is water. Although small amounts of water do not prevent succinates from forming, water definitely increases the production of carbon dioxide, as seen in Table II.

TABLE II
EFFECT OF ADDITION OF ORTHOFORMATE[a]

Wt of methyl orthoformate, g	Mol of product produced		
	Methyl succinate	Carbon dioxide	Other
0	0.17	0.17	Methyl formate, 0.02
100	0.33	0.068	
200	0.18	0.0044	
200[b]	0.24[b]	0.0088	Ethyl acetate, 0.19

[a] At 300 psig CO, 700 psig C_2H_4, methanol to a total of 400 ml in a 0.5-gal stirred titanium autoclave with 1 g of $PdCl_2$, 10 g of $FeCl_2 \cdot 4H_2O$, and oxygen addition to 125–175 psig in increments at 85°. [b] The corresponding ethyl esters and ethyl alcohol.

Alkyl orthoformates can be added to suppress the carbon dioxide formation. In this way yields of succinate of over 90% based upon both ethylene and carbon monoxide are achieved.

Although eq 1 shows the need for 2 mol of carbon monoxide for 1 mol of ethylene, it was shown that slightly higher partial pressures of ethylene to carbon monoxide give better yields of succinates, as shown in Table III, for butyl succinate. Also, lower yields of

TABLE III
EFFECT OF CHANGES IN THE CARBON MONOXIDE–ETHYLENE RATIO[a]

Pressure, psig			Wt of butyl succinate product, g
Carbon monoxide	Ethylene	CO/C_2H_4	
300	700	0.43	0[b]
500	750	0.67	26
500	400	1.25	23
800	500	1.60	12

[a] 1 g of $PdCl_2$, 5 g of $CuCl_2$, 5 g of LiCl, and 400 ml of butanol, at 125–150° in a 0.5-gal stirred steel autoclave with 150–200 psig oxygen added in increments. [b] 15 g of butyl acrylate produced.

carbon dioxide are produced at lower CO/C_2H_4 ratios. However, at still lower CO/C_2H_4 ratios, instead of succinates, acrylates are produced. However, with the same carbon monoxide–ethylene ratio using the ferrous system without excess chloride ion, succinates were made (Tables I and II). Thus the product distribution depends significantly on the CO/C_2H_4 ratio. This dependence on CO/C_2H_4 ratio was previously noted for the synthesis of acrylic acid[4] starting from ethylene and carbon monoxide, according to eq 6,

$$CH_2{=}CH_2 + CO + {}^1/_2O_2 \longrightarrow CH_2{=}CHCO_2H \quad (6)$$

using a similar palladium redox catalyst with an acetic acid solvent. Here β-acetoxypropionic acid was also produced, particularly at higher temperatures and pressures and also at higher CO/C_2H_4 ratios. However, succinic acid was not a significant product.

Other olefins may also be used in place of ethylene. The results of two of these runs are shown in Table IV.

(4) D. M. Fenton, K. L. Olivier, and G. Biale, *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **14** (4), C77 (1969).

TABLE IV
USE OF OTHER OLEFINS[a]

Olefin	Wt, g: Olefin	Wt, g: Ethyl orthoformate	Pressure, psig carbon monoxide	Wt of products, g
Propylene	238	200	600	Diethyl methylsuccinate, 30; Ethyl crotonate, 30
1-Octene	100	100	700	Diethyl hexylsuccinate, 22

[a] 1 g of $PdCl_2$, 5 g of $CuCl_2$, 5 g of LiCl, and enough ethanol to make 600 ml of liquid, in a 0.5-gal stirred steel autoclave at 125–150° with 100–200 psig oxygen.

Experimental Section

The reactions were carried out in 0.5-gal stirred autoclaves made of either steel or titanium. The steel autoclaves exhibited some corrosion and so titanium was preferred. The catalyst and liquids were charged to the autoclave and ethylene (where used) and carbon monoxide were added to the desired pressures. Stirring was commenced and the autoclave was heated to the desired temperature. Oxygen was then added (controlled from behind a suitable barracade) in 10-psig increments. In almost all cases an immediate exotherm was noted and cooling water was circulated to bring the temperature under control. Pressure drops were noted. Oxygen was added until 150–200 psi had been added or until the reaction slowed down. In those cases where no noticeable reaction occurred no more than 40 psi of oxygen was added. After oxygen addition, the autoclave was cooled to room temperature and the gases were collected and analyzed by gas chromatography. The liquid was weighed and analyzed by gas chromatography and occasionally by distillation.

Registry No.—Palladium chloride, 7647-10-1; sodium acetate, 127-09-3; hydrochloric acid, 7647-01-0; methyl orthoformate, 34405-39-5; carbon monoxide, 630-08-0; ethylene, 74-85-1.

Effect of α-Methyl Substitution in the Beckmann and Schmidt Rearrangement of 1-Hydrindanones[1]

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In this paper we report the results of a study of (1) the Beckman rearrangement on the oximes of *cis*- and *trans*-1-hydrindanones (**1**), *cis*- and *trans*-8-methyl-1-hydrindanones (**4**), *cis*- and *trans*-2,8-dimethyl-1-hydrindanones (**8**), and 16-methylestrone 3-methyl ether (**13**); and (2) the Schmidt reaction on *cis*- and *trans*-**8**. *cis*- and *trans*-**1**,[3] *cis*- and *trans*-**4**[4–6] and **13** are known compounds, and the oximes of the former, respectively

(1) This research was supported by Public Health Service Grant No. 5RO1 AI-108063-01-03 from the National Cancer Institute.

(2) Graduate Research Assistant (1963–1967) on grants[1] supported by NIH; taken entirely from the Ph.D. Thesis of M. A. Stemniski, Fordham University, New York, N. Y., 1967.

(3) W. Hückel and W. Egerer, *Justus Liebigs Ann. Chem.*, **645**, 162 (1961).

(4) W. S. Johnson, *J. Amer. Chem. Soc.*, **65**, 1317 (1943).

(5) W. S. Johnson, *ibid.*, **66**, 215 (1944).

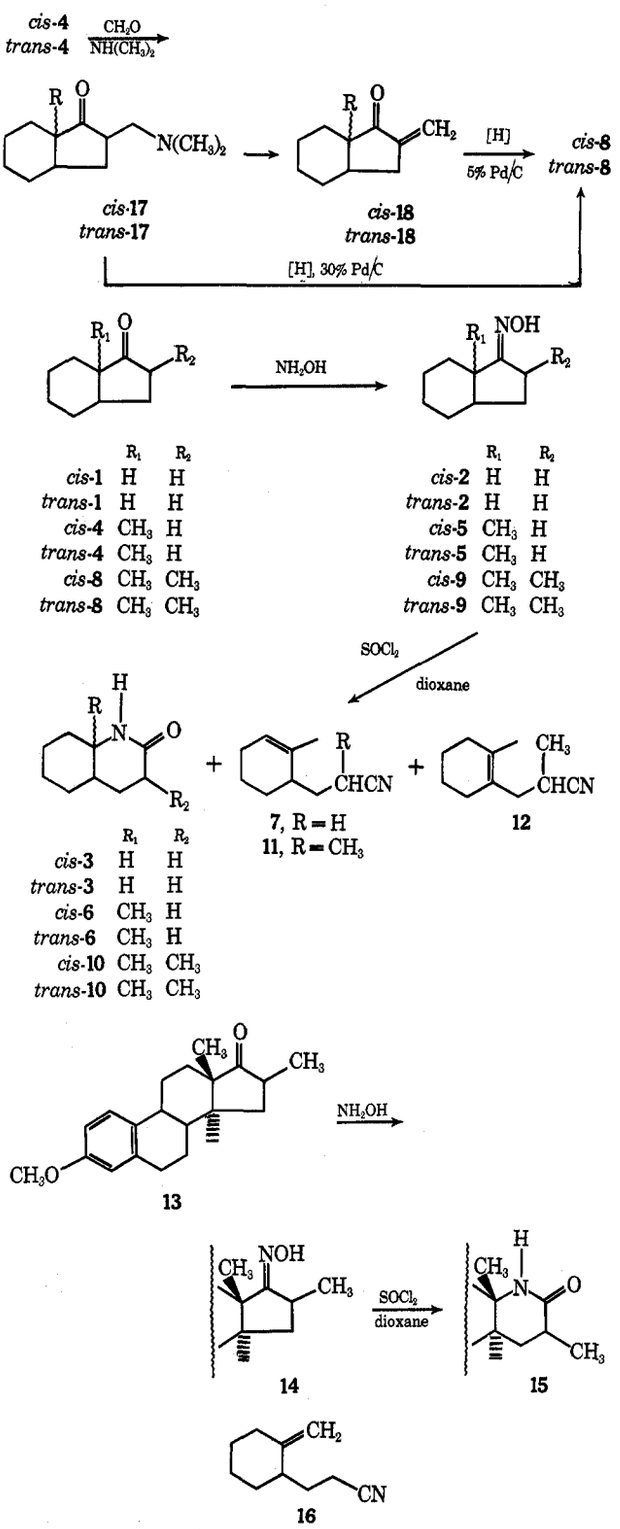
(6) W. E. Bachmann and S. Kushner, *J. Amer. Chem. Soc.*, **65**, 1963 (1943).

cis- and *trans*-**2**[7] and *cis*- and *trans*-**5**,[5,6] also have been reported. Conventional treatment of **13** with hydroxylamine afforded oxime **14**. Ketones *cis*- and *trans*-**8** were prepared from *cis*- and *trans*-**4**, respectively, *via* the well-trod Mannich pathway.[8,9] Thus, treatment of *cis*- and *trans*-**4** with dimethylamine hydrochloride and paraformaldehyde in 95% ethanol afforded the Mannich bases *cis*- (61%) and *trans*-**17** (39%), respectively. Since the Mannich reaction proceeds *via* the enol tautomer, recovery of considerable starting material from the trans reaction suggests that *cis*-**4** can enolize more readily than the trans isomer. Decomposition of *cis*- and *trans*-**17** either by steam distillation or refluxing in acetic acid–acetic anhydride led to *cis*- (55–57%) and *trans*-2-methylene-8-methyl-1-hydrindanone (**18**) (61–62%), respectively. Both *cis*- and *trans*-**18** were unstable and polymerized on standing at room temperature. Reduction of *cis*- and *trans*-**18** over 5% Pd/C led to *cis*- and *trans*-**8**, respectively, both isolated as stable oils (85%). Alternatively, both *cis*- and *trans*-**8** were prepared directly from the Mannich bases, respectively *cis*- (56%) and *trans*-**17** (46%), by hydrogenolysis over 30% Pd/C. The stereochemistry of the C-2 methyl substituent in *cis*- and *trans*-**8** is unknown. Since models indicate equal ease of hydrogen attack on both sides of both *cis*- and *trans*-**18**, it is assumed that each isomer of **8** is a mixture of α and β configurations. Oximation of *cis*- and *trans*-**8** occurred slowly (steric hindrance by the α,α'-methyl groups) and yields of oximes *cis*- (25%) and *trans*-**9** (46%) were comparatively low.

Models suggest less congestion in the geometric isomer of both *cis*- and *trans*-**9**,[10] and **14** where the hydroxyl group is anti to the six-membered ring.[11] In this configuration, the oximino group occupies a staggered conformation relative to the C-2 hydrogen and methyl substituents.

Beckmann rearrangement (thionyl chloride in dioxane) of oximes *cis*- and *trans*-**2** and **14** afforded the expected lactams *cis*- (66%)[12] and *trans*-3,4,4a,5,6,7,8,-8a-octahydrocarbostyril (**3**, 66%)[13] and 16-methyl-17a-aza-D-homoestrone 3-methyl ether (**15**, 32%).[14]

Rearrangement of *cis*-**5** led to lactam *cis*-8a-methyl-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (**6**, 40%) and fragmentation product 3-(2-cyanoethyl)-2-methylcyclohexene (**7**, 40%). Di Maio and Permutte[15] have noted in passing that treatment of *cis*-**5** with PCl_5 in ether afforded *cis*-**6** and 3-(2-methylenecyclohexyl)-propanenitrile (**16**) in undisclosed yields.[16] Since the latter authors easily converted *cis*-**6** to **16** under the



(7) W. Hückel, M. Sachs, J. Yantschulewitsch, and F. Nerdel, *Justus Liebigs Ann. Chem.*, **518**, 155 (1935).

(8) F. A. Kincl and M. Garcia, *Ber.*, **92**, 595 (1959).

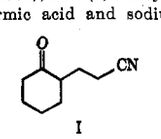
(9) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, pp 230–234.

(10) *trans*-**9** is configurationally identical with the trans-fused C,D rings in **14**.

(11) P. T. Lansbury and N. R. Mancuso, *Tetrahedron Lett.*, 2445 (1965); P. T. Lansbury, J. G. Colson, and N. R. Mancuso, *J. Amer. Chem. Soc.*, **86**, 5225 (1964); P. T. Lansbury and N. R. Mancuso, *ibid.*, **88**, 1205 (1966).

(12) Identical with the lactam obtained by C. A. Grob, H. P. Fischer, H. Link, and E. Renk, *Helv. Chim. Acta*, **46**, 1190 (1963), on treatment of the tosylate of *cis*-**2** with base.

(13) *trans*-**3** has been obtained (1) as one of the products of the Schmidt reaction on a mixture of *cis*- and *trans*-**1** [G. DiMaio and P. A. Tardella, *Gazz. Chim. Ital.*, **91**, 1345 (1961), and (2) *via* cylization of 2-(2-cyanoethyl)-cyclohexanone (I) with formic acid and sodium formate [A. N. Kost,



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T. A. Shelegoleva, and L. G. Yudin, *Zh. Obshch. Khim.*, **25**, 2464 (1955); *Chem. Abstr.*, **50**, 9410*i* (1956)].

(14) B. M. Regan and F. N. Hayes, *J. Amer. Chem. Soc.*, **78**, 639 (1956).

(15) G. DiMaio and V. Permutti, *Tetrahedron*, 2059 (1966).

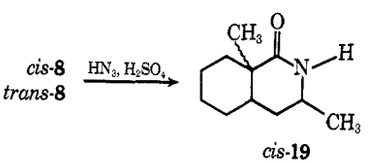
(16) A comparison of the properties of **7** and **16** is not possible since the authors[15] proved the structure of **16** by hydrolysis to 3-(2-methylenecyclohexyl)propanoic acid and then transformed the latter into its benzylisothiouronium salt. Our **7** clearly showed both a single vinyl proton at δ 4.61 coupled to the adjacent CH_2 and a CH_3 singlet at δ 2.29. The discrepancy between our melting point for *cis*-**6** (82–84°) and that reported by Di Maio and Permutti (mp 48–49°) should be noted.

reaction conditions,[15] the latter is a secondary reaction product and not a true Beckmann fragmentation product, as is **7**.

Similarly, Beckmann rearrangement of *trans*-**5** afforded *trans*-**6** (37%) and **7** (35%).

Finally, rearrangement of *cis*- and *trans*-**9** produced lactams *cis*- (41%) and *trans*-3,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (**10**, 40%), respectively. In the former case, fragmentation product 3-(2-cyanopropyl)-2-methylcyclohexene (**11**, 12%) was also obtained; in the latter an inseparable mixture of **11** and the isomeric 2-(2-cyanopropyl)-1-methylcyclohexene (**12**) was isolated in 17% yield.

Treatment of benzene solutions of *cis*- and *trans*-**8** with hydrazoic acid in the presence of concentrated sulfuric acid afforded the expected lactams, *cis*- (27%) and *trans*-3,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydroisocarbostyril (**19**, 30%), respectively. Worthy of



cis-**19**
trans-**19**

comparison is the position of the C-3 methine proton in the nmr. In carbostyrils *cis*- and *trans*-**10**, this proton appears as a complex multiplet in the range δ 2.65–1.90. In isocarbostyrils *cis*- and *trans*-**19**, it is deshielded by the adjacent N and appears downfield at δ 3.70–3.25.

To sum up a general observation, models indicated and these experiments confirmed that methyl substituents on C-2,8 of **1** have little or no effect on the direction of the Beckmann rearrangement (aryl migration) leading to carbostyril products. In the Schmidt reaction, however, methyl substitution on C-2,8 of **1** led *via* alkyl migration to isocarbostyrils.

Experimental Section[17]

In the preparation of *cis*-1-hydrindanone (**1**),[3] reduction of 1-indanone was accomplished at 60 psi using 5% rhodium on alumina catalyst.[18] The reduction product mixture containing *cis*-1 and 1-hydrindanol was oxidized with chromic acid to yield *cis*-1 in 73% overall yield.

Oxime of 16-Methylestrone 3-Methyl Ether (14).—A mixture of 2.8 g (9.4 mmol) of 16-methylestrone 3-methyl ether (**13**), mp 90–93° (lit.[19] mp 95–96°), 1.40 g (20 mmol) of $NH_2OH \cdot HCl$, and 3.0 g of NaOAc in 300 ml of 95% C_2H_5OH was stirred and refluxed for 3 hr. The reaction was diluted with H_2O and cooled to yield a white solid which was filtered and air dried. Several recrystallizations from 95% C_2H_5OH gave white crystals of **14** (1.3 g, 44%): mp 181–185° dec (15–20 min); ir (KBr) 6.25 μ (C=N); nmr ($CDCl_3$) δ 8.70 (s, 1, NOH), 7.32–6.60 (m, 3, aromatic), 3.78 (s, 3, OCH_3), 3.10–1.34 (m, 14, CH_2 and CH), 1.22 (d, J = 6.5 Hz, 3, CH_3), and 1.07 (s, 3, CH_3).

Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.54; H, 8.70; N, 4.58.

(17) Melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 grating spectrophotometer. Potassium bromide wafers were used for all solid compounds and sodium chloride plates were used for all liquid compounds. The nmr spectra were obtained on a Varian Associates A-60 spectrometer; chemical shifts are expressed in parts per million (δ) downfield from TMS as an internal standard. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(18) A. I. Meyers, W. Beverung, and G. Garcia-Munoz, *J. Org. Chem.*, **29**, 3427 (1964).

(19) D. A. Tyner, U. S. Patent 3,049,555 (1962); *Chem. Abstr.*, **59**, 1712*h* (1963).

cis-**2-(Dimethylaminomethyl)-8-methyl-1-hydrindanone (17).**—A mixture of 5.0 g (33 mmol) of *cis*-8-methyl-1-hydrindanone (**4**), bp 70° (3 mm) [lit.[5] bp 106° (20 mm)], 5.0 g (0.17 mol) of paraformaldehyde, 17.8 g (0.22 mol) of $(CH_3)_2NH \cdot HCl$, and 85 ml of 95% C_2H_5OH was stirred and refluxed for 3 hr. An additional 5.0 g (0.17 mol) of paraformaldehyde was added to the clear solution and refluxing was continued for an additional 15–17 hr. Evaporation *in vacuo* afforded a semisolid residue to which was added 100 ml of 10% HCl, and the whole was extracted with ether. The aqueous layer was neutralized with concentrated NH_4OH and extracted with ether. The ether extracts were dried (Na_2SO_4), filtered, and evaporated *in vacuo* to give 4.2 g (61%) of *cis*-**17** as a colorless oil: bp 108–110° (2 mm); ir (neat) 5.76 μ (C=O); nmr (CCl_4) δ 2.75–2.21 (m, 3, CH_2 and CH), 2.17 [s, 6, $N(CH_3)_2$], 2.00–1.00 (m, 11, CH_2 and CH), and 0.93 (s, 3, CH_3).

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.49; H, 11.04; N, 6.99.

trans-**2-(Dimethylaminomethyl)-8-methyl-1-hydrindanone (17).**—Similar treatment of *trans*-8-methyl-1-hydrindanone (**4**, 2.0 g, 13 mmol), bp 64–65° (1.5 mm) [lit.[5] bp 109° (20 mm)], afforded *trans*-**17** (1.1 g, 39%): bp 105–109° (2 mm); ir (neat) 5.76 μ (C=O); nmr (CCl_4) δ 2.90–2.25 (m, 3, CH_2 and CH), 2.15 [s, 6, $N(CH_3)_2$], 1.95–1.20 (m, 11, CH_2 and CH), and 0.89 (s, 3, CH_3).

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.52; H, 10.97; N, 6.69.

cis-**2-Methylene-8-methyl-1-hydrindanone (18).**—Indirect steam distillation (short path distillation head) of 1.75 g of *cis*-**17** into ice-cold ether was continued until the distillate was a single phase. The ether solution was extracted with 10% HCl, dried (Na_2SO_4), and evaporated *in vacuo* to an oil which was fractionated to give *cis*-**18** (0.78 g, 57%), bp 75–76° (2.5 mm).

Alternatively, 1.75 g (8.3 mmol) of *cis*-**17** in 10 ml each of glacial acetic acid and acetic anhydride was heated on a steam bath for 2 hr. After the solvent was evaporated *in vacuo*, the residue was dissolved in ether and successively washed with 10% NaOH, H_2O, and a saturated solution of NaCl. Evaporation of solvent ether *in vacuo* then fractionation gave 0.75 g (55%) of *cis*-**18**: bp 74–76° (2.5 mm); ir (neat) 5.78 (C=O) and 6.11 μ (C=C); nmr (CCl_4) δ 6.08 (distorted q, J = 2.5 Hz, 1, =CH), 5.34 (distorted q, J = 2.5 Hz, 1, =CH), 2.85–1.22 (m, 11, CH_2 and CH), and 1.02 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.24; H, 10.05.

trans-**2-Methylene-8-methyl-1-hydrindanone (18).**—Similar treatment of *trans*-**17** (2.6 g, 12 mmol) afforded *trans*-**18** in 62% yield by steam distillation and 61% *via* acetic acid–acetic anhydride reflux: bp 69–70° (0.8 mm) and 76–78° (2 mm); ir (neat) 5.78 (C=O) and 6.10 μ (C=C); nmr (CCl_4) δ 5.92 (distorted q, J = 2.5 Hz, 1, =CH), 5.25 (distorted q, J = 2.5 Hz, 1 =CH), 2.50–1.20 (m, 11, CH_2 and CH), and 0.85 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.26; H, 9.62.

cis-**2,8-Dimethyl-1-hydrindanone (8). Hydrogenation of *cis*-18.**—A mixture of 4.0 g (12 mmol) of *cis*-**18** in 150 ml of absolute C_2H_5OH and 2.0 g of 5% Pd/C was hydrogenated (10 psi) in a Paar apparatus for 2 hr. After catalyst removal by filtration through Filter-cel, the solvent was removed *in vacuo* and the oily residue was distilled to give 3.44 g (85%) of *cis*-**8** as a colorless oil, bp 58° (0.6 mm).

Hydrogenolysis of *cis*-17.—The 30% Pd/C catalyst (2.0 g) in 200 ml of absolute C_2H_5OH was reduced under 45 psi H_2 pressure for 2 hr. To this suspension was added 3.8 g (18 mmol) of *cis*-**17** and reduction was continued at 30 psi for 24 hr. After catalyst and solvent removal, the residual oil was dissolved in ether and washed with 10% HCl. Neutralization of the aqueous layer followed by extraction led ultimately to recovery of 1.15 g of unreacted *cis*-**17**. The ether layer was evaporated *in vacuo* and distilled to give 1.70 g (56%) of *cis*-**8**: bp 67–68° (2 mm); ir (neat) 5.75 μ (C=O); nmr (CCl_4) δ 2.40–1.31 (m, 12, CH_2 and CH), 1.12 (d, J = 6.5 Hz, 3, CH_3), and 1.04 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.65; H, 10.68.

trans-**2,8-Dimethyl-1-hydrindanone (8).**—Similar hydrogenation of *trans*-**18** (2.0 g, 12 mmol) and hydrogenolysis of *trans*-**17** (3.75 g, 18 mmol) afforded *trans*-**8** in 85 and 46% yields, respectively, as a colorless oil: bp 63° (0.7 mm) and 67–68° (1 mm); ir (neat) 5.75 μ (C=O); nmr (CCl_4) δ 2.20–1.25 (m, 12, CH_2 and CH), 1.13 (d, J = 6.5 Hz, 3, CH_3), and 0.78 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.37; H, 10.63.

***cis*-2,8-Dimethyl-1-hydrindanone Oxime (9).**—A mixture of 2.0 g (12 mmol) of *cis*-**8**, 1.64 g (24 mmol) of $NH_2OH \cdot HCl$, 3.74 g of NaOAc, and 100 ml of 95% C_2H_5OH was refluxed for 7 hr. The solution was diluted with an equal volume of H_2O and cooled to precipitate crude *cis*-**9**. Several recrystallizations of this material from 95% C_2H_5OH afforded 0.55 g (25%) of *cis*-**9**: mp 114–116°; ir (KBr) 6.90 μ (C=N); nmr ($CDCl_3$) δ 9.75 (s, 1, OH), 3.20–2.60 (broad s, 1, CH_2 or CH), 1.44 (s, 11, CH_2 and CH), 1.40 (d, downfield peak hidden under band at δ 1.44, J = 6.5 Hz, 3, CH_3), and 1.18 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: 72.85; H, 10.39; N, 7.48.

***trans*-2,8-Dimethyl-1-hydrindanone Oxime (9).**—Similar treatment of *trans*-**8** (0.50 g, 3.0 mmol) with $NH_2OH \cdot HCl$ (0.41 g, 5.9 mmol) and NaOAc (0.94 g) in 25 ml of 95% C_2H_5OH ultimately afforded *trans*-**9** (0.25 g, 46%): mp 114–116° (from CH_3OH); ir (KBr) 6.83 μ (C=N); nmr ($CDCl_3$) δ 9.03 (s, 1, OH), 3.15–2.55 (m, 1), 2.10–1.37 (m, 11, CH_2 and CH), 1.30 (d, downfield peak partially obscured by band at CH_2 resonances, J = 6.5 Hz, 3, CH_3), and 0.93 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 73.18; H, 10.61; N, 7.69.

Beckmann Rearrangements.—The general procedure was as follows. Thionyl chloride (5–10 molar equiv) was added slowly to a solution of the oxime in anhydrous, freshly distilled dioxane at room temperature. The temperature of the resulting yellow solution rose 8–10°. After stirring for 10–20 min, the solution was decomposed with aqueous $NaHCO_3$ solution and extracted with $CHCl_3$ or ether. The extracts were dried (Na_2SO_4) and evaporated to dryness, leaving a residue that was recrystallized (solid) or distilled (liquid). Variations on isolation and purification procedure are noted under each oxime.

cis-**2** (2.0 g, 13 mmol), mp 97–99° (lit.[6] mp 100°), in 140 ml of dioxane and 5 ml (67 mmol) of $SOCl_2$ afforded crude ***cis*-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (3)** as a crude solid after liquid–liquid extraction with ether for 48 hr. Recrystallization from acetone gave pure *cis*-**3**, mp 127–129° (lit.[12] mp 128–130°).

Similarly, *trans*-**2** (1.0 g 6.5 mmol), mp 145–147° (lit.[6] mp 146°), 70 ml of dioxane, and 2.5 ml (34 mmol) of $SOCl_2$ gave 0.66 g (33%) of ***trans*-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (3)**, mp 151.5–153° (from acetone) (lit.[13] mp 151°). After liquid–liquid extraction with ether and evaporation, the initial crude *trans*-**3** had been isolated as white crystals in a brown oil. This negligible amount of residual oil showed the presence of a nitrile and unreacted *trans*-**2**.

cis-**5** (2.0 g, 12 mmol), mp 85–87° (lit.[7] mp 85.5–87°), in 140 ml of dioxane and 4.5 ml (62 mmol) of $SOCl_2$ led after evaporation of the ether extract (liquid–liquid extractor) to a viscous brown residual oil. Vacuum distillation of this material afforded two fractions. Fraction i consisted of **3-(2-cyanoethyl)-2-methylcyclohexene (7**, 0.71 g, 40%): bp 57° (0.10 mm); ir (neat) 4.46 (C=N) and 6.10 μ (C=C); nmr (CCl_4) δ 4.61 (d, J = 6.5 Hz, 1, C=CH), 2.20–1.80 (m, 5, CH_2 and CH), 1.63 (s, 6, CH_2), and 2.29 (s, 3, CH_3).

Anal. Calcd for $C_{10}H_{15}N$: C, 80.48; H, 10.13; N, 9.38. Found: C, 80.47; H, 10.06; N, 9.23.

Fraction ii, bp 118–120° (0.15 mm), gave 0.80 g (40%) of a nearly colorless viscous oil which gradually crystallized on standing. Recrystallization of this material from ether gave ***cis*-8a-methyl-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (6)**: mp 82–84°; ir (KBr) 3.14 (NH) and 6.02 μ (C=O); nmr (CCl_4) δ 7.53 (s, 1, NH), 2.50–2.18 (m, 2, CH_2) 2.12–1.31 (m with sharp peak at 1.50, 11, CH_2 and CH) and 1.26 (s, 3, CH_3).

Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37. Found: C, 72.00; H, 10.10; N, 8.60.

Similarly, *trans*-**5** (2.0 g, 12 mmol), mp 115–116° (lit.[7] mp 113–115°), in 140 ml of dioxane and 5 ml (67 mmol) of $SOCl_2$ gave, after evaporation of the $CHCl_3$ extracts, a residual brown oil from which crystals separated on standing. The crystals were filtered and washed with ether; the ether wash was slowly evaporated to yield an additional crop of crystals in a brown oil. The combined solids were recrystallized from acetone to give 0.75 g (37%) of ***trans*-8a-methyl-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (6)**: mp 150–152°; ir (KBr) 3.12 (NH), 6.01 and 6.15 μ (C=O); nmr (CCl_4) δ 9.20 (s, 1, NH), 2.40–2.10 (m, 2, CH_2), 1.90–1.35 (m, 11, CH_2 and CH), and 1.13 (s, 3, CH_3).

Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37. Found: C, 71.82; H, 10.01; N, 8.62.

Fractional distillation of the brown oil afforded **7** (0.63 g, 35%) as a colorless oil, bp 71° (0.80 mm).

cis-**9** (1.0 g, 5.5 mmol) in 60 ml of dioxane and 4.0 ml (55 mmol) of $SOCl_2$ led, after evaporation of the $CHCl_3$ extracts, to an oil which gradually crystallized on standing. The filtered crystals were washed with cold ether and dried. Slow evaporation of the ether wash yielded an additional crop of crystals in a viscous oil. The combined solids were recrystallized from acetone to give 0.41 g (41%) of ***cis*-3,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (10)**: mp 149–151°; ir (KBr) 3.12 (NH) and 6.01 μ (C=O); nmr (CCl_4) δ 8.10 (s, 1, NH), 2.40–1.90 (m, 1, CH), 1.85–1.40 (m, 11, CH_2 and CH), 1.30 (s, 3, CH_3), and 1.16 (d, J = 6.5 Hz, 3, CH_3).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: C, 72.71; H, 10.63; N, 7.48.

Fractional distillation [pot temperature 95–100° (1.2 mm)] of the viscous oil afforded 0.11 g (12%) of **3-(2-cyanopropyl)-2-methylcyclohexene (11)**: ir (neat) 4.47 (C≡N) and 6.10 μ (C=C); nmr (CCl_4) δ 4.62 (d, J = 6.5 Hz, 1, =CH), 2.80–2.40 (m, 1, CH), 2.40–2.00 (m, 3, CH_3), 2.00–1.48 (m, 9, CH_2 and CH), and 1.30 (d, J = 6.5 Hz, 3, CH_3).

Anal. Calcd for $C_{11}H_{17}N$: C, 80.92; H, 10.50; N, 8.58. Found: C 81.07; H, 10.62; N, 8.83.

Similar treatment of *trans*-**9** (1.0 g, 5.6 mmol) in 60 ml of dioxane and 4.0 ml (55 mmol) of $SOCl_2$ ultimately afforded 0.40 g (40%) of ***trans*-3,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydrocarbostyril (10)**: mp 158–160° (from acetone); ir (KBr) 3.15 (NH), 6.00 and 6.23 μ (C=O); nmr ($CDCl_3$) δ 6.44 (s, 1, NH), 2.65–2.10 (m, 1, CH), 1.98–1.38 (m, 11, CH_2 and CH), 1.24 (d, upfield peak under CH_3 resonance, J = 6.5 Hz, 3, CH_3), and 1.16 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: C, 72.60; H, 10.61; N, 7.71.

Fractional distillation of the oil [pot temperature 90–100° (0.8 mm)] afforded 0.15 g (17%) of a mixture (nmr) of **11** and **2-(2-cyanopropyl)methylcyclohexene (12)**: ir (neat) 4.48 (C≡N) and 6.12 μ (C=C); nmr (CCl_4) δ 4.62 (d, J = 6.5 Hz, =CH), 2.40–1.79 (m, CH_3), 1.64 (s, CH_2), 1.30 (d, J = 6.5 Hz), and 1.25 (d, J = 6.5 Hz).

Oxime **14** (0.88 g, 2.8 mmol) in 35 ml of dioxane rearranged in 15 min with 1.0 ml (14 mmol) of $SOCl_2$. After decomposition with 100 ml of saturated aqueous $NaHCO_3$, the precipitate which formed was filtered and dried. Repeated recrystallization from CH_3OH gave 0.28 g (32%) of **16-methyl-17a-aza-*D*-homoestrone 3-methyl ether (15)**: mp 212–214°; ir (KBr) 3.13 (NH) and 6.02 μ (C=O); nmr ($CDCl_3$) δ 7.21–6.71 (m, 3, aromatic), 6.32 (s, 1, NH), 3.75 (s, 3, OCH_3), 3.00–1.40 (m, 14, CH_2 and CH), 1.20 (d, upfield peak under CH_3 resonance, J = 6.5 Hz, 3, CH_3), and 1.15 (s, 3, CH_3).

Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.69; H, 8.64; N, 4.33.

Schmidt Reaction on *cis*- and *trans*-8.—Concentrated H_2SO_4 (5.6 ml) was added to a cooled (<10°), stirred solution of 2.0 g (12 mmol) of *cis*-**8** in 96 ml of anhydrous C_6H_6. Twenty milliliters of a solution of freshly prepared HN_3 [13 g (0.20 mol) of NaN_3, 13 ml of H_2O, 100 ml of C_6H_6, and 9.8 g (0.10 mol) of concentrated H_2SO_4] in benzene was added to the yellow solution over a 1-hr period. The temperature was maintained at 6–7° during addition and for 30 min more until N_2 evolution ceased. The reaction mixture was poured onto 300 ml of ice water and extracted with a large excess of $CHCl_3$. The combined organic extracts were successively washed with 2 N NaOH solution and H_2O and dried (Na_2SO_4). Filtration and evaporation of solvent *in vacuo* left a brown oil which crystallized on standing. The crystals were washed with cold ether and dried. Recrystallization from acetone (or CH_3OH) gave 0.58 g (27%) of ***cis*-3,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydroisocarbostyril (19)**: mp 112–114°; ir (KBr) 3.14 (NH) and 6.04 μ (C=O); nmr ($CDCl_3$) δ 6.17 (s, 1, NH), 3.70–3.25 (broad mound, 1, CH), 2.26–1.37 (m, 11, CH_2 and CH), 1.28 (s, 3, CH_3), and 1.15 (d, J = 6.5 Hz, 3, CH_3).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: C, 72.30; H, 10.73; N, 7.76.

Some unidentified material (0.20 g, 10%) was isolated from the mother liquors.

Similar treatment of *trans*-**8** (2.0 g, 12 mmol) in 96 ml of benzene with 5.6 ml of concentrated H_2SO_4 and 20 ml of a freshly prepared solution of HN_3 in C_6H_6 provided 0.67 g (31%) of ***trans*-3,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydroisocarbostyril (19)**: mp 121–123° (from acetone); ir (KBr) 3.13 (NH) and 6.05 μ (C=O);

nmr (CCl_4) δ 8.09 (s, 1, NH), 3.70–3.25 (broad mound, 1, CH), 1.60–1.30 (m, 11, CH_2 and CH), 1.18 (d, J = 6.5 Hz, 3, CH_3), and 1.08 (s, 3, CH_3).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.72. Found: C, 72.76; H, 10.53; N, 7.84.

Registry No.—*cis*-**6**, 34387-94-5; *trans*-**6**, 34387-95-6; **7**, 34387-96-7; **8**, 34387-97-8; **9**, 34387-98-9; **10**, 34387-99-0; **11**, 34388-00-6; **14**, 34388-01-7; **15**, 34388-02-8; **17**, 34388-03-9; *cis*-**18**, 34388-04-0; *trans*-**18**, 34388-05-1; **19**, 34388-06-2.

Intramolecular Cyclization of *N*-Alkyl-3,3′,4,4′-tetrahydro-1,1′-biisoquinolinium Salts

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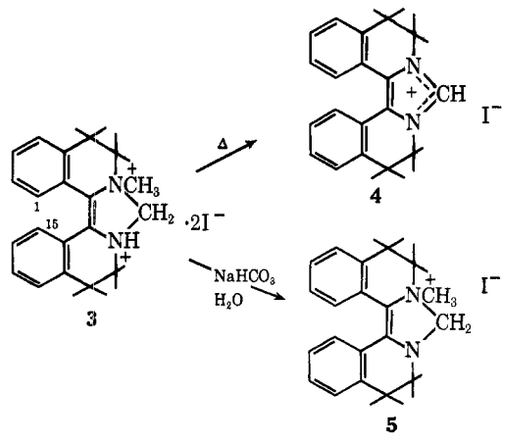
The preparation and chemiluminescence of 2,2′-dimethyl-3,3′,4,4′-tetrahydro-1,1′-biisoquinolinium diiodide (**1**) have recently been described.[1] Although 3,3′,4,4′-tetrahydro-1,1′-biisoquinoline (**2**) very readily forms a monomethiodide, its conversion to the dimethiodide requires more drastic reaction conditions. As a consequence, a competing, intramolecular cyclization, which will be described in this note, also occurs.

When **2** and excess methyl iodide were refluxed in acetonitrile for 18 hr, in addition to **1** (52% yield), there was recovered in approximately 10% yield an isomeric compound whose ^1H nmr spectrum and chemical behavior are consistent with those expected for 7-methyl-5,6,10,11-tetrahydro-8*H*-diisoquino[1,2-*c*:2′,1′-*e*]imidazolidiinium diiodide (**3**). The proton count on **3** indicated only one methyl group. The nmr spectrum was characterized by two other significant changes. One was the appearance of an AB quartet, which, although it is the chemical shift region assigned to 3 and 4 protons in 1,2-dihydroisoquinoline derivatives,[2] is due to the methylene in the imidazole ring, split because of the adjacent asymmetric nitrogen atom in the fused ring system. The other is a marked downfield shift of two of the aromatic ring protons, ascribed to an overlap of the 1,15 protons in the rigid, fused ring system of **3**.



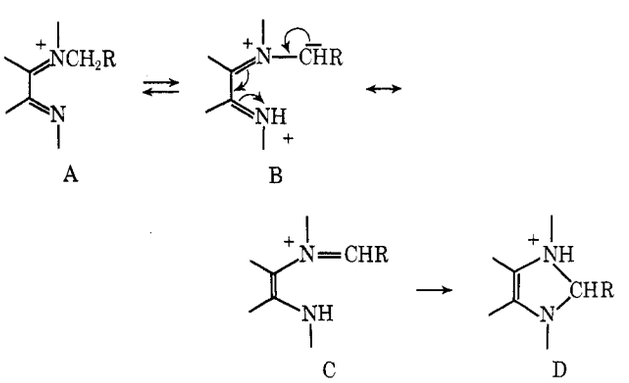
In **1**, rotation about the 1,1′ bond can still occur and the 8,8′ protons do not overlap.

When **3** was heated to 165–170°, both loss of methyl iodide and oxidation occurred to give 5,6,10,11-tetrahydrodiisoquino[1,2-*c*:2′,1′-*e*]imidazolium iodide (**4**). Its ^1H nmr spectrum (see Experimental Section) reflected these changes. Heating an aqueous solution of **3** with sodium bicarbonate yielded the monoquaternary salt **5**, whose nmr spectrum, except for one less proton, was the same as that for **3**.

It appears that the cyclization which leads to **3** can occur in either of two ways. (1) The monomethiodide of the 1,1′-biisoquinoline cyclizes intramolecularly and the resulting product is further methylated. (2) The dimethiodide **1** is first formed and then undergoes cyclization. There is evidence for both routes. For example, when preformed monomethiodide was refluxed in dry acetonitrile for various lengths of time, the proton nmr spectra on the recovered mixture of salts showed decreasing methyl signals, increasing signals characteristic of a methylene group, and the downfield shift of two aromatic protons as a consequence of the 1,15 proton overlap which develops as the fused ring system forms. Similarly, when 2-benzyl-3,3′,4,4′-tetrahydro-1,1′-biisoquinolinium bromide was refluxed in acetonitrile, the benzyl methylene signal disappeared; in addition the generally complicated nmr spectrum of the starting compound (because of unsymmetrical substitution) became simpler and more symmetrical as the cyclization occurred. One of the products recovered from this latter reaction was the 8-phenyl-5,6,10,11-tetrahydrodiisoquino[1,2-*c*:2′,1′-*e*]imidazolium salt (as the perchlorate).

When purified dimethiodide **1** was refluxed in methanol, ethanol, or 2-propanol, the dark red-orange colored solutions gradually faded. Although the recovered pale yellow product was a difficultly separable mixture, one compound isolated and identified was **5**.

2-Benzyl-1,1′-biisoquinolinium bromide remains essentially unchanged under conditions which effect the complete loss of the corresponding 3,3′,4,4′-tetrahydro compound. This fact suggests that the greater basicity of the 3,4-dihydroisoquinoline moiety over that of the unreduced isoquinoline is an important factor in the cyclization process. One possible route for cyclization of a monoalkyl salt is depicted in the following simplified scheme.



Abstraction of a proton from the alkyl group on A leads to the ylide B, which through charge redistribution gives the immonium salt C. Intramolecular addition of the nucleophile to the latter in a manner

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(2) J. L. Neumeyer, M. McCarthy, K. K. Weinhardt, and P. L. Levins, *J. Org. Chem.*, **33**, 2890 (1968).