in carbon tetrachloride containing 0.1 M pyridine, was degassed, sealed, and heated for 14 hr at 134°. The infrared spectrum of the reaction mixture was largely that of the epoxide plus a small amount of α-phenylpropionaldehyde. Analysis by vpc on column A at 107°, 15 psi of helium, showed small peaks (relative to *p*-bromotoluene = 1.00) at 1.42 and 2.38, and a major peak at 1.73 (starting material, 85%). The small peaks at 1.42 and 2.38 are not present in the peroxylactone decomposition and were not further investigated.

Subjection of the epoxide to the above conditions, omitting pyridine, resulted in conversion of the epoxide to α-phenylpropionaldehyde. Heating the epoxide in carbon tetrachloride with pyridine (0.1 M) at 180° for 20 hr afforded a complex mixture derived, in part, from reaction of the pyridine with the solvent.

B. Decomposition of the Peroxylactone in the Presence of α-Methylstyrene Oxide.—A solution of peroxylactone (0.05 M), epoxide (0.0496 M), and pyridine (0.1 M) in carbon tetrachloride was heated at 134° for 14 hr. Analysis by vpc on column A showed peaks (relative to *p*-bromotoluene = 1.00) at 1.43 (small, unknown), 1.54 (acetophenone, 8%), 1.73 (α-methylstyrene oxide, 84%), 2.24 (benzyl methyl ketone, 15%), 2.38 (small, unknown), and 2.48 (propiophenone, 69%).

C. α-Methoxystyrene. Thermal Stability.—A solution of α-methoxystyrene (0.05 M) and pyridine (0.01 M) in carbon tetrachloride was degassed, sealed, and heated at 134° for 14 hr. Analysis by vpc on column A showed two unresolved peaks at 1.55 and 1.6 (relative to *p*-bromotoluene = 1.00); no peak or shoulder was observed at 1.63, the relative retention time for α-methoxystyrene.

D. Decomposition of the Peroxylactone in the Presence of α-Methoxystyrene.—A solution of peroxylactone (0.058 M), α-methoxystyrene (0.05 M), and pyridine (0.1 M) in carbon tetrachloride was degassed, sealed, and heated at 134° for 14 hr. The reaction mixture (extensive tar formation) was analyzed by vpc on column A; peaks (relative to *p*-bromotoluene = 1.00) were observed at 0.47, 1.54 (large), 1.70 (large), 2.20 (small), 2.42 (small); these peaks do not correspond to those from decomposition of peroxylactone alone or of the enol ether alone.

Ring Expansion of 2-Substituted 1-Indanones to 2-Hydroxyisocarbostyril Derivatives. Scope and Mechanism of Reaction. A Spectral Study of the Lactam–Lactim Tautomerism in Isocarbostyrils[1]

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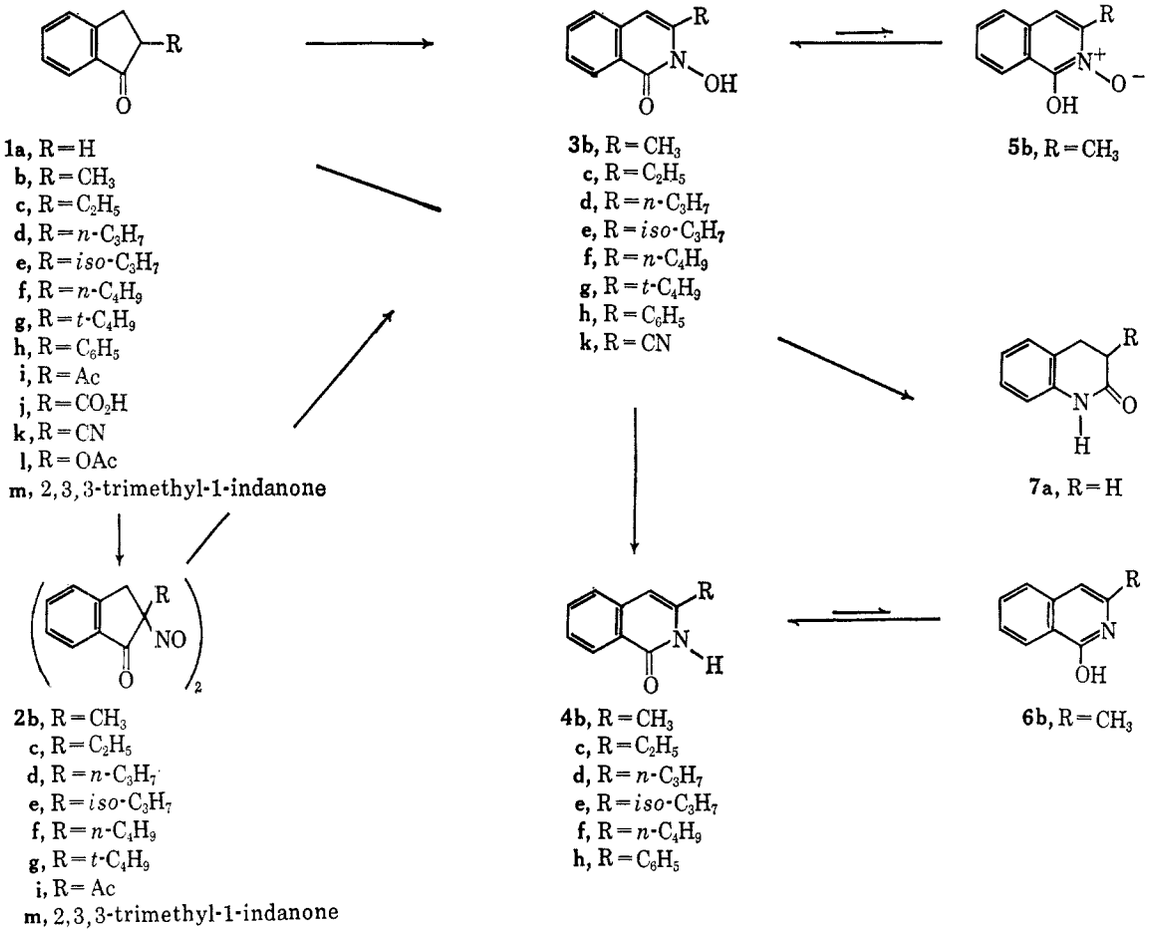
The addition of *n*-butyl nitrite to a 1:1 molar equivalent of 2-alkyl-1-indanone [R = CH_3 (**1b**), C_2H_5 (**1c**), C_3H_7 (**1d**), *iso*-C_3H_7 (**1e**), *n*-C_4H_9 (**1f**), and *t*-C_4H_9 (**1g**)]–hydrochloric acid, and to a 2-phenyl- (**1h**) and 2-cyano-1-indanone (**1k**)–sodium alkoxide mixture, produced 2-hydroxy-3-alkyl- or -arylisocarbostyrils (**3b–3h** and **3k**, respectively) in decreasing yields (69–14%). Reverse addition of acid to an indanone–nitrite mixture led to the isolation of the stable dimeric 2-alkyl-2-nitroso-1-indanones [**2b–2g** and **2i** (R = Ac)] in decreasing yields (90–20%). Since **2b–2g** were isomerized to **3b–3g**, respectively, in both acid (92–96%) and base (90–96%), the nitrosation step (**1** → **2**) clearly determines product yield in the conversion **1** → **3**. Reduction of **3b–3f** and **3h** with iodine and red phosphorus in glacial acetic acid led to the known 3-alkyl- or -arylisocarbostyrils (**4b–4f** and **4h**). Both hydrochloric acid and methanolic sodium methoxide converted **2i** to 2-oximino-1-indanone (**2a**), as did nitrosation of 1-indanone (**1a**). 2-Carboxy-1-indanone (**1j**) underwent nitrosative decarboxylation to **2a**. Ring-opened intermediates in the isomerization **2b** → **3b** are suggested by the conversion of *o*-carboxy- (**19**) and *o*-carbomethoxybenzyl methyl ketoxime (**24**) to **3b**, in acid and base, respectively. 2,3,3-Trimethyl-1-indanone (**1m**), 2-methyl- (**32a**), and 2-ethyl-1-tetralone (**32b**) were converted to their respective nitroso dimers, **2m**, **33a**, and **33b**. Acid treatment of **2m** and base treatment of **33a** and **33b** led to ring-opened hydrolysis products, 3-methyl-3-(*o*-carboxyphenyl)-2-butanone oxime (**29**), 4-(*o*-carboxyphenyl)-2-butanone (**34a**), and 1-(*o*-carboxyphenyl)-3-pentanone (**34b**), respectively. A similarity of ultraviolet spectra, the presence of a C-4 vinyl proton signal in the nmr of **3b**, **4b**, and 2,3-dimethylisocarbostyril (**35**), and the lack of N→O absorption in **3b**, is consistent with the existence of 2-hydroxy-3-methylisocarbostyril and 3-methylisocarbostyril predominantly in their respective lactam forms, **3b** and **4b**. Infrared, ultraviolet, and nmr data are reported for compounds in the series **1–4**, inclusive.

In the first description of this novel ring expansion,[2] we reported that addition of *n*-butyl nitrite to a 1:1 molar equiv of 2-methyl- (**1b**) and 2-ethyl-1-indanone (**1c**)–hydrochloric acid mixture produced 2-hydroxy-3-alkylisocarbostyrils (**3b** and **3c**, respectively). With lower acid concentrations and reversal of the mode of addition (acid to indanone–nitrite mixture), the stable dimeric precursors, 2-methyl- (**2b**) and 2-ethyl-2-nitroso-1-indanone (**2c**) were isolated. Compounds **2b** and **2c** isomerized to **3b** and **3c**, respectively, rapidly in refluxing methanolic sodium methoxide solution and more slowly in concentrated hydrochloric acid. Reduction of **3b** and **3c** in glacial acetic acid with iodine and red phosphorus led to isocarbostyrils **4b** and **4c**, respectively.

(1) This research was supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research, under Grants AF-AFOSR 62-18 and 488-64.

(2) E. J. Moriconi, F. J. Creegan, C. K. Donovan, and F. A. Spano, *J. Org. Chem.*, **28**, 2215 (1963).

SCHEME I



The uniqueness and utility of this ring expansion reaction derives from the fact that the 3,4-dihydro reduction products of the isocarbostyrils (**4**) are isomeric with the Beckmann and Schmidt rearrangement products (**7a**) and are not normally accessible by these latter routes. Thus, Beckmann rearrangement of 1-indanone oxime,[3] and the Schmidt reaction on 1-indanone (**1a**)[4] have led predominantly[5] to the *aryl* migration product, 3,4-dihydrocarbostyril (**7a**). To produce isocarbostyrils of the type **3** and **4** *via* these same reaction routes would require preferential *alkyl* migration.[8]

In this paper we report on (i) proximity effects on the nitrosation (**1** → **2**) and ring expansion reactions (**2** → **3**; **1** → **3**) by both electron-donating substituents of increasing bulk (**1c**, R = C_2H_5; **1d**, R = *n*-C_3H_7; **1e**, R = *iso*-C_3H_7; **1f**, R = *n*-C_4H_9; **1g**, R = *t*-C_4H_9; and **1h**, R = C_6H_5) and electron-withdrawing substituents (**1i**, R = Ac; **1j**, R = CO_2H; **1k**, R = CN; and **1l**, R = OAc); (ii) presumptive evidence for a mechanism by which the ring expansion could proceed; and (iii) a spectral study of the lactam–lactim tautomerism possible in 3-methyl-2-hydroxyisocarbostyril (**3b** ⇄ **5b**) and in the parent heterocyclic 3-methylisocarbostyril (**4b** ⇄ **6b**). (See Scheme I.)

trans-**2-Nitroso-1-indanone Dimers** (**2**).[12]—The addition of concentrated hydrochloric acid to an ice-bath-cooled solution of 2-substituted-1-indanones (**1a–1g**, **1i**, and **1m**) and freshly prepared *n*-butyl nitrite invariably produced a green solution of the monomeric nitroso compounds, from which, after several

(3) F. S. Kipping, *Proc. Chem. Soc.*, 240 (1893); *J. Chem. Soc.*, **65**, 480 (1894).

(4) L. H. Briggs and G. C. De Ath, *ibid.*, 456 (1937).

(5) However, increasing the bulk of *peri* (C-7) substitutents in **1a** from H to *t*-butyl, changed the per cent aryl/per cent alkyl migration ratios from 9.0 to 0.33 in the Beckmann rearrangement and from 3.2 to 0.15 in the Schmidt reaction.[6] In fact, 4-bromo-7-*t*-butyl-1-indanone oxime is such a rigid molecule that the major reaction product (70–75%) under Beckmann conditions results from a bond insertion by electron-deficient nitrogen. Only minor amounts of both possible lactams are formed. The Schmidt reaction of 4-bromo-7-*t*-butyl-1-indanone led to all three products, but lactams were now the major components.[7]

(6) P. T. Lansbury and N. R. Mancuso, *Tetrahedron Letters*, 2445 (1965).

(7) P. T. Lansbury, J. G. Colson, and N. R. Mancuso, *J. Am. Chem. Soc.*, **86**, 5225 (1964).

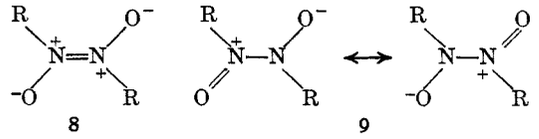
(8) As seems to occur in the conversion of 2-nitro-3-oximino-1-indanone to 1-chloro-4-hydroxy-3-nitroisoquinoline;[9] alkyl migration also occurs in the conversion of 2-nitro-1,3-indandione to 3,4-diketo-3,4-dihydro-2-hydroxyisoquinolone,[10] and 2-nitro-1-indanone oxime to N-hydroxyhomophthalimide and 3-chloro-2-hydroxyisocarbostyril.[11]

(9) G. Ya. Vanag and V. N. Vitol, *J. Gen. Chem. USSR* (Eng. Transl.), **25**, 1899 (1955).

(10) G. Ya. Vanag and E. Vanag, *Proc. Acad. Sci. USSR, Chem. Tech. Sect.* (Eng. Transl.), **90**, 59 (1953).

(11) T. Kametani and H. Sugahara, *J. Chem. Soc.*, 3856 (1964).

(12) Despite the theoretically calculated[13] and experimentally reported[14] free-radical nature of some dimeric nitroso compounds, the preferred structure for *trans*-nitroso dimers seems to be the azo dioxide **8**[15a] rather than the hybrid **9**.[15b]



8 **9**

(13) J. W. Linnett and R. M. Rosenberg, *Tetrahedron*, **20**, 53 (1964).

(14) W. Theilacker, *Angew. Chem. Intern. Ed. Engl.*, **4**, 688 (1965).

(15) (a) See R. R. Holmes, *et al.*, *J. Org. Chem.*, **30**, 3837 (1965), for leading references; (b) as originally proposed by D. Ll. Hammick, R. G. A. New, and R. B. Williams, *J. Chem. Soc.*, 29 (1934), and most recently quoted in J. D. Roberts and M. C. Caserio," Basic Principles of Organic Chemistry" W. A. Benjamin, Inc., New York, N. Y., 1964, p 687.

TABLE I

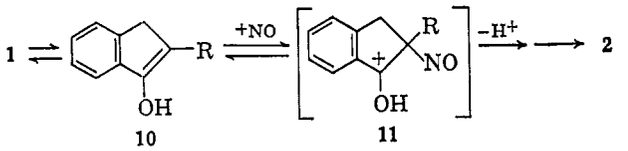
PRODUCTS OF NITROSATION, RING EXPANSION, AND REDUCTION

Reactant, 1-indanones (1), substituent	Nitrosation, *trans*-nitroso dimers (2), % yield	Ring expansion, isocarbostyrils (3), % yield — From 2 — Acid	Base	From 1	Reduction, isocarbostyrils (4), % yield
2-CH_3 (1b)	2b, 90	3b, 71[a] (92)[b]	80[a] (90)[b]	69	4b, 32
2-C_2H_5 (1c)	2c, 68	3c, 71 (94)	80 (90)	65	4c, 38
2-*n*-C_3H_7 (1d)	2d, 64	3d, 74 (95)	87 (93)	64	4d, 36
2-*iso*-C_3H_7 (1e)	2e, 46	3e, 81 (96)	84 (94)	49	4e, 64
2-*n*-C_4H_9 (1f)	2f, 29	3f, 91 (93)	95 (95)	45	4f, 35
2-*t*-C_4H (1g)	2g, 19	3g, 96 (96)	96 (96)	20	
2-C_6H_5 (1h)				3h, 18[c]	4h, 57
2-Ac (1i)	2i, 20				
2-CN (1k)				3k, 14[c]	
2,3.3-Trimethyl (1m)	2m, 10				

[a] Based on product formation. [b] Based on recovered starting material. [c] Under alkaline conditions.

hours, precipitated the colorless dimeric nitroso products, **2b–2g**, **2i**, and **2m**, respectively, in decreasing yields (90–10%, Table I).

The decreasing yield of nitroso dimers in the homologous series **2b–2g** can be attributed entirely to the progressively increasing steric congestion which makes itself felt in both the initial nitrosation and subsequent dimerization steps. Thus, acid-catalyzed nitrosation has been envisioned as an electrophilic attack by nitrosonium ion (or its carrier) on the enol form **10** to presumably lead to **11**.[16] Irreversible proton loss therefrom would yield the nitroso monomer which could then dimerize to the thermodynamically more stable



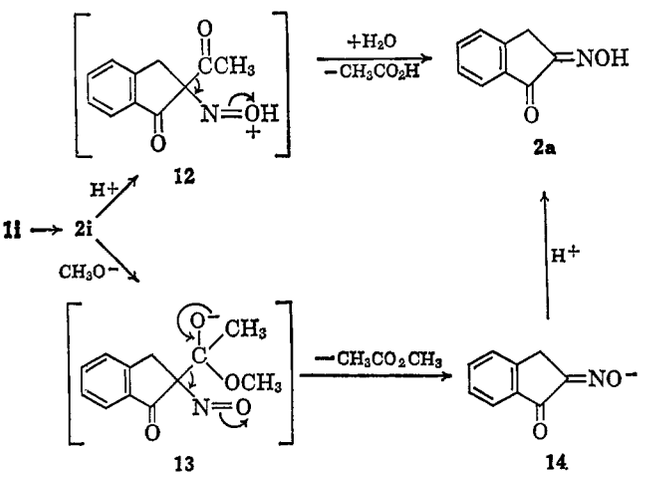
10 11

trans-nitroso dimer. It seems reasonable to assume that increasing the size of R in **1** would sterically hinder initial approach by the nitrosonium electrophile to the α-carbon atom in enol **10**. The bulk effect would also make itself felt in the dimerization to **2**, and enhance its reversible dissociation in solution to the monomer. It is relevant to note that the solubility of the nitroso dimers qualitatively increased in the series **2b–2g** such that the *t*-butyl derivative (**2g**) dissolved in warm solvents (chloroform, carbon tetrachloride, ethanol, and dioxane) to produce green solutions of the monomer.

In the infrared, each of **2b–2g** displayed a strong, sharp N→O absorption in the 7.68–7.78-μ region (indicative of *trans*-nitroso dimers),[19a,b] in addition to the characteristic ultraviolet band in the 293–295-mμ range.[19c] Alcoholic solutions of **2b–2g**, maintained in the ultraviolet beam at 294 mμ over a 45–60-min period showed a decisive decrease in extinction coefficient due to dissociation to the monomer.

The addition of acid to a mixture of 2-phenyl-1-indanone (**1h**)–*n*-butyl nitrite led only to recovery of starting material. It is of interest to report that the recrystallizing solvent played a significant role in determining the presence of the enol tautomer **10h** (R = C_6H_5). Thus, recrystallization of **1h** from nonpolar benzene–hexane solvent led to a keto–enol tautomeric mixture (mp 90–92°) which showed strong bands in the infrared (KBr) at 2.94 (OH) and 5.84 μ (C=O). With aqueous ethanol as the recrystallizing solvent, the product (mp 77–78°) showed only a single strong keto carbonyl absorption (KBr) at 5.85 μ. Clearly the implied stability of the enol form **10h** (even to nitrosation) must be a consequence of the enhanced conjugation possible between the *endo* double bond and the coplanar fused and substituted phenyl rings.

2-Acetyl-1-indanone (**1i**) in benzene solution was sufficiently acidic for nitrosation to proceed to dimer **2i** by the addition of *n*-butyl nitrite. Nitrosation of **1i** in hydrochloric acid led to the rapid precipitation of 2-oximino-1-indanone (**2a**), as did treatment of **2i** in acid, both reactions presumably proceeding *via* a protonated species such as **12**. Methanolic sodium methoxide converted **2i** to the oximino salt of **2a**, (**14**), possibly *via* **13**.[20] Compound **2i** displayed the appropriate *trans*-nitroso dimer absorption at 299 mμ



(16) N. V. Sidgwick, "The Organic Chemistry of Nitrogen," Clarendon Press, London, 1937, p 171; A. T. Austin, *Sci. Progr.* (London), **49**, 619 (1961). It should be noted that this mechanism requires that the rates of acid-catalyzed nitrosation and enolization be the same. Although a number of aryl alkyl ketones of the 1-indanone type have been nitrosated,[17] no such kinetic data is available in these systems. In fact, kinetic data on a number of simple aliphatic ketones indicate a considerable difference in such rates, and the suggestion has been made that the nitrosonium electrophile initially attacks the carbonyl oxygen atom of the keto form (**1**).[18]

(17) O. Touster, *Org. Reactions*, **7**, 327 (1953).

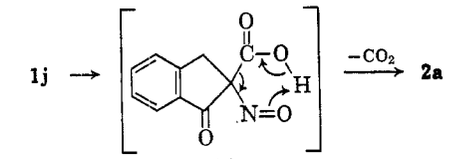
(18) K. Singer and P. A. Vamplew, *J. Chem. Soc.*, 3052 (1957).

(19) (a) B. G. Gowenlock and W. Lüttke, *Quart. Rev.* (London), **12**, 321 (1958); (b) J. F. Brown, Jr., *J. Am. Chem. Soc.*, **77**, 6341 (1955); (c) P. Kabaskalian and E. Townley, *ibid.*, **84**, 2723 (1962), and three preceding papers.

(20) A. G. Wilson [U. S. Patent 2,515,482 (1950)] was similarly able to convert 17-acetyl steroids (20-ketopregnanes) directly to 17-keto steroids with ethyl nitrite and sodium alkoxide–alcohol.

in the ultraviolet and the N→O stretching vibration appeared at 7.78 μ in the infrared.

2-Carboxy-1-indanone (**1j**) in benzene, on treatment with *n*-butyl nitrite and concentrated hydrochloric acid, underwent nitrosative decarboxylation, presumably *via* the precedented cyclic transition state **15**,[21] to precipitate gradually 2-oximino-1-indanone (**2a**). The



15

addition of acid to a mixture of *n*-butyl nitrite and 2-cyano- (**1k**) or 2-acetoxy-1-indanone (**1l**) led only to the recovery of small quantities of starting material and considerable polymeric products.

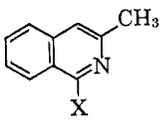
2-Hydroxyisocarbostyrils (3).—As previously noted for **2b** and **2c**, the *trans*-nitroso dimers **2c–2g** were ring expanded to their respective hydroxyisocarbostyrils, **3c–3g** under acidic [**2** (1 g) refluxed in 50 ml of concentrated hydrochloric acid for 5 hr] and alkaline [**2** (1 g) refluxed in a solution of 0.25 g of sodium in 50 ml of absolute methanol for 2.5 hr] conditions. On the basis of recovered starting material, isomerization of **2** to **3** in both media occurred in virtually quantitative yield (Table I). All these ring expansion reactions, however, began in heterogeneous media. In the case of **2b**, complete solution in concentrated hydrochloric acid had not occurred even after 5 hr. When the reaction period was extended until dissolution was complete (*ca.* 8 hr) the actual product yield of **3b** increased from 71 to 95%. At the other extreme, 2-*t*-butyl-2-nitroso-1-indanone dimer (**2g**) had completely dissolved by the end of the 5-hr (acid) and 2.5-hr (base) reactions, with a 96% yield of **3g** obtained in both cases. We conclude from these results that the difference in reaction time between the two isomerization media, and the increasing yields of hydroxyisocarbostyril products [**3b–3g** (71–96%), respectively, in acid, and 80–96%, in base)] must merely reflect the increasing solubility of the *trans*-nitroso dimers as the bulk of the alkyl substituent becomes larger.

In the direct conversion of **1b–1g** to **3b–3g**, respectively, the progressive decrease in product yield parallels a similar decrease in yields of **2b–2g** from the nitrosation of **1b–1g**. Since the nitroso dimers (**2b–2g**) are undoubtedly intermediates in the conversion of **1b–1g** to **3b–3g**, the nitrosation step clearly determines product yields.

The reaction **1b** → **3b** required 4 days for completion. In a brief study, we found that the use of nitrosonium tetrafluoroborate[22] in dry chloroform cut this reaction time to several hours but led to a lower yield (40–50%) of pure product.

The addition of *n*-butyl nitrite to **1h**–sodium methoxide–methanol, and sodium ethoxide to **1k**–*n*-butyl nitrite–ethanol solutions, led directly to 2-hydroxy-3-phenylisocarbostyril (**3h**, 18%) and 3-cyano-2-hydroxyisocarbostyril (**3k**, 14%), respectively.

The nmr spectra of **3b–3g** show, in addition to the expected alkyl proton signals in the *ca.* δ 1–3.5 region, four resonances with area ratios of 1:3:1:1, a vinyl proton singlet (δ 6.38–6.84 region), an aromatic proton multiplet (δ 7.47–7.58 region), a *peri* hydrogen (on C-8) multiplet (δ 8.32–8.42 region), and a deuterium exchangeable broad NOH proton signal (δ 9.3–10.71 region).[23] 2-Hydroxy-3-phenylisocarbostyril (**3h**) expectedly shows these same four signals in an area ratio of 1:8:1:1. The C-8 proton signal in all these isocarbostyrils appears downfield from the normal aromatic proton envelope. As it is in the plane of the C-1 carbonyl group, it must be subject to further anisotropic deshielding arising from the carbonyl ring current. This unresolved multiplet can be considered the X proton of an ABCX pattern. A similar chemical shift of the C-8 proton (relative to the three remaining benzene ring protons) due to the anisotropic effect of both Cl and OCH_3 groups was also observed in 1-chloro- (**16**) and 1-methoxy-3-methylisoquinoline (**17**).



16, X = Cl
17, X = OCH_3

Proof of structure of the hydroxyisocarbostyrils (**3**) was based on elemental analysis, conversion to their respective N-benzoate esters, reduction to the known isocarbostyrils (**4**), and spectral data. In the ultraviolet, each of **3d–3h** showed a main peak in the 225–230-mμ region (ϵ 10,000–20,000), in addition to longer wavelength bands of lower extinction at 241–242, 248–249, 291–292, 318, 327–328, and 340–343 mμ. In the infrared, each of **3d–3h**, and **3k** displayed a strong carbonyl band in the 6.02–6.10-μ region and doublet ring absorptions in the 6.13–6.32-μ range.[24] Chloroform solutions of **3b–3f** show broad, undoubtedly inter- and intramolecularly bonded OH absorptions in the 3.1–3.6-μ region. The 2-hydroxy-3-*t*-butylisocarbostyril (**3g**), however, displayed a sharp, bonded OH band at 3.39 μ. Since **3b–3g** showed no free OH absorptions below 3.0 μ, we interpret the spectrum of **3g** to mean that the size of the 3-*t*-butyl substituent prevented intermolecular OH---O bonding between hydroxyisocarbostyril molecules and constrained the hydrogen bridge solely to an intramolecular one.

Reaction Mechanism.—Based on evidence presented to date, we feel that the ring expansion **1** → **3** proceeds first to the nitroso monomers which can be isolated as dimers (**2**). The further reactions of these monomers in acid and base to **3**, however, permits speculation as to the intermediacy of the respective ring-opened oximino acid (**19**) or oximino ester (**24**). Alternatively, a concerted elimination–ring expansion without ring opening can be envisaged.[2] The precursors of **19** and **24**, *o*-carboxybenzyl (**20**) and *o*-carbomethoxylbenzyl

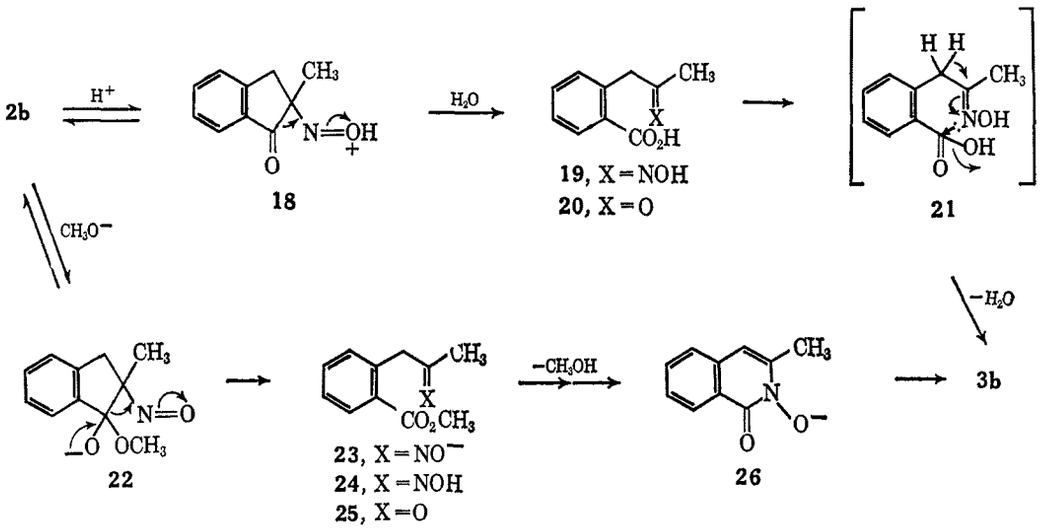
(21) As does cyclohexanecarboxylic acid on treatment with nitrosonium sulfate: C. R. Noller "Chemistry of Carbon Compounds," 3rd ed, W. B. Saunders, Philadelphia, Pa., 1965, p 937; W. Muench, L. Notarbartolo, and G. Silvestri, U. S. Patent 3,022,291 (1962); *Chem. Abstr.*, **57**, 7112e (1962).

(22) G. A. Olah and J. A. Olah, *J. Org. Chem.*, **30**, 2386 (1965), and preceding papers. The nitrosonium tetrafluoroborate was purchased from the Ozark-Mahoning Co., Tulsa, Okla.

(23) Previously and erroneously reported to be under the aromatic ring multiplet.[2]

(24) M. M. Robison and B. L. Robison [*J. Org. Chem.*, **21**, 1337 (1956) and *J. Am. Chem. Soc.*, **80**, 3443 (1958)] reported similar infrared absorptions for the parent 2-hydroxyisocarbostyril: 6.14 (C=O), 6.21, and 6.29 μ (ring).

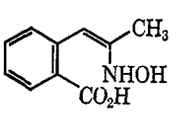
SCHEME II



methyl ketone (**25**) (see Scheme II), respectively, were prepared by alkaline hydrolysis of 3-methylisocoumarin.[25] Ketones **20** and **25** were converted directly to their respective oximes **19** and **24** with hydroxylamine. Refluxing either a solution of **19** in concentrated hydrochloric acid for 5 hr or a solution of **24** in absolute methanol–sodium methoxide for 2.5 hr led to **3b** in 71 and 80% yield, respectively. These yields are strikingly identical with those for the isomerization of **2b** → **3b** under both acidic and alkaline conditions (Table I) and are presumptive evidence that the ring expansion may proceed *via* ring-opened routes **19** and **23**, *i.e.*, **2b** → **18** → **19** →→ **3b**, and **2b** → **22** → **23** → **26** → **3b**.[26] Further, heating **19** above its melting point for 30 min cyclodehydrated it to Gottlieb's "anhydro derivative," actually **3b**, in 83% yield.

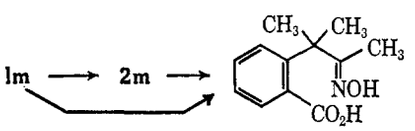
Several attempts to trap **19** by quenching the reaction at various intervals led only to the recovery of **2b**, in addition to product **3b**. When the ring expansion of **2b** was conducted in buffered solution (sodium acetate–acetic acid–acetic anhydride), only **3b** was obtained; under these conditions **19** also led to **3b**. Similar attempts to isolate **23** or **24** were unsuccessful.

The cyclodehydration of **19** → **3b** can be viewed as occurring by a concerted process (**21**) or perhaps *via* an initial enolization of **19** to the hydroxylenamine **28**. From either route, the product **3b**



28

contains a double bond conjugated with the benzene ring. When such elimination or enolization is prevented, as in 2,3,3-trimethyl-1-indanone (**1m**), the reaction terminates with the formation of the open-chain oximino acid **29**. Thus, addition of concentrated



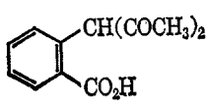
29

hydrochloric acid to a solution of **1m** and *n*-butyl nitrite led to the precipitation of the nitroso dimer **2m**. When *n*-butyl nitrite was added to a mixture of **1m** and concentrated hydrochloric acid, or **2m** was treated alone with concentrated hydrochloric acid, only the cleavage product, 3-methyl-3-(*o*-carboxyphenyl)-2-butanone oxime (**29**) was obtained.[27]

In the obvious extension of our ring expansion studies to the higher ring homologs 2-methyl- (**32a**) and 2-ethyl-1-tetralone (**32b**), nitrosation led to the very insoluble dimers, **33a** and **33b**, respectively. Isomerization of **33a** and **33b** under acid conditions led only to intractable tars; in base, however, the dimers dissolved slowly (20-hr reflux), after which acidification led only to the ring-opened, keto acid hydrolysis products **34a** and **34b** (94 and 90%, respectively). No ring-expanded dihydrobenzazepinone products were isolated.

(25) J. Gottlieb, *Ber.*, **32**, 958 (1899).

(26) In our previous paper,[2] we came to the opposite view that **19** (and by analogy, **23**) were not intermediates in the ring expansion **2b** → **3b** because "treatment of **19** under the conditions of acid-catalyzed isomerization.... led (only) to a recovery of **19**..." The keto acid (**20**) precursor of **19** had been prepared using W. R. H. Hurtley's procedure [*J. Chem. Soc.*, 1870 (1929)]: "Boiling aq. alkali produced from it [phenylacetylacetone-*o*-carboxylic acid (**27**)] a poor yield of *o*-carboxybenzyl methyl ketone, mp 115°...." Since



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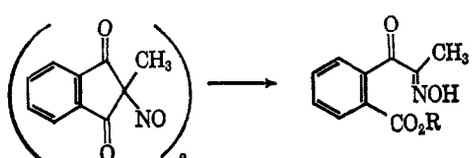
the melting point (119–120°) of the product obtained by us coincided with the literature[25] melting point (118–119°) of **20**, we assumed the compound was as indicated. It seems not, however, since the conversion of **20** to **19** "in the usual manner"[2] did not lead to the same oxime obtained from Gottlieb's keto acid.[25] We propagated the error then by not exercising the most fundamental of checks, elemental and spectral analysis of Hurtley's **20** and its oximation product.

(27) Ya. F. Freimanis and G. Ya. Vanag [*J. Gen. Chem. USSR* (Eng. Transl.), **31**, 1828 (1961)] similarly observed that treatment of 2-methyl-2-nitroso-1,3-indandione dimer **30** with base led to **31**.



30 **31**

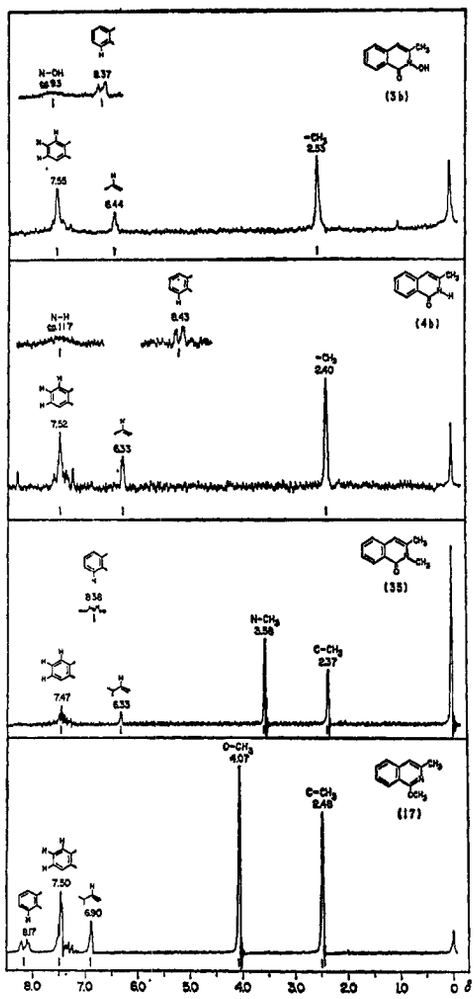
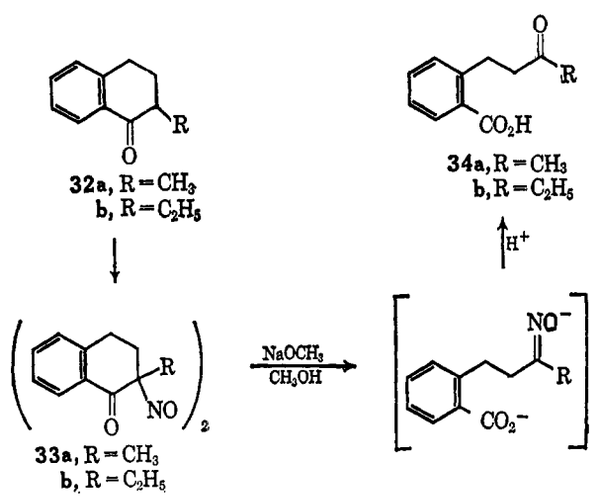


Figure 1.—Nmr spectra of 2-hydroxy-3-methylisocarbostyril (**3b**), 3-methylisocarbostyril (**4b**), 2,3-dimethylisocarbostyril (**35**), and 1-methoxy-3-methylisoquinoline (**17**).



Finally, nitrosation of 2-methylindoxyl led to unidentifiable polymeric products.[28]

Lactam–Lactim Tautomerism.—Jones, Katritzky, and Lagowski[29] have demonstrated the structural delineation of a potentially tautomeric compound by a comparison of its nmr spectrum with alkylated derivatives of the alternative structure. We have compared the nmr (Figure 1) and ultraviolet spectra (Figure 2) of 3-methyl-2-hydroxyisocarbostyril (**3b** ⇄ **5b**) and its reduction product, 3-methylisocarbostyril (**4b** ⇄ **6b**),[30] with that of 2,3-dimethylisocarbostyril (**35**) and 1-methoxy-3-methylisoquinoline (**17**) where such lactam–lactim tautomerism is precluded.

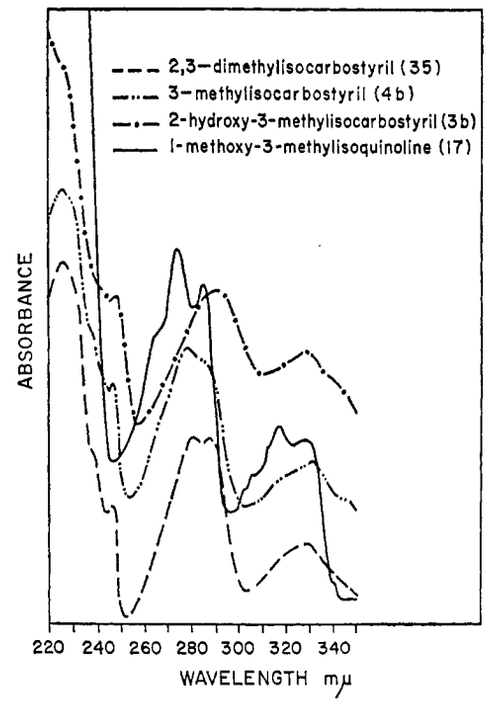
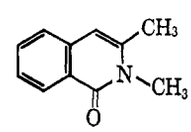


Figure 2.—Ultraviolet spectra of 2-hydroxy-3-methylisocarbostyril (**3b**), 3-methylisocarbostyril (**4b**), 2,3-dimethylisocarbostyril (**35**), and 1-methoxy-3-methylisoquinoline (**17**).



35

In addition to the signals for CCH_3 (δ 2.37), NCH_3 (δ 3.58), and aromatic and *peri* H (δ 7.47 and 8.38, respectively), the most salient feature of the nmr spectrum of **35** is the *C-4 vinyl proton singlet at δ 6.33.* This same signal for a vinyl proton appears at δ 6.33 in **4b** and δ 6.44 in **3b**. The 6.6-cps downfield shift for this same proton in **3b** relative to **4b** and **35** can be attributed entirely to the greater inductive[31] and resonance[32] effect of the NOH group compared with those of NH and NCH_3.

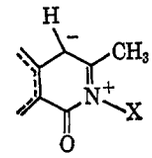
(28) Similar results were reported by A. S. Endler and E. I. Becker [*J. Am. Chem. Soc.*, **77**, 6608 (1955)] for the nitrosation of 3-methyloxindole.

(29) R. A. Y. Jones, A. R. Katritzky, and J. M. Lagowski, *Chem. Ind.* (London), 870 (1960).

(30) Both tautomers would show strong intramolecular hydrogen bonding.

(31) Note also the paramagnetic shift of adjacent CCH_3 protons in the nmr of **3b** (δ 2.53) relative to **4b** (δ 2.40).

(32) Possibly due to the relative stability and importance of structures **a** compared with **b** and **c**.



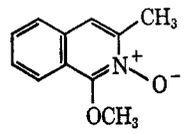
a, X = OH
b, X = H
c, X = CH_3

Further, the ultraviolet spectra of **3b**, **4b**, and **35** are quite similar, and differ considerably from that of the aromatic **17** (Figure 2). Thus **17** displays a strong K band at 217 mμ (ε 28,000) in the ultraviolet[33] (main peak not shown in Figure 2), and aromatic fine structure in the 270–330-mμ region, neither of which appears in **3b**, **4b**, or **35**.

Finally, the infrared spectrum of **3b** shows no N→O stretching band, as is found, *e.g.*, at 7.81 and 7.55 μ for 1-methyl- and 3-methylisoquinoline 2-oxides, respectively.[34]

The sum total of this spectral data is consistent only with the existence of 2-hydroxy-3-methylisocarbostyril and 3-methylisocarbostyril predominantly in the lactam forms **3b** and **4b**, respectively. Since **3c–3f** and **3h** also display the vinyl proton singlet in the nmr, they too must exist in the lactam form.

The nontautomeric 1-methoxy-3-methylisoquinoline 2-oxide (**36**) would have been desirable for nmr spectral



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comparison of its C-4 aromatic ring proton with the corresponding vinyl protons in **4b** and especially **3b**. We were unable to prepare **36** by the peracid oxidation of **17**. It is noteworthy that in the completely aromatic and nontautomeric **17**, the resonance effect of the 1-OCH_3 group shifts the resonance line for the C-4 aromatic ring proton upfield approximately 36 cps. removing it positionally from the normal aromatic proton envelope. It is clearly too far down field to be vinylic, and must be considered a diamagnetically shielded aromatic ring proton.

Experimental Section[35]

1-Indanones and 1-Tetralones.—The preparation and properties of 2-methyl-1-indanone (**1b**) and 2-ethyl-1-indanone (**1c**) have been reported.[2] Both displayed infrared carbonyl frequencies (film) at 5.82 μ. Other ketones prepared include **2-*n*-propyl-1-indanone** (**1d**), a light yellow oil, bp 110° (5 mm) [lit.[37] bp 100° (3 mm)], infrared absorption (film) at 5.85 μ (C=O); **2-isopropyl-1-indanone** (**1e**), a light yellow oil, bp 135° (10 mm) [lit.[38] bp 138° (12 mm)], infrared absorption (film) at 5.85 μ (C=O); **2-butyl-1-indanone** (**1f**), a semiviscous, light yellow oil, bp 118–120° (1.5 mm) [lit.[39] bp 154° (14 mm)], infrared absorption (film) at 5.82 μ (C=O); **2-*t*-Butyl-1-indanone** (**1g**), a yellow oil, bp 99–100° (0.9 mm), $n^{20}D$ 1.5338 [lit.[40] bp 113–115° (2.5 mm), $n^{20}D$ 1.5332], infrared absorption (film) at 5.83 μ (C=O); **2-phenyl-1-indanone** (**1h**), white plates, mp 78° from aqueous ethanol (lit.[41] mp 77°), mp 90–92° from benzene–hexane; each isomer led to the same 2,4-dinitrophenylhydrazone as ruby red cubes, mp 227–228° (lit.[41] mp 227–228°); **2-acetyl-1-indanone** (**1i**), light yellow flakes, mp 76–78° (lit.[42] mp 77°), infrared absorptions ($CHCl_3$) at 6.01 (acetyl C=O) and 6.17 μ (C=O); **2-carboxy-1-indanone** (**1j**), light yellow plates, mp 96–99° [lit.[43] mp 98–100°], infrared absorption (KBr) at 5.82 μ (C=O, broad); **2-cyano-1-indanone** (**1k**), light yellow plates, mp 67–68° [lit.[44] mp 68–69°], infrared absorptions (KBr) at 4.45 (C≡N) and 5.84 μ (C=O); **2-acetoxy-1-indanone** (**1l**), a light yellow, viscous oil, bp 130–133° (1.0 mm) [lit.[45] bp 137° (1.0 mm)], infrared absorptions (film) at 5.71 (ester C=O) and 5.77 μ (C=O); **2,3,3-trimethyl-1-indanone** (**1m**), a viscous, yellow oil, bp 125–127° (9 mm) [lit.[46] bp 133–136° (18 mm)], infrared absorption ($CHCl_3$) at 5.81 μ (C=O); **2-methyl-1-tetralone** (**32a**), bp 136–138° (16 mm) [lit.[47] bp 136–138° (16 mm)], infrared absorption (film) at 5.93 μ (C=O); **2-ethyl-1-tetralone** (**32b**), bp 125° (3 mm) [lit.[47] bp 147–148° (15 mm)], infrared absorption (film) at 5.94 μ (C=O).

2-Nitroso-1-indanone and 2-Nitroso-1-tetralone Dimers.—The general method of preparation of **2b–2g**, **2m**, **33a**, and **33b** was as follows. Freshly prepared *n*-butyl nitrite (3.5 ml) was added to an ice-bath-cooled solution of 20 mmoles of the 2-substituted 1-indanone or 1-tetralone in 25 ml of benzene, followed by 10 drops of concentrated hydrochloric acid. After a few minutes, the deep green color of the nitroso monomer in solution appeared. After standing for 2 hr at ice-bath temperature, the white precipitate which deposited was filtered, washed with cold ethanol, and dried. Evaporation of the colored filtrate invariably led to additional white, solid product. The combined white solids were triturated with absolute ethanol to lead to the following nitroso dimers (per cent yield in parenthesis).

2-Methyl-2-nitroso-1-indanone[2] (**2b**, 89.7%) had mp 145–147° dec; ultraviolet maxima at 249 mμ (ε 26,700) and 293 mμ (ε 6300); infrared absorptions (KBr) at 7.70 (N→O) and 5.81 μ (C=O).

2-Ethyl-2-nitroso-1-indanone[2] (**2c**, 68.4%) had mp 134–135° dec; ultraviolet maxima at 247 mμ (ε 24,450) and 295 mμ (ε 5800); infrared absorptions (KBr) at 7.70 (N→O) and 5.77 μ (C=O).

2-Propyl-2-nitroso-1-indanone (**2d**, 64.1%) was obtained as white plates: mp 104–105° dec; ultraviolet maxima at 252 mμ (ε 29,000) and 295 mμ (ε 7100); infrared absorptions (KBr) at 7.75 (N→O) and 5.78 μ (C=O). *Anal.* Calcd for $C_{24}H_{26}N_2O_4$: C, 70.92; H, 6.45; N, 6.89. Found: C, 71.13; H, 6.67; N, 6.69.

2-Isopropyl-2-nitroso-1-indanone (**2e**, 45.9%) was obtained as white plates, mp 94–95° dec, with ultraviolet maxima at 252 mμ (ε 25,500) and 295 mμ (ε 6400); and infrared absorptions (KBr) at 7.78 (N→O) and 5.81 μ (C=O). *Anal.* Calcd for $C_{24}H_{26}N_2O_4$: C, 70.92; H, 6.45; N, 6.89. Found: C, 71.13; H, 6.44; N, 6.85.

2-*n*-Butyl-2-nitroso-1-indanone (**2f**, 28.6%) was obtained as white plates, mp 105–106° dec, with ultraviolet maxima at 252 mμ (ε 25,600) and 294 mμ (ε 6400); and infrared absorptions (KBr) at 7.75 (N→O) and 5.79 μ (C=O). *Anal.* Calcd for $C_{26}H_{30}N_2O_4$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.89; H, 6.88; N, 6.34.

2-*t*-Butyl-2-nitroso-1-indanone (**2g**, 19.0%) was obtained as white plates, mp 90–91° dec, with ultraviolet maxima at 247 mμ (ε 25,200) and 294 mμ (ε 3750); and infrared absorptions (KBr) at 7.68 (N→O) and 5.81 μ (C=O). *Anal.* Calcd for $C_{26}H_{30}N_2O_4$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.93; H, 6.92; N, 6.34.

2,3,3-Trimethyl-2-nitroso-1-indanone (**2m**, 10.0%) was obtained as white plates, mp 113–114° dec, with ultraviolet maxima at 247 mμ (ε 12,600) and 292 mμ (ε 2650); and infrared absorptions (KBr) at 7.83 (N→O) and 5.80 μ (C=O). *Anal.* Calcd

(33) Reminiscent of the K band at 216 mμ (log ε 4.07) in isoquinoline: R. A. Morton and A. J. A. De Gouveia, *J. Chem. Soc.*, 916 (1934); "Ultraviolet Spectra of Aromatic Compounds" R. A. Friedel and M. Orchin, Ed., John Wiley and Sons, Inc., New York, N. Y., 1951, Spectrum 271.

(34) E. J. Moriconi and F. A. Spano, *J. Am. Chem. Soc.*, **86**, 38 (1964).

(35) Melting points and boiling points are corrected. The infrared spectra were obtained on Perkin-Elmer 21 and 337 spectrophotometers. The microanalyses were determined by Schwarzkopf Microanalytical Laboratory. The ultraviolet spectra were recorded in 95% ethanol solution on a Cary 15 spectrophotometer. Molar absorptivities parenthetically follow each wavelength reported. The nmr spectra were obtained on a Varian A-60 spectrometer[35] using dilute deuteriochloroform solutions; chemical shifts are given in parts per million downfield from tetramethylsilane.

(36) We acknowledge with pleasure the assistance of a National Science Foundation Grant GP 1482 to the Department of Chemistry toward the purchase of this instrument.

(37) J. H. Burchalter and R. C. Fuson, *J. Am. Chem. Soc.*, **70**, 4184 (1948).

(38) P. A. Plattner, A. Fürst, J. Wyss, and R. Sandrin, *Helv. Chim. Acta.*, **30**, 689 (1947).

(39) A. Maillard, A. Deluzarchi, and H. El-Ass, *Compt. Rend.*, **245**, 85 (1957).

(40) W. Herz, *J. Am. Chem. Soc.*, **80**, 1243 (1958).

(41) P. A. Plattner, R. Sandrin, and J. Wyss, *Helv. Chim. Acta.*, **29**, 1604 (1946).

(42) H. Burton and D. A. Munday, *J. Chem. Soc.*, 1718 (1957).

(43) R. H. Wiley and P. H. Hobson, *J. Am. Chem. Soc.*, **71**, 2429 (1949).

(44) W. S. Johnson and W. E. Shelberg, *ibid.*, **67**, 1745 (1945).

(45) F. I. Ishiwara, *J. Prak. Chem.*, **108**, 195 (1924).

(46) J. Colonge and J. Chambion, *Bull. Soc. Chim. France*, 999 (1947).

(47) H. Adkins and J. W. Davis, *J. Am. Chem. Soc.*, **71**, 2955 (1949).

for $C_{24}H_{26}N_2O_4$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.64; H, 6.48; N, 6.76.

2-Acetyl-2-nitroso-1-indanone (**2i**, 10.0%) was prepared from 0.5 g (2.9 mmoles) of **1i** in 15 ml of benzene and 4 ml of freshly prepared *n*-butyl nitrite. Work-up to product was the same as for all other nitroso dimers. **2i** was obtained as white plates: mp 123–125° dec; ultraviolet maxima at 253 mμ (ε 18,200) and 299 mμ (ε 5400); infrared absorptions (KBr) at 7.78 (N→O) and 5.78 μ (C=O). *Anal.* Calcd for $C_{22}H_{18}N_2O_6$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.09; H, 4.42; N, 6.99.

2-Methyl-2-nitroso-1-tetralone (**33a**, 76%) was obtained as white plates, mp 131–132° dec, with infrared absorptions (KBr) at 7.78 (N→O) and 5.95 μ (C=O). *Anal.* Calcd for C_{22}-$H_{22}N_2O_4$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.85; H, 5.77; N, 7.61.

2-Ethyl-2-nitroso-1-tetralone (**33b**, 37%) was obtained as white plates, mp 106–107° dec, with infrared absorptions (KBr) at 7.82 (N→O) and 5.90 μ (C=O). *Anal.* Calcd for $C_{24}H_{26}$-N_2O_4: C, 70.95; H, 6.40; N, 6.89. Found: C, 71.22; H, 6.48; N, 6.75.

2-Hydroxyisocarbostyrils (**3b–3h** and **3k**) were obtained by one or more of four procedures: from the nitroso dimers by (A) acid isomerization and (B) base isomerization; from the nitrosative ring expansion of **1** in (C) acid and (D) base (**3h** and **3k**). Examples of procedures A, B, and C have been detailed in ref 2 for the preparation of **3b** and **3c**. Only additional physical data are reported on these latter compounds. Other 2-hydroxyisocarbostyrils, prepared using these three procedures, and their N-benzoate esters, are listed below.

2-Hydroxy-3-methylisocarbostyril (**3b**)[2] showed ultraviolet maxima at 225 mμ (ε 13,500), 241 (5750), 248 (5300), 290 (5000), 318 (2500), 327.5 (1750) and 342 (1600); infrared absorptions ($CHCl_3$) at 6.04 (C=O), 6.15 and 6.26 μ (ring); and nmr peaks at *ca.* δ 9.3 (1 H, broad singlet, OH), 8.32 (1 *peri* H, multiplet), 7.47 (3 H, aromatic multiplet), 6.40 (1 H, vinyl singlet), and 2.53 (3 H, singlet, CH_3).

The N-benzoate ester of **3b**[2] displayed ultraviolet maxima at 231 mμ (ε 31,400), 277 (10,500), 286 (10,200), and 320 (4600); and nmr peaks were found at δ 8.31 (3 H, *peri* H and two H *ortho* to C=O group, multiplet), 7.56 (6 H, aromatic multiplet), 6.33 (1 H, vinyl singlet), and 2.35 (3 H singlet, CH_3).

2-Hydroxy-3-ethylisocarbostyril (**3c**)[2] showed ultraviolet maxima at 225 mμ (ε 16,400), 241 (8700), 248 (8300), 291 (7800), 318 (4250), 327 (4600), and 342 (3000); infrared absorptions ($CHCl_3$) at 6.07 (C=O), 6.16, and 6.26 μ (ring); and nmr peaks at *ca.* δ 9.3 (1 H broad singlet, OH), 8.42 (1 *peri* H, multiplet), 7.58 (3 H, aromatic multiplet), 6.47 (1 H, vinyl singlet), 2.92 (2 H quartet, J = 7 cps CH_2), and 1.38 (3 H triplet, J = 7 cps, CH_3).

The N-benzoate ester of **3c**[2] displayed ultraviolet maxima at 231 mμ (ε 31,000), 277 (8500), 286 (8000), and 320 (4600).

2-Hydroxy-3-propylisocarbostyril (**3d**), was obtained as white plates, mp 139–141°, with ultraviolet maxima at 226 mμ (ε 20,300), 242 (9500), 249 (9300), 291 (8300), 327 (5300), and 343 (3700); infrared absorptions ($CHCl_3$) at 6.08 (C=O), 6.17, and 6.29 μ (ring); and nmr peaks at *ca.* δ 9.8 (1 H, broad singlet, OH), 8.37 (1 *peri* H, multiplet), 7.53 (3 H, aromatic multiplet), 6.43 (1 H, vinyl singlet), 2.84 (2 H, triplet, J = 7 cps, α-CH_2), 1.83 (2 H, sextet, J = 7 cps, β-CH_2), and 1.03 (3 H triplet, J = 7 cps, CH_3).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.98; H, 6.62; N, 6.73.

The N-benzoate ester of **3d** was obtained as white plates, mp 122–123°, with ultraviolet maxima at 233 mμ (ε 36,000), 278 (12,700), 286 (11,000), and 326 (4900); and infrared absorptions (KBr) at 5.65 (ester C=O) and 5.95 μ (C=O).

Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.28; H, 5.54; N, 4.56. Found: C, 74.47; H, 5.76; N, 4.70.

2-Hydroxy-3-isopropylisocarbostyril (**3e**) was obtained as light yellow plates, mp 107–108°, with ultraviolet maxima at 226 mμ (ε 11,650), 249 (5650), 287 (5500), 291 (5250), 317 (2300), 327 (2750), and 343 (1750); infrared absorptions (KBr) at 6.10 (C=O), 6.17, and 6.29 μ (ring); and nmr peaks at *ca.* δ 8.8 (1 H, broad singlet, OH), 8.38 (1 *peri* H, multiplet), 7.58 (3 H, aromatic multiplet), 6.48 (1 H, vinyl singlet), 3.45 (1 H, heptet, J = 6.5 cps, CH), and 1.38 (6 H, doublet, J = 6.5 cps, CH_3).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.67; H, 6.30; N, 6.89.

The N-benzoate ester of **3e** was obtained as light pink needles, mp 77–78°, with ultraviolet maxima at 232 mμ (ε 53,200), 277 (18,500), 285 (18,400), and 327 (8700); and infrared absorptions (KBr) at 5.67 (ester C=O) and 5.93 μ (C=O).

Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.28; H, 5.54; N, 4.56. Found: C, 74.26; H, 5.80; N, 4.29.

2-Hydroxy-3-*n*-butylisocarbostyril (**3f**) was obtained as pink plates, mp 108–109°, with ultraviolet maxima at 226 mμ (ε 20,000), 242 (9100), 248 (9400), 292 (8000), 327 (4800), and 343 (3400); infrared absorptions ($CHCl_3$) at 6.10 (C=O), 6.16, and 6.29 μ (ring); and nmr peaks at *ca.* δ 10.7 (1 H, broad singlet, OH), 8.35 (1 *peri* H, multiplet), 7.48 (3 H, main peak of aromatic multiplet), 6.38 (1 H, vinyl singlet), 2.85 (2 H, triplet, J = 6 cps, CH_2), 1.62 (4 H, multiplet, CH_2CH_2), and 0.98 (3 H, triplet, J = 5 cps, CH_3).

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.90; H, 6.96; N, 6.45. Found: C, 72.14; H, 7.11; N, 6.57.

The N-benzoate ester of **3f** was obtained as pale pink needles mp 75–76°, with ultraviolet maxima at 232 mμ (ε 9200), 277 (3600), 287 (3200), and 320 (1600); and infrared absorptions ($CHCl_3$) at 5.63 (ester C=O) and 5.99 μ (C=O).

Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.74; H, 5.96; N, 4.36. Found: C, 74.99; H, 5.95; N, 4.38.

2-Hydroxy-3-*t*-butylisocarbostyril (**3g**) was obtained as white plates, mp 104–106°, with ultraviolet maxima at 227 mμ (ε 10,000), 242 (5850), 249 (5250), 291 (3700), 328 (2450), and 340 (1800); and infrared absorptions ($CHCl_3$) at 3.39 (bonded OH), 6.09 (C=O), 6.17, and 6.32 μ (ring).

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.90; H, 6.96; N, 6.45. Found: C, 72.03; H, 6.89; N, 6.45.

2-Hydroxy-3-phenylisocarbostyril (**3h**) was prepared by procedure D. A solution of 1.0 g (4.8 mmoles) of 2-phenyl-1-indanone (**1h**) in 10 ml of absolute ethanol was added to a solution of 0.4 g (0.0174 g-atom) of sodium in 25 ml of absolute ethanol. Freshly prepared *n*-butyl nitrite (2.0 ml) was then added to the golden yellow solution cooled in an ice bath. After standing for 1 hr, the white solid which precipitated from the now green solution was filtered and dried. The filtrate was evaporated to dryness to give a gummy solid which was crystallized with ether. The combined solids were dissolved in hot water, cooled, and acidified with dilute acid. The resulting solid was filtered, dried, and recrystallized from ethanol (Norit) to give 0.20 g (17.7%) of **2-hydroxy-3-phenylisocorbostyril** (**3h**) as snow-white flakes, mp 137–138° (lit.[48] mp 137–138°), with ultraviolet maxima at 230 mμ (ε 11,700), 252 (6850), 302 (5200), and 332 (3950); infrared absorptions ($CHCl_3$) at 6.06 (C=O), 6.21, and 6.29 μ (ring); and nmr peaks at *ca.* δ 10.1 (1 H, broad singlet, OH), 8.32 (1 *peri* H, multiplet), *ca.* 7.5 (8 H, aromatic multiplet), and 6.84 (1 H, vinyl singlet).

2-Hydroxy-3-cyanoisocarbostyril (**3k**) was also prepared by procedure D. Freshly prepared *n*-butyl nitrite (3.5 ml) was added to a solution of 2.0 g (12.7 mmoles) of **1k** in 25 ml of ethanol. Upon addition of 4 ml of 5% ethanolic sodium ethoxide solution, a succession of color changes was observed (green, orange, and red) after which a solid began to precipitate from solution. After standing for 1 hr, the mixture was diluted with 20 ml of water, and acidified with dilute hydrochloric acid. The solution was extracted with 20 ml of ether, and the ether extracts were dried. Filtration and evaporation of the filtrate left a yellow solid which was recrystallized from aqueous methanol to give 0.34 g (14.3%) of **2-hydroxy-3-cyanoisocarbostyril** (**3k**) as straw-like needles, mp 232–234°, with ultraviolet maxima at 262 mμ (ε 4700), 277 (2900), 308 (5300), 322 (5100), and 335 (4000); and infrared absorptions (KBr) at 4.48 (C≡N), 6.02 (C=O), 6.13 (shoulder), and 6.24 μ (ring).

Anal. Calcd for $C_{10}H_6N_2O_2$: C, 64.51; H, 3.25; N, 15.04. Found: C, 64.24; H, 3.48; N, 15.00.

3-Alkyl- and -arylisocarbostyrils (**4d–4f and 4h**) were prepared by the reduction of the corresponding 2-hydroxyisocarbostyrils (**3d–3f** and **3h**) with a mixture of iodine and red phosphorus in glacial acetic acid as previously detailed for **4b** and **4c**.[2] Additional physical data are reported for these latter two compounds.

3-Methylisocarbostyril (**4b**) showed ultraviolet maxima at 226 mμ (ε 9450), 240 (5450), 247 (4000), 278 (5450), 286 (5200), 318 (1500), and 332 (2250); infrared absorptions ($CHCl_3$) at 6.02 (C=O), 6.10, and 6.21 μ (ring); and nmr peaks at *ca.* δ 11.7 (1 H, broad singlet exchangeable in D_2O, NH), 8.43 (1 *peri* H, multiplet), 7.72 (3 H, aromatic multiplet), 6.33 (1 H, vinyl singlet), and 2.40 (3 H, singlet, CH_3).

(48) S. Gabriel, *Ber.*, **18**, 2448 (1885).

3-Ethylisocarbostyril (**4c**) had ultraviolet maxima at 226 mμ (ε 14,100), 239 (8300) 247 (5550), 278 (7850), 286 (6850), 317 (3250), 331 (3950), and 345 (2800); and infrared absorptions (KBr) at 5.99 (C=O), 6.09, and 6.20 μ (ring).

3-Propylisocarbostyril (**4d**, 36.2% yield) was obtained as white needles, mp 132.8–133.8° (lit.[49] mp 130–131°), with ultraviolet maxima at 227 mμ (ε 19,950), 239 (11,900), 248 (9350), 280 (11,250), 287 (10,950), 319 (4650), 332 (5700), and 347 (3850); and infrared absorptions (KBr) at 6.01 (C=O), 6.09, and 6.20 μ (ring).

3-Isopropylisocarbostyril (**4e**, 64.3% yield) was obtained as white needles, mp 186–188° (lit.[50] mp 186–189°), with ultraviolet maxima at 226 mμ (ε 17,100), 239 (10,800), 248 (8350), 278 (10,000), 287 (9800), 319 (4400), 331 (4200), and 347 (3500); and infrared absorptions (KBr) at 6.02 (C=O), 6.11, and 6.26 μ (ring).

3-*n*-Butylisocarbostyril (**4f**, 35.3%) was obtained as white lustrous plates, mp 139–140° (lit.[51] mp 138–139°), with ultraviolet maxima at 227 mμ (ε 19,900), 238 (11,650), 247 (9050), 278 (11,200), 287 (11,250), 320 (4650), 332 (5450) and 347 (3500); and infrared absorptions (KBr) at 5.99 (C=O), 6.06, and 6.17 μ (ring).

3-Phenylisocarbostyril (**4h**, 56.5%) was obtained as tiny white needles, mp 199.5–200° (lit.[52] mp 199.5–200°), with ultraviolet maxima at 232 mμ (ε 22,400), 305 (14,500), and 337 (8900); and infrared absorptions ($CHCl_3$) at 6.06 (C=O), 6.10, and 6.19 μ (ring).

1-Chloro-3-methylisoquinoline (**16**) was obtained in 92.2% yield by the treatment of 3-methylisocarbostyril (**4b**) with phosphorus oxychloride. Pure **16** distilled, bp 110–112° (2 mm) [lit.[53] bp 280–281° (756 mm)], as a colorless oil which solidified on standing, mp 36° (lit.[53] mp 36°), with infrared absorption ($CHCl_3$) at 6.13, 6.27, and 6.41 μ (ring); and nmr peaks at δ 8.18 (1 *peri* H, multiplet), 7.63 (main peak of 3 H aromatic multiplet), 7.32 (1 H, singlet, C-4 aromatic ring proton), and 2.60 (3 H, singlet, CH_3).

1-Methoxy-3-methylisoquinoline (**17**) was obtained in 70.8% yield by the treatment of **16** with methanolic sodium methoxide. Pure **17** distilled, bp 102–103° (2 mm) [lit.[53] bp 258° (764 mm)], as a colorless, sweet-smelling liquid which solidified on standing, with ultraviolet maxima (Figure 2) at 217 mμ (ε 28,000), 232 (1400), 237 (4650), 263 (5000), 273 (6300), 283 (5550), 303 (2400), 310 (3300), and 328 (2950); infrared absorptions ($CHCl_3$) at 6.15, 6.25, and 6.35 μ (ring); and nmr peaks that are shown in Figure 1.

***o*-Carboxybenzyl methyl ketoxime** (**19**) was obtained as white needles, mp 159–160° (lit.[25] mp 162°), with ultraviolet maxima at 224 mμ (ε 16,600) and 275 mμ (ε 2900). Its conversion to **3b** was accomplished in the following three ways.

(i) Two grams (10.4 mmoles) of **19** was heated in a crucible at 170° for 30 min. The white solid formed a red melt at 160° and began to foam slightly; beads of water condensed at the crucible top. Upon cooling, the melt solidified to a blood-red solid; recrystallization from aqueous acetone (Norit) gave 1.5 g (83.3%) of peach-colored plates. Sublimation of this material gave white plates, mp 172–173°, identical by all the usual criteria with **3b**.

(ii) The successive addition of 7 ml of 3 *N* hydrochloric acid in ethyl acetate, and then 0.8 ml of freshly prepared *n*-butyl nitrite, to a solution of 1.0 g (5.5 mmoles) of **19** in 10 ml of toluene maintained at 0° led, after the usual hydroxyisocarbostyril work-up, to **3b** in 69% (0.66 g) yield.

(iii) Similarly, a refluxing solution (5 hr) of 0.193 g (1.0 mmole) of **19** in 20 ml of concentrated hydrochloric acid ultimately led to **3b** in 71% yield.

(49) J. M. Albahary, *Ber.*, **29**, 2391 (1896).

(50) J. N. Lehmkuhl, *ibid.*, **30**, 889 (1897).

(51) J. W. Wilson, III, E. L. Anderson, and G. E. Allyot, *J. Org. Chem.*, **16**, 800 (1957).

(52) S. Gabriel, *Ber.*, **18**, 3470 (1885).

(53) S. Gabriel and A. Neumann, *ibid.*, **25**, 3563 (1892).

***o*-Carbomethoxybenzyl Methyl Ketone** (**25**).—A solution of 1.0 g (6.24 mmoles) of 3-methylisocoumarin in 25 ml of 50% methanolic sodium methoxide was refluxed for 2 hr. Upon cooling, the solution was acidified with dilute hydrochloric acid. The yellow precipitate was filtered and recrystallized from aqueous ethanol to give 0.580 g (48.7%) of **25** as yellow needles, mp 102–105°.

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.28. Found: C, 68.58; H, 6.41.

***o*-Carbomethoxybenzyl methyl ketoxime** (**24**) was obtained by heating a solution of 0.5 g of **25**, 3 ml of 5 *M* hydroxylamine hydrochloride solution, 3 ml of 5 *M* sodium acetate solution, and 5 ml of ethanol, on a steam bath for 3 hr. Upon cooling, the precipitated material was filtered, and the residue was recrystallized from aqueous ethanol to give 0.34 g (63.2%) of **24**, mp 149–152°.

Anal. Calcd for $C_{11}H_{13}NO_3$: C, 64.06; H, 5.87; N, 6.79. Found: C, 64.31; H, 5.89; N, 6.85.

A solution of 0.38 g (2.85 mmoles) of **24**, 50 ml of absolute methanol, and 0.25 g of sodium was heated under reflux for 2.5 hr. Evaporation of the solution left a sodium salt, acidification of which with dilute acid gave 0.40 g (80%) of **3b**.

Ring Opening of 1m and 2m to 3-Methyl-3-(*o*-carboxyphenyl)-2-butanone Oxime (**29**).—Thirty five milliliters of 3 *N* hydrochloric acid in ethyl acetate and 4.0 ml of freshly prepared *n*-butyl nitrite were added successively to a cooled (0°) solution of 4.7 g (28.0 mmoles) of **1m** in 100 ml of toluene. The two-phase system turned green, then yellow. After 1 hr at 0° and 1 additional hr at room temperature, the layers were separated and refrigerated. The precipitate formed from both portions was filtered, and recrystallized from aqueous methanol to give 3.96 g (64.4%) of pure **29** as white needles, mp 144–146°, with an ultraviolet maximum at 231 mμ (ε 7650) and infrared absorption (KBr) at 5.89 μ (C=O).

Anal. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.84; N, 6.33. Found: C, 65.44; H, 6.57; N, 6.60.

Refluxing 1 g of **2m** for 5 hr in concentrated hydrochloric acid also converted it to **29** in 84% yield.

Ring Opening of 33a to 4-(*o*-Carboxyphenyl)-2-butanone (**34a**).—Nitroso dimer **33a** (0.5 g, 2.6 mmoles) was added to a solution of 1.7 g of sodium in 50 ml of absolute methanol. The mixture was refluxed for 20 hr. The methanol was removed *in vacuo* and the solid residue was dissolved in water. The cold, aqueous solution was acidified with concentrated hydrochloric acid. After about 1 hr, crude **34a** began to precipitate. Recrystallization from methanol led to 90% of **34a** as white needles, mp 115° (lit.[54] mp 113°), with ultraviolet maxima at 228 mμ (ε 6800) and 277 mμ (ε 1300); and infrared absorption (KBr) at 5.87 μ (C=O).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.28. Found: C, 68.96; H, 6.47.

Ring Opening of 33b to 1-(*o*-Carboxyphenyl)-3-pentanone (**34b**).—Nitroso dimer **33b** (1.0 g, 2.46 mmoles) was added to a solution of 3.4 g of sodium in 50 ml of absolute methanol. The mixture was also heated for 20 hr but solution was attained very slowly. Work-up of **34b** was the same as **33b**, and led to 0.96 g (94.1%) of pure **34b**, mp 100–100.5°, with ultraviolet maxima at 228 mμ (ε 6500) and 277 mμ (ε 1050); and infrared absorption (KBr) at 5.88 μ (C=O).

Anal. Calcd for $C_{12}H_{14}NO_3$: C, 69.89; H, 6.84. Found: C, 70.01; H, 6.59.

2,3-Dimethylisocarbostyril (**35**) was obtained using the procedure of Brooker and White[55] as a yellow oil: bp 150–154° (1.6 mm); yellow rods, mp 101–102° [from petroleum ether (bp 30–60°)] [lit.[55] bp 153–163° (1 mm), mp 101–102°]; infrared absorptions (KBr) at 6.05, 6.12, and 6.26 μ (ring). The nmr and ultraviolet spectra are shown in Figures 1 and 2, respectively.

(54) C. Bülow and M. Deseniss, *ibid.*, **40**, 187 (1907).

(55) L. G. S. Brooker and F. L. White, *J. Am. Chem. Soc.*, **73**, 1094 (1951).