On the Stereochemistry of Conjugate Addition. I. Addition to $\Delta^{1,9}$-2-Octalone

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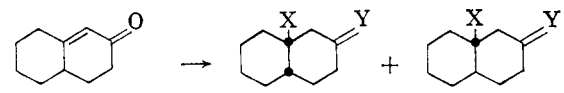
Reaction of potassium cyanide with $\Delta^{1,9}$-2-octalone in aqueous methanol affords a 3.6:1 ratio of *trans*- to *cis*-2-decalone-9-carboxamide. Structures of these products are assigned on the basis of degradative and physical evidence.

In synthesis of polycyclic molecules with angular substituents, such as the steroids and terpenoids, conjugate addition of a nucleophilic reagent to an α,β-unsaturated carbonyl function, *if it is a stereoselective process*, represents a potentially powerful but until recently[1] relatively neglected method for introduction of the angular group. A particularly attractive feature of such an approach is that it allows synthesis of angular functional substituents as well as the ubiquitous methyl group. The existence of a number of natural products containing angular functions has prompted us to investigate the general synthetic and stereochemical suitability of such nucleophilic conjugate addition processes.

The potential of conjugate addition reactions for this purpose was early realized by Birch and Robinson,[2] who examined cuprous bromide-catalyzed 1,4-addition of the methyl iodide Grignard reagent to $\Delta^{1,9}$-2-octalone (I). The sole product, isolated in 60% yield, was *cis*-9-methyl-2-decalone. While the reaction was thus ascertained to be highly stereoselective, it was so in the wrong sense for application to steroid synthesis, and the study was not extensively pursued.

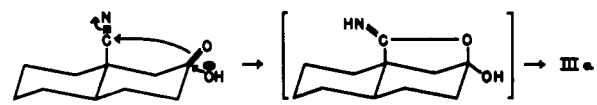
Suspecting that the stereoselectivity of such a reaction might be influenced by the nature of the nucleophile, we initiated our study with the addition of hydrogen cyanide to the octalone I. Indeed, although a mixture of *cis*- and *trans*-fused 2-decalone derivatives was produced, in this case it was the *trans* isomer which predominated. Reaction of potassium cyanide with I at 75° in aqueous methanol proceeded smoothly, and after five hours there was isolated in 75% yield a mixture of products devoid of the 240-mμ absorption of I. After separation of an insoluble high-melting by-product, formed in 10% yield,[3] crystallization and chromatography of the products afforded *cis*- (IIa), m.p. 135–136°, and *trans*-2-decalone-9-carboxamide (IIIa), m.p. 171–172°, in 15% and 37% yields, respectively. Gas-liquid chromatographic analysis of the crude reaction mixture (after separation of the insoluble by-product) indicated the ratio of IIIa to IIa to be approximately 3.6 to 1.[4,5]



I II III

a. X = $CONH_2$; Y = O
b. X = $CONH_2$; Y = S—CH_2CH_2—S
c. X = $CONH_2$; Y = H_2
d. X = CO_2H; Y = H_2

It is interesting that the initially formed rather hindered angular nitriles are converted completely to the amides under these mildly basic conditions. Although reaction at room temperature allowed isolation of some ketonitrile, m.p. 44–46°, as indicated by its absorption at 4.45 and 5.85 μ, in addition to the ketoamides, we found no conditions which prevented appreciable hydrolysis to the ketoamides in alkaline medium.[1b,c,4] It is possible that hydrolysis of the nitrile is facilitated by participation of the ketonic function.[6]



Configurations of IIa and IIIa were ascertained by degradation to the known *cis*- and *trans*-decalin-

(1) (a) Since initiation of our program, W. Nagata *et al.*, *Tetrahedron Letters*, No. 17, 27 (1960) and subsequent papers, have made elegant use of the reaction in steroid synthesis. These results, like ours, indicate a certain degree of stereoselectivity favoring the *trans*-fused isomer in the cyanide addition reaction. See also (b) A. Bowers, *J. Org. Chem.*, **26**, 2043 (1961) and (c) W. Nagata, S. Hirai, H. Itazaki, and K. Takeda, *J. Org. Chem.*, **26**, 2413 (1961) for work in Δ^4-3-keto steroid series, and (d) S. Mukherjee, *J. Sci. Ind. Research* (India), **19B**, 94 (1960).

(2) A. J. Birch and R. Robinson, *J. Chem. Soc.*, 501 (1943). See also A. J. Birch and R. Robinson, *J. Chem. Soc.*, 503 (1944), and S. M. McElvain and D. C. Remy, *J. Am. Chem. Soc.*, **82**, 3960 (1960).

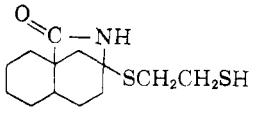
(3) The homogeneity and structure of this material have not been examined in the course of our work. However, dimeric by-products have often been isolated from similar reactions, *cf.* refs. 1b,c.

(4) W. Nagata, I. Kikkawa, and M. Fujimoto, *Chem. and Pharm. Bull.* (Tokyo), in press, have found even greater predominance of the *trans*-fused product from cyanide addition to I under reaction conditions quite different from ours. We are grateful to Dr. Nagata for communication of his results prior to publication, and for comparison and confirmation of identity of samples of our IIa and IIIa with his.

(5) All compounds described herein are racemic. But one enantiomer is depicted in each of the structural formulas.

(6) Although relative rate data for the nonketonic analogs are not available, it is significant that a small (23%) yield of a product tentatively presumed to be 9-cyano-*trans*-decalin, based on its infrared absorption at 4.4 μ and lack of NH or carbonyl absorption, was obtained on attempted Wolff-Kishner reduction of IIIa. The literature does not lack analogy for base-catalyzed conversion of a hindered amide to a nitrile, *cf.* E. Wenkert and B. G. Jackson, *J. Am. Chem. Soc.*, **80**, 211 (1958). This, of course, implies that the reverse (hydrolysis) reaction would be quite slow in the absence of the ketone.

9-carboxylic acids. On treatment with ethanedithiol and boron fluoride etherate,[7] IIa and IIIa were converted to the corresponding ethylenedithioketals, IIb and IIIb, m.p. 156–157° and 161–162° respectively. Although these isomers have similar melting points, there is no doubt of their nonidentity, since a mixture melting point is considerably depressed and solution infrared spectra, while showing identical amide carbonyl (5.97 μ) and NH_2 (2.82 and 2.92 μ) absorption, are considerably different in the 7–12-μ region. These infrared spectra, which lack the 4.1 μ absorption of SH[8] and have a normal amide rather than the shorter wave length γ-lactam carbonyl absorption, confirm that the derivatives are true dithioketals as formulated rather than β-mercaptoethylthio-γ-lactams (IV), as was found by Nagata[1c] to be the case for similar ethylene glycol derivatives in the cholesterol series. Nuclear magnetic resonance spectra show strong sharp peaks at 6.75 τ[9,10] (that of the *cis* isomer having two very closely spaced satellites) attributable to the four nearly equivalent protons of the ethylene group, rather than the more complex pattern expected for IV.



IV

Desulfurization of IIb and IIIb with Raney nickel afforded the corresponding *cis*-(IIc) and *trans*-decalin-9-carboxamides (IIIc), m.p. 131–132° and 127–128°, respectively. Again, these compounds are functionally similar but structurally different as indicated by their nonsuperimposable solution infrared spectra. Further, the infrared data clearly indicate that neither isomer is contaminated by the other and that as expected configurational homogeneity has been maintained throughout the degradation.

The *cis*-amide IIc was recovered unchanged after one and one-half hours at 80° in aqueous methanolic potassium hydroxide. Nitrous acid deamination, on the other hand, proceeded smoothly in 50% sulfuric acid, and each amide produced its corresponding carboxylic acid. Although Bartlett[11] has shown that these acids are interconvertible in stronger sulfuric acid solutions, under the conditions of our degradation they must be configurationally stable. Thus each amide gave a single acid, uncontaminated by the other as shown by infrared spectroscopy. The two acids IId and IIId were unequivocally identified by comparisons with authentic samples[11] through mixture melting point and solution infrared spectroscopic data. That acid derived from IIa, the minor conjugate addition product, was *cis*-decalin-9-carboxylic acid (IId), while the major addition product IIIa led to *trans*-decalin-9-carboxylic acid (IIId). As no reaction in the degradative sequence would be expected to alter the stereochemistry at C-9 and C-10, IIa is thus *cis*- and IIIa is *trans*-2-decalone-9-carboxamide.

Thus the conjugate addition of cyanide to the octalone I is quite stereoselective, the *trans*-fused product being preferentially produced.[1,4] It is mechanistically interesting, as well as of obvious synthetic importance, that this steric result is the reverse of that observed with the methyl Grignard reagent.[2] We do not yet have sufficient evidence to discern the relative importance to steric control of (a) approach of the nucleophile to the less hindered face of the bicyclic ketone,[12] (b) formation of the thermodynamically more stable product, and (c) approach of the nucleophile from that direction which leads to formation of the less hindered transition state having efficient orbital overlap between the developing β-carbon–nucleophile bond and the π system of the developing enolate anion.[13] The greater stereoselectivity observed here than with the Δ^4-3-keto steroids[1b,c] would seem to argue against *a* (steric approach control) as the most important factor. However the conversion of 5α- to 5β-cyanocholestan-3-one observed by the Japanese workers[1c] makes such a conclusion tenuous, since the extent of reversibility of the cyanide addition under our conditions is not known. Further experiments are in progress to examine these factors with other nucleophiles and acceptors.

We have thus far considered only the ketoamide structures for the conjugate addition products IIa and IIIa. The proximity of the angular carboxamide and the 2-ketone when the amide is axial with respect to the ketonic ring facilitates possible tautomerism between the ketoamide and a hydroxy-γ-lactam, *e.g.* IIIa $\rightleftharpoons$ V in the *trans* series. Indeed, in the 3-keto steroid series, Nagata[1c,14] and Bowers[1b] have shown by means of optical rotatory dispersion and infrared data that with either a 5α- or a 5β-carboxamide group the hydroxylactam form pre-

(7) L. F. Fieser, *J. Am. Chem. Soc.*, **76**, 1945 (1954).

(8) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., Methuen and Co., London, 1958, p. 351.

(9) NMR resonances are expressed throughout in terms of the τ scale of G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

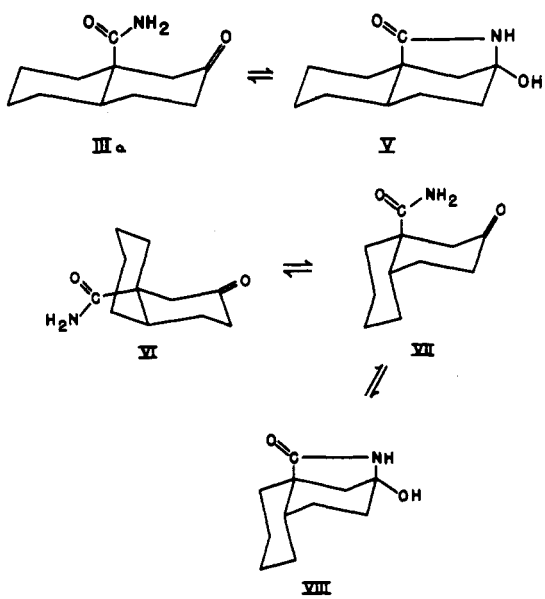
(10) L. F. Fieser, C. Yuan, and T. Goto, *J. Am. Chem. Soc.*, **82**, 1996 (1960) find the ethylenedithioketal group gives a single resonance line 118–129 c.p.s. from benzene at 40 Mc. However, it is not clear whether benzene as an internal or external standard was used. If the benzene was an external standard, this corresponds to the range 6.52–6.78 τ.

(11) R. E. Pincock, E. Grigat, and P. D. Bartlett, *J. Am. Chem. Soc.*, **81**, 6332 (1959). We express our thanks to Professor Bartlett for samples of the two acids for comparison purposes.

(12) This would superficially seem incompatible with the different results with cyanide and the Grignard reagent. However, the degree and nature of complex formation (with the Grignard reagent or cuprous bromide) in the latter reaction is not clear, and thus the possibility that quite different species are being attacked in the two processes cannot be ruled out.

(13) See G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **82**, 1512 (1960) for discussion of this last type of control on a somewhat similar electrophilic attack.

(14) W. Nagata, S. Hirai, H. Itazaki, and K. Takeda, *Ann.*, **641**, 184, 196 (1961).



dominates to the exclusion of the ketoamide structure.

Our *cis*- and *trans*-"ketoamides" IIa and IIIa appear to exist in chloroform solution almost entirely in the hydroxylactam forms, V and VIII. Thus, although all the true angular amides (IIb, c, IIIb, c) examined in the course of this work have solution infrared spectra characteristic of the amide, with a sharp doublet at 2.82 μ and 2.92 μ due to NH_2, a sharp carbonyl absorption at 5.97–6.01 μ, and the 6.31 μ "amide II" band[15] characteristic of amides but not lactams, the spectra of IIIa $\rightleftharpoons$ V and the *cis* analog VI $\rightleftharpoons$ VII $\rightleftharpoons$ VIII are quite different from this. The short wavelength region is characterized by sharp bands at 2.78 and 2.92 μ and a broad band near 3.0 μ, which could be due to free and hydrogen bonded NH_2 or NH and OH. The sharp carbonyl absorptions are shifted to 5.90 μ, ascribable to γ-lactam, and as is known to be the case for γ-lactams there are no absorptions in the 6.3-μ region.[16]

In an attempt to obtain further evidence on this structural point, NMR spectra of the series IIa–c and IIIa–c were examined. Resonances due to NH and OH are frequently broad and variable in position as the result of hydrogen bonding, chemical exchange, and in the case of NH the quadrupole moment of nitrogen. We have not yet been able to make specific assignments of such peaks in the spectra of the two "ketoamides." However, *trans*-decalin derivatives characteristically show a broad series of resonances due to the ring methylene protons which as a consequence of the rigid skeleton

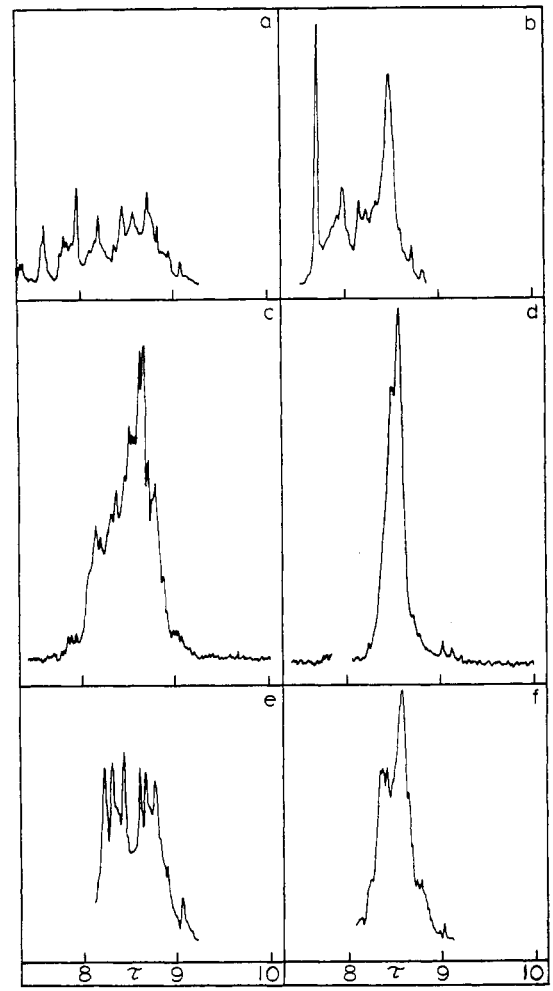


Fig. 1.—Partial NMR spectra of a: *trans*-thioketalamide (IIIb); b: *cis*-thioketalamide (IIb); c: *trans*-amide (IIIc); d: *cis*-amide (IIc); e: *trans*-"ketoamide" (V); f: *cis*-"ketoamide" (IIa). Spectra a, b, and c from deuterochloroform solutions, and d, e, and f from deuteroacetone solutions.

are environmentally different (axial or equatorial) and chemically shifted and observably spin-coupled to one another.[17] *cis*-Decalins, on the other hand, can undergo rapid rotational conformational interconversion (*e.g.*, VI $\rightleftharpoons$ VII), and the environmental differences of axial and equatorial hydrogens are averaged out to produce a much narrower resonance band.[17] For example, in the present work we find the skeletal CH resonances of the *cis*-thioketalamide IIb and the *cis*-amide IIc occur over much narrower ranges than do those of the *trans* isomers (Fig. 1). The conformationally fixed *trans*-hydroxylactam V has a broad ring proton resonance band. If the *cis*-"ketoamide" exists as the hydroxylactam VIII the chair-chair interconversion is restricted just as it is with a *trans* ring fusion and the ring protons have fixed axial and

(15) Ref. 8, p. 216 *ff*.

(16) On one occasion we obtained a sample of the *cis* isomer IIa which had an infrared spectrum with sharp bands at 2.86 and 2.94 μ, broad absorption at 3.0 μ, a broad unresolved carbonyl band between 5.85 and 6.0 μ, and a band at 6.26 μ. Thus this sample, m.p. 133–135°, seemed to contain at least some of the true ketoamide tautomer, IIa. However, all attempts to obtain further samples of this material have resulted only in isolation of the hydroxylactam VIII.

(17) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, p. 399. For a further recent discussion see J. I. Musher, *J. Am. Chem. Soc.*, **83**, 1146 (1961).

equatorial character. It was thus hoped that a broad resonance band resembling that of the *trans* isomer would confirm the *cis*-hydroxylactam assignment. In fact, a somewhat narrower resonance band was observed from a deuteroacetone solution of IIa ⇌ VIII (Fig. 1). The result is thus inconclusive, as it is consistent with either a shifted equilibrium favoring IIa in acetone as compared to chloroform solution, a sufficiently rapid mobile equilibrium VI ⇌ VII ⇌ VIII so the NMR technique is sensitive only to the average environment of the protons,[17] or naturally smaller chemical shift differences in V and VIII. Studies on the tautomerism are continuing.

The $\Delta^{1,9}$-2-octalone (I) used in this work was prepared from cyclohexanone and methyl vinyl ketone by the enamine method of Stork.[18] As was found by Baisted and Whitehurst[19] for I prepared by other routes, we have observed saturated ketone absorption at 5.85 μ in the infrared spectrum of the product. Repeated careful distillation diminishes the intensity of this absorption but we have not yet been successful in obtaining a sample in which it is completely absent. Gas-liquid chromatographic analysis shows the presence of one major impurity and a second minor one with shorter retention times than the octalone itself. Presumably[19] these are the unconjugated Δ^9 and Δ^8 isomers. The NMR spectrum of the mixture is devoid of absorption in the vinyl region except for the major peak at 4.20 τ due to I, thus suggesting the absence of appreciable quantities of the Δ^8 isomer unless its chemical shift is coincident with that of I. Until the pure minor components of this mixture have been isolated, however, their identities must be considered speculative only.

Experimental[20]

Addition of Potassium Cyanide to $\Delta^{1,9}$-2-Octalone.—To 10.0 g. of potassium cyanide in 40 ml. of water there was added a solution of 10.12 g. (0.0675 mole) of $\Delta^{1,9}$-2-octalone (I),[18] b.p. 134–135° (15 mm.), $\lambda_{max}^{95\%\ C_2H_5OH}$ 240 mμ (ϵ 12,500), in 140 ml. of methanol. After being stirred at 75° for 5 hr., the mixture was cooled and a white precipitate, weighing 0.877 g. (9% by weight), m.p. approximately 350°, λ_{max}^{KBr} 2.85 μ, 3.05, 5.9, 6.0, was separated by filtration and washed with methanol. The combined filtrate and washings were concentrated *in vacuo* until precipitation occurred, and then extracted with ether. Evaporation of the dried ethereal solution yielded 6.81 g. (52%) of solid residue. Recrystallization from ethyl acetate–cyclohexane afforded a first crop of 2.516 g., m.p. 174–177°, and a second crop of 0.952 g., m.p. 168–170°, of *trans*-2-decalone-9-carboxamide (IIIa). Repeated chromatography of the mother liquors on Florisil, eluting with benzene–ethyl acetate mixtures, allowed isolation of a further 0.583 g. of IIIa and 1.140 g. of the *cis*-ketoamide IIa, pure as shown by infrared and gas chromatographic analysis. In a center fraction, 0.123 g. of the mixture remained unresolved, IIa and IIIa being present in approximately equal quantities as estimated from the infrared spectrum.

Continuous ether extraction of the original aqueous solution for 2 days afforded a further 1.57 g. (12%) of the ketoamide mixture, bringing the total yield to 64%. Chromatographic fractionation of this material afforded 0.617 g. of *trans*-ketoamide IIIa, 0.505 g. of the *cis* isomer IIa, and 0.115 g. of a 60:40 mixture of IIa to IIIa as estimated from the infrared spectrum. The total isolated yield of *cis*-ketoamide IIa was 14% and of *trans*-ketoamide was 36%.

Recrystallization of the combined fractions of IIa from ethyl acetate–cyclohexane gave material of m.p. 144–146°. Repeated recrystallization from the same solvent pair gave colorless prisms, m.p. 135.5–136°; $\lambda_{max}^{CHCl_3}$ 2.78 μ, 2.92, 3.0 (broad), 5.90.[21]

Anal. Calcd. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found[22]: C, 67.7; H, 8.6; N, 7.2.

Recrystallization of the combined fractions of IIIa from ethyl acetate–cyclohexane gave colorless prisms of m.p. 169–172°. Repeated recrystallization sharpened the m.p. to 171–172°; $\lambda_{max}^{CHCl_3}$ 2.78 μ, 2.92, 3.0 (broad), 5.90.

Anal. Calcd. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found[22]: C, 67.4; H, 8.6; N, 7.1.

When the addition reaction was carried out as described above and processed by filtration of the precipitated by-product and then continuous ether extraction for 40 hr., gas-liquid chromatograms showed the ratio of IIIa to IIa in the total crude ether extract to be 3.6 ± 0.2 to 1.

9-Carboxamido-2,2-ethylenedithio-*trans*-decalin (IIIb).—A solution consisting of 1.01 g. (5.18 mmoles) of *trans*-ketoamide IIIa, m.p. 168–170°, 15 ml. of glacial acetic acid, 2.0 ml. of 1,2-ethanedithiol, and 2.0 ml. of boron fluoride etherate[7] was allowed to stand at room temperature overnight. The white crystalline precipitate was collected and weighed 1.487 g. (100%), m.p. 185–195°. Recrystallization from methanol gave in two crops a total of 0.914 g. (65%) of the thioketal IIIb as colorless prisms, m.p. 161–161.5°, and repeated recrystallization raised the melting point to 161–162°; $\lambda_{max}^{CHCl_3}$ 2.82 μ, 2.92, 5.96, 6.29; τ ($CDCl_3$) 6.75 (SCH_2-CH_2S).

Anal. Calcd. for $(C_{13}H_{21}NOS_2)_2 \cdot CH_3OH$: C, 56.40; H, 8.07; N, 4.87; S, 22.31. Found[22]: C, 56.4, 56.5; H, 7.8, 7.7; N, 4.6, 5.1; S, 21.4.

A sample was recrystallized from ethyl acetate–cyclohexane to remove the methanol of crystallization, giving flat needles, m.p. 154–156°.

Anal. Calcd. for $C_{13}H_{21}NOS_2$: C, 57.52; H, 7.80; N, 5.16; S, 23.63. Found[22,23]: C, 57.8; H, 7.9; N, 5.2; S, 23.5.

9-Carboxamido-2,2-ethylenedithio-*cis*-decalin (IIb).—Reaction conditions were similar to those used with the *trans*-ketoamide. Reaction of 126 mg. (0.65 mmole) of *cis*-ketoamide IIa, m.p. 134–135.5°, with 1,2-ethanedithiol yielded an oil which was chromatographed on Florisil to obtain 153 mg. (87%) of crystalline material, m.p. 154–159°. After recrystallization from ethyl acetate–cyclohexane, 93 mg. (53%) of pure *cis*-thioketal IIb was obtained as colorless prisms, m.p. 156–157°; $\lambda_{max}^{CHCl_3}$ 2.82 μ, 2.92, 5.97, 6.31;

(18) G. Stork and H. Landesman, *J. Am. Chem. Soc.*, **78**, 5129 (1956).

(19) D. J. Baisted and J. S. Whitehurst, *J. Chem. Soc.*, 4089 (1961).

(20) Melting points are corrected for stem exposure. Infrared spectra were obtained on Perkin-Elmer Models 21 and 137-G spectrophotometers. NMR spectra were obtained from dilute solutions in deuterochloroform or deuteroacetone using a Varian DP-60 spectrometer operating at 60 Mc. and equipped with a Model 3506 flux stabilizer. Resonance positions were determined by the audio sideband technique relative to tetramethylsilane as an internal standard. Vapor chromatograms were carried out at 230° on a 2-m. column containing 9% silicone gum SE-30 on Chromosorb W.

(21) On some occasions, dissolution of this material in chloroform or deuterochloroform was rapidly followed by reprecipitation of colorless needles, m.p. 119–120°, apparently a polymorphic modification of IIa. This form was too sparingly soluble in chloroform to allow solution infrared measurements to be made. A melt of the 120° form resolidified on cooling, producing prisms which remelted from 131–133°.

(22) Microanalysis by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(23) Microanalysis by Midwest Microlab, Inc., Indianapolis 20, Ind.

τ ($CDCl_3$) 6.73. On admixture with IIIb, the melting point was depressed more than 25°.

Anal. Calcd. for $C_{13}H_{21}NOS_2$: C, 57.52; H, 7.80; N, 5.16; S, 23.63. Found[22,23]: C, 57.5; H, 7.9; N, 5.1; S, 23.6.

***trans*-Decalin-9-carboxamide (IIIc).**—A mixture consisting of 285 mg. (1.05 mmoles) of *trans*-thioketal IIIb, m.p. 161–162°, 3.0 g. of Raney nickel and 20 ml. of absolute ethanol was refluxed for a period of 12.5 hr.[24] The mixture was cooled, Raney nickel was removed by centrifugation and washed thoroughly with hot absolute ethanol, and the combined reaction solution and washings were evaporated to dryness. An ether solution of the residual oil was centrifuged to remove turbidity and evaporated to dryness, affording 178 mg. (94%) of crude *trans*-amide IIIc, m.p. 115–121°, with an infrared spectrum which differed from that of the *cis* isomer. Repeated recrystallization from ethyl acetate–cyclohexane yielded 89 mg. (47%) of colorless prisms, m.p. 127–128° (reported[25] 125–126°); $\lambda_{max}^{CHCl_3}$ 2.82 μ, 2.92, 5.97, 6.31.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found[22]: C, 72.5; H, 10.3; N, 7.3.

***cis*-Decalin-9-carboxamide (IIc).**—Reaction conditions were similar to those used with the *trans*-thioketal IIIb. Reaction of 84 mg. (0.31 mmole) of *cis*-thioketal IIb, m.p. 161–162°, with 1.0 g. of Raney nickel in 5 ml. of absolute ethanol yielded 48 mg. (86%) of a crystalline residue, m.p. 128.5–130°, devoid of infrared absorptions characteristic of the *trans* isomer. After several recrystallizations from cyclohexane, 32 mg. (57%) of analytically pure *cis*-amide IIc was obtained as colorless prisms, m.p. 131–132°; $\lambda_{max}^{CHCl_3}$ 2.82 μ, 2.92, 6.01, 6.32.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found[22]: C, 72.7; H, 10.3; N, 7.6.

***trans*-Decalin-9-carboxylic Acid (IIId).**—To 49 mg. (0.27 mmole) of *trans*-amide IIIc, m.p. 128–129°, in 0.5 ml. of concd. sulfuric acid was added dropwise 0.5 ml. of a solution of 1 g. of sodium nitrite in 5 ml. of water.[26] After addition was complete the solution was heated on a steam bath for 5 min., cooled, diluted with 20 ml. of water, and extracted with three 75-ml. portions of ether. The ether extracts were washed with water, dried with sodium sulfate, and evaporated to dryness to afford 44 mg. (90%) of a pale yellow crystalline residue, m.p. 133–136°, which lacked infrared absorption at 11.26 μ characteristic of the *cis* isomer. After recrystallization from aqueous ethanol, 28 mg. (58%) pure *trans*-acid IIId was obtained as white platelets, m.p. 136.5–137° (reported[11] 135°); $\lambda_{max}^{CHCl_3}$ 3.4 μ (sh), 3.7 (broad), 5.90, 10.28. On admixture with an authentic sample,[11] there was no melting point depression. The infrared spectrum of a chloroform solution was rich in detail, identical in all respects with that of the authentic sample, and quite different in the 7–12-μ region from that of the *cis* isomer.

***cis*-Decalin-9-carboxylic Acid (IId).**—The *cis*-acid IId was prepared in the manner described above for the *trans* isomer. From 30 mg. (0.17 mmole) of *cis*-amide IIc, m.p. 129–130.5°, was obtained 32 mg. (100%) of crude solid IId devoid of the 10.28 μ infrared band characteristic of IIId. One recrystallization from aqueous ethanol yielded 15 mg. (50%) of white plates, m.p. 117–121°, and further recrystallization raised the m.p. to 123–124° (reported[11] 122°); $\lambda_{max}^{CHCl_3}$ 3.3 μ (broad), 3.8 μ (broad), 5.90. A mixture melting point with an authentic sample[11] was undepressed, although when mixed with the *trans* acid IIId the melting point was depressed more than 20°. The solution infrared spectrum was identical with that of the authentic sample.

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(24) F. Sondheimer and D. Rosenthal, *J. Am. Chem. Soc.*, **80**, 3995 (1958).

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Production of a Fused-Ring System by an Intramolecular Michael Condensation

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The unsaturated diketone IV has been prepared from the succinoylation product (VIII) of *m*-cresyl methyl ether. Wolff-Kishner reduction gave the acid X; this was converted into the methyl ketone XI which was in turn transformed into the ketal XII, then submitted to the Birch reduction followed by acid hydrolysis. The resulting unsaturated diketone IV was treated under basic conditions in order to effect an intramolecular Michael condensation. The major product was shown to be the ketol XV arising from the *cis*-fused diketone XIV.

Friedmann and Robinson[1] have studied in a preliminary manner an ingenious scheme for synthesizing the steroid nucleus containing an 11-keto group. The approach consisted of a Michael condensation of an appropriate donor species with the bicyclic ketone I, followed by an intramolecular aldol reaction to produce the tricyclic intermediate II, and finally an intramolecular Michael condensation to complete ring D. The product was a complex mixture, and although no evidence has been advanced for the structure or stereochemisty of this product, it was presumed to contain the steroidal compound III.

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