However, the independence of the rate of ND_4^+ and pyridinium-d_5 casts doubt upon this alternative. Further, the numerous examples of other heteroatomic aromatic substrates[6,15-20] that appear to undergo hydrogen exchange in α positions through ylide intermediates support this mechanism for the 3(5) position in pyrazole. Of particular interest, 1,2-dimethylpyrazolium cation undergoes deuteration in the 3(5) position at 31° in alkaline solution.[6] Here, the much smaller rate of deuteration of the 3(5) position in pyrazole in terms of the ylide path is a consequence of the very weak base strength of pyrazole.[2]

The experimental activation energy for the 4 position is 21.8 ± 1.6 kcal and that for the 3(5) position is 38.8 ± 6.4 kcal. Corresponding pseudo-unimolecular collision factors are 7.6 ± 10^5 sec^{-1} and 2.1 × 10^{12} sec^{-1}, respectively. The activation energy for the 3(5) position is unexpectedly large;[21] the smaller exchange reactivity for the 3(5) position compared to the 4 position is due to the great difference in activation energies of these positions, partially offset by the larger preexponential factor of the 3(5) position.

It is evident that two types of exchange mechanism are operative in aromatic heterocyclic systems. The first type involves base-catalyzed proton removal from the exchange site of the substrate. The second type involves acid-catalyzed Wheland intermediate formation. In general, in neutral, weakly acidic, or weakly alkaline solutions, positions next to nitrogen, oxygen, or sulfur heteroatoms undergo exchange by the first type,[6,7,15-20] whereas positions with carbon neighbors may react through the first[22] or the second type.[10,12,23] The relative reactivities of the conjugate acid, conjugate base, and molecule forms of the substrates differ, depending upon which type mechanism is operative. Thus, for the proton abstraction mechanism, the conjugate acid is most reactive, the molecule next,[7,19] and the conjugate base apparently unreactive. Here protonation of the heteroatom leads to rate enhancement in two ways: first, by increased inductive stabilization of transition states leading to ylide or anion intermediates[6,7,20] and second, by the increased entropy of activation attending reactions between ions of opposite charge. For the Wheland intermediate mechanism, the conjugate base is most reactive, the molecule next, and the conjugate acid least. In the latter case, deprotonation of the heteroatom appears to stabilize transition states leading to the Wheland intermediate, and also to cause the entropy of activation to increase for positively charged electrophiles.

(15) H. S. Staub, *Tetrahedron Lett.*, 845 (1964).
(16) P. Beak and J. Bonham, *J. Amer. Chem. Soc.*, **87**, 3365 (1965).
(17) P. Haake and W. B. Miller, *ibid.*, **85**, 4044 (1963).
(18) R. Breslow, *Ann. N. Y. Acad. Sci.*, **98**, 445 (1962).
(19) R. A. Olofson, J. M. Landesberg, K. N. Houk, and J. S. Michelman, *J. Amer. Chem. Soc.*, **88**, 4265 (1966).
(20) P. Haake, L. S. Bauscher, and W. B. Miller, *ibid.*, **91**, 1113 (1969).
(21) For example, the activation energy for exchange in the 4(5) position in imidazole is about 22 kcal.[7]
(22) J. A. Zoltewicz, G. Grahe, and C. L. Smith, *J. Amer. Chem. Soc.*, **91**, 5501 (1969).
(23) The β position in 4-aminopyridines exhibits mechanism type 1 in alkaline solution and type 2 in acid solution. See ref 13.

Registry No.—Pyrazole, 288-13-1.

The Azodiformate Adduct of Indene and the Stereochemistry of Some 1,2-Disubstituted Indans[1]

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It has been shown by chemical degradations that the structure of the adduct of indene and diethyl azodiformate is correctly formulated as an oxadiazine. The stereochemical structure assigned to a 2-amino-1-indanol by interpretation of nmr data has been shown to be erroneous. The generalizations proposed to deduce the stereochemistry of 1,2-disubstituted indan on the basis of nmr spectra have been shown to be an oversimplification.

A recent study on Diels–Alder reactions of indene[3] presented physical data on whose basis the long-known adduct of indene and diethyl azodiformate[4] was formulated as diazetidine **1**. Chemical evidence now, however, shows this substance to be represented properly by the oxadiazine structure.[5] In this connection it is noteworthy that reaction of indene with sterically restricted phthalazine-1,4-dione leads to 1,2 addition and hence to the formation of an authentic diazetidine **2**,[6] while reactions of azodiformates with other olefins have been shown recently to yield both 1,2 and 1,4 adducts.[7]

Structure **1** became untenable when a hydrazino alcohol was obtained upon its reduction by lithium aluminum hydride. Proof of the nature of the reduction product and formulation of its structure as **4** emerged from the following observations. Its nmr spectrum showed the presence of two replaceable hydrogens and two N-methyl groups. Acetylation gave an O,N-diacetyl derivative. Hydrogenation of **4** over platinum oxide in acetic acid gave an amino alcohol

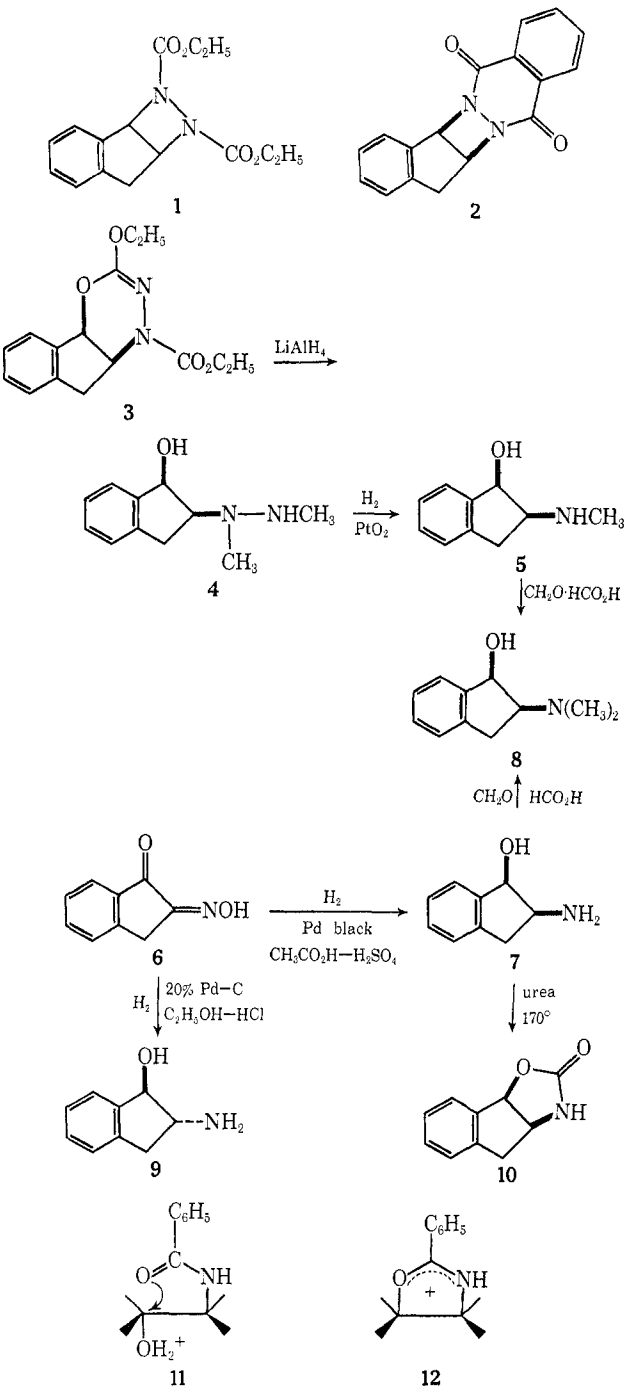
(1) Delay in publication of this paper was the responsibility of the editor. Since acceptance of this paper for publication the correct structures for **1** and **7** have been proposed by others: (a) H. M. R. Hoffmann, *Angew. Chem. Int. Ed. Engl.*, **8**, 556 (1969); (b) H. Rimek, T. Yupraphat, and F. Zymalkowski, *Justus Liebigs Ann. Chem.*, **725**, 116 (1969); (c) H. Rimek, T. Yupraphat, and F. Zymalkowski, *ibid.*, **726**, 25 (1969).
(2) (a) CIBA Pharmaceutical Co.; (b) Indiana University.
(3) C. F. Huebner, P. L. Strachan, E. M. Donoghue, N. Cahoon, L. Dorfman, R. Margerison, and E. Wenkert, *J. Org. Chem.*, **32**, 1126 (1967).
(4) O. Diels and K. Alder, *Justus Liebigs Ann. Chem.*, **450**, 237 (1926).
(5) Dr. E. Koerner von Gustorf also concluded that this new structure is the correct one (private communication). He has since then completed his evidence for this structure: E. K. von Gustorf, D. White, B. Kim, D. Hess and J. Leitich, *J. Org. Chem.*, **35**, (155 197). His earlier paper, E. K. von Gustorf and B. Kim, *Angew. Chem.*, **76**, 592 (1964), proposing the diazetidine structure, was neither abstracted nor indexed by *Chemical Abstracts*.
(6) O. L. Chapman and S. J. Dominianni, *J. Org. Chem.*, **31**, 3862 (1966).
(7) J. J. Tufariello, T. F. Mich, and P. S. Miller, *Tetrahedron Lett.*, 2293 (1966); G. Ahlgren and B. Akermark, *Acta Chem. Scand.*, **21**, 2910 (1967).

$C_{10}H_{13}NO$ (**5**), with loss of methylamine. The positions of the alcohol and amino groups were shown by formaldehyde–formic acid methylation of **5** to a dimethylamino alcohol **8** identical with that obtained by similar methylation of the known 2-amino-1-indanol (**7**) (mp 107–108°) prepared by the method of Rosen and Green,[8] hydrogenation of 2-oximino-1-indanone (**6**) in acetic acid–sulfuric acid over palladium black. To rule out any acid-catalyzed rearrangement of the amino alcohols **5** and **7**, especially at the benzyl alcohol position,[9] both compounds were methylated under basic conditions with methyl iodide, and an identical quaternary ammonium salt was obtained. Thus, the gross structure of the indene adduct is indicated by **3**, with only the stereochemistry of the ring fusion to be defined. Since no stereochemical change would be expected to occur during the reaction sequence **3** → **8**, the stereochemistry of the 2-amino-1-indanol **7** is that of the ring fusion in the adduct **3**. The *trans* structure has been assigned to **7** by Rosen, *et al.*,[10] on the basis of its nmr spectrum, now requiring **3** also to be *trans*. Since this appeared most improbable, the stereochemical assignment of **7** was reexamined and means of establishing the stereochemistry by methods other than nmr spectroscopy were sought.

In previous work we had obtained the isomeric 2-amino-1-indanol **9** (mp 104–105°) as the major product from the hydrogenation of 2-oximino-1-indanone (**6**) in ethanol containing hydrochloric acid over palladium on carbon, even though hydrogenation of **6** under the not too dissimilar conditions of acetic acid containing sulfuric acid over palladium black gave the other isomer **7** as the major product (see Scheme I). The reason for this divergence in results under the described empirically determined hydrogenation conditions is not apparent. Having on hand both the isomeric amino alcohols **7** and **9**, stereochemical assignments could be made more rigorously. The infrared spectrum of **7** in methylene chloride at successive dilutions showed band shifts associated with intramolecular hydrogen bonding. A broad hydroxyl stretching band at 3590 cm^{-1} with an inflection at 3650 cm^{-1} due to the unbonded form is seen. There was no material change in the shape of the curve on successive dilutions. The spectrum of **9** showed the bonded hydroxyl band at 3580 cm^{-1} and a distinct band due to the unassociated hydroxyl at 3680 cm^{-1}. Successive dilutions increased the intensity of the latter at the expense of the 3580-cm^{-1} band. These measurements indicated **7** to be the *cis* and **9** the *trans* amino alcohol. This difference in infrared spectra could be seen more clearly on the dimethylamino alcohols **8** and **13**. The broad bonded hydroxyl stretching band at 3375 cm^{-1} seen in the spectrum of **8** was not changed by dilution, while the corresponding band of **13** at 3380 cm^{-1} virtually disappeared on dilution and the sharp band at 3580 cm^{-1} due to unbonded hydroxyl grew in intensity.

Chemical evidence indicating the *cis* stereochemistry of **7** is also available. Close[11] has shown that

SCHEME I



pseudoephedrine, in which the hydroxyl and amino groups in their preferred conformations are closer to each other than in ephedrine,[12] gives an oxazolone on reaction with urea. By contrast, ephedrine gives an imidazolone. We found **7** to give the oxazolone **10** in good yield on reaction with urea. Under the same reaction conditions **9** gave an intractable resinous material.

Acid-catalyzed N → O acyl migrations are well known in systems in which the interacting groups are close. N-Benzoylpseudoephedrine rearranges very readily to the O-benzoate under conditions which leave the ephedrine derivative unchanged.[13] However, applying

(8) W. E. Rosen and M. J. Green, *J. Org. Chem.*, **28**, 2797 (1963).

(9) It is known that the ephedrine ⇌ pseudoephedrine equilibration with a similarly situated benzyl hydroxyl is acid catalyzed by 25% hydrochloric acid; see H. Emde, *Helv. Chim. Acta*, **12**, 377 (1929).

(10) W. E. Rosen, L. Dorfman, and M. P. Linfield, *J. Org. Chem.*, **29**, 1723 (1964).

(11) W. J. Close, *ibid.*, **15**, 1131 (1950).

(12) J. B. Hyne, *Can. J. Chem.*, **39**, 2536 (1961).

(13) G. Fodor, V. Bruckner, J. Kiss, and G. Óhegyi, *J. Org. Chem.*, **14**, 337 (1949).

this technique to the differentiation of **7** and **9** was of no value. The N-benzoates of **7** and **9** both rearranged under acid catalysis to a single O-benzoate and at about equal rates. Acyl migration of the *trans* benzoate (**11**) must readily occur *via* the intermediate **12** with inversion at C-1 to give the *cis* O-benzoate.

During the course of the present work a publication reinforcing our data appeared.[14] Thrift found that reductive acetylation of **6** followed by sodium borohydride reduction of the ketone gave an acetamidoindanol which on acid hydrolysis gave one aminoindanol and on basic hydrolysis another. It was reasoned that the acid-catalyzed hydrolysis proceeding *via* an intermediate of the type of **12** would yield the inverted or *cis* compound. However, it is also possible that the acetamidoindanol could have the *cis* configuration and acid hydrolysis would give the *trans* amino alcohol, since it is known[9] that acid may invert the benzyl alcohol. The N-acyl group is not necessary for inversion to occur.[15]

Despite several descriptions of the two 2-amino-1-indanols[16] their distinction by the melting points of the isomeric bases and hydrochlorides is not possible: melting point of **7**, 107–108°; hydrochloride, 206°; O-N-diacetate, 118–120°; melting point of **9**, 102–104°; hydrochloride, 229–230°; O-N-diacetate, 210–212°. They can be distinguished, however, by the melting points of the diacetyl derivatives. Judged solely on the basis of melting points, previous reports[16] probably dealt with mixtures.

The methylamino alcohol **5** is identical (mixture melting points and infrared spectra) with one of unspecified stereochemistry described by Heinzelmann, *et al.*[17] It had been prepared by substitution of *trans*-1,2-dibromoindane first at the 1 position by a benzyloxy and then at the 2 position by a benzylmethylamino group, followed by removal of the benzyl groups. The configuration of the amino alcohol resulting from these two consecutive nucelophilic substitution reactions could not be predicted with certainty, although it is recognized that the bromo group is a stronger participating neighboring group than is alkoxy.[18] Since the structure of this amino alcohol **5** is now shown to be *cis*, it is evident that the first substitution reaction proceeded with retention and the second with inversion.

Two incidental observations of chemical behavior of the aminoindanols remain to be described. When either *cis*-2-dimethylamino-1-indanol (**8**) or the *trans* isomer **13** was dissolved in trifluoroacetic acid, complete esterification had occurred within the time required for a nmr spectral determination (2 min). The esters **14** and **15** were shown to be present by the downfield shift of the C-1 proton in their nmr spectra and by the ester carbonyl bands in the infrared spectra.

(14) R. I. Thrift, *J. Chem. Soc.*, 288 (1967).

(15) The configurational assignments of the amino indanols parallel those of the amino tetralols [F. Zymalkowski and H. J. Rimek, *Arch. Pharm.* (Weinheim), **294**, 581 (1961)]. The stereochemistry of the latter was confirmed recently by interpretation of their nmr spectra [R. Violland, R. Gaige, and H. Pacheco, *Bull. Soc. Chim. Fr.*, 2105 (1967)].

(16) *Cf.* N. Levin, B. E. Graham, and H. G. Kolloff, *J. Org. Chem.*, **9**, 380 (1944); T. Kametani, H. Sugahara, and S. Asagi, *Chem. Pharm. Bull.* (Tokyo), **14**, 1409 (1966).

(17) R. V. Heinzelmann, B. O. Aspergren, and J. H. Hunter, *J. Org. Chem.*, **14**, 906 (1949). We thank Dr. Heinzelmann for a sample with which to make this comparison.

(18) C. A. Bunton, "Nucleophilic Substitution at a Saturated Carbon," Elsevier Publishing Co., New York, N. Y., 1963, p 53.

In order to confirm that the unusually large C_1 proton shift caused by the dissolution of **8** and **13** in trifluoroacetic acid was indeed due to a combination of esterification and protonation and not purely a protonation effect, a number of comparisons were made. Though the spectra were not taken in trifluoroacetic acid, it could be seen that the downfield effect of protonation of the C-2 nitrogen from compounds **5**, **7**, **8**, **9**, and **13** in deuterium oxide was in the order of 52–67 cps (Table I), the smaller value being the N-methyl compounds. Compounds **14** and **15**, the trifluoroacetic esters, exhibit a downfield shift of 102 and 99 cps, respectively. The additional shift of 50 cps over that seen by N-protonation alone is due to esterification. It should be noted that O-acetylation of compound **8** shifts the C-1 proton 78 cps downfield. Making the salt (spectrum in sulfuric acid-d_2: deuterium oxide) produced an additional effect of 30 cps or a total of 108 cps.

Since a unique ester is formed from each alcohol, esterification must have been taken place without inversion. If it had occurred *via* a benzyl carbonium ion, the same ester or mixture of esters should have been present from either **8** or **13**. During attempts to isolate the pure trifluoroacetate esters by basification of the amine salt mixture obtained by removal of either excess trifluoroacetic acid or anhydride, such rapid hydrolysis occurred that only a mixture of predominantly alcohol plus a minor amount of ester could be obtained. Ester could be recognized by the infrared spectra but could not be separated in a pure state from the mixture. The fact that the starting alcohol was obtained is additional evidence that esterification occurred without inversion.

When a trifluoroacetic acid solution of **8** or **13** was allowed to stand, equilibration of the esters was observed and within 3 days the same 55–45% mixture of esters, with the *trans* isomer predominating, was obtained. Refluxing of **8** in 2 *N* hydrochloric acid causes equilibration of the alcohols. Because the extremely rapid esterification at 25° of **8** and **13** by trifluoroacetic acid was somewhat unexpected, it was considered of interest to briefly examine the esterification of simpler benzyl alcohols. 1-Indanol immediately forms an insoluble polymer in trifluoroacetic acid. Benzyl alcohol is esterified considerably slower in trifluoroacetic acid under the same conditions as used for **8** and **13** with a half-life at 42° of about 12 min. Addition of one molar equivalent of triethylamine caused no change in this rate of esterification. Finally, it might be noted that by ring opening of **3** mild acid hydrolysis yields the amino alcohol derivative **16**. Since there is no reason to believe that hydrolysis has taken place with inversion, **16** most probably belongs to the *cis* series.

Since the *cis*-2-aminoindanol (**7**) had been assigned erroneously, the *trans* configuration by Rosen, *et al.*,[10] a reevaluation of the nmr data on 1,2-disubstituted indanes became necessary. The previous authors noted that a small series of simple 1,2-disubstituted indanes could be divided into two groups on the basis of the complexity of the nmr signals of the C-3 methylene protons. These protons in the *cis* compounds were seen as a doublet and in the *trans* compounds as an octet. Since **7** showed a multiplicity of bands which

TABLE I

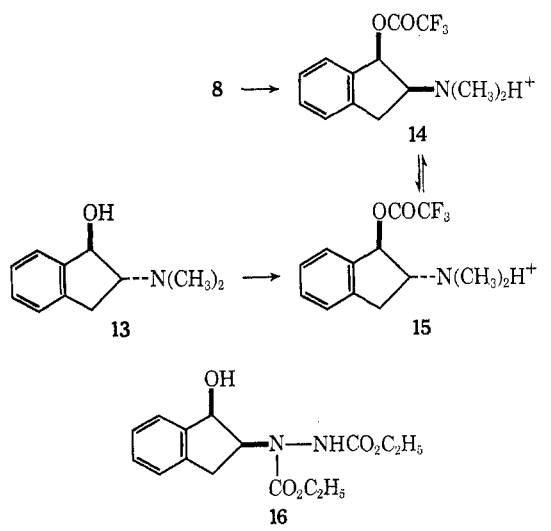
NUCLEAR MAGNETIC RESONANCE DATA OF *cis*- AND *trans*-1,2-DISUBSTITUTED INDANS[a]

Compd	Substituent C1	Substituent C2		H_{3a}		H_{3b}	H_2	H_1	Other hydrogens	
7	OH	NH_2	*cis*[b]		172[c] m		215 q	285 d (5.4)	OH, NH_2	153
	OH	$NH_2 \cdot HCl$	*cis*[d]		220[c] m		270 q	346 d (5.8)		
9	OH	NH_2	*trans*[b]	147 q		~186 m	~203 m	281 d (6.1)	OH, NH_2	173
	OH	$NH_2 \cdot HCl$	*trans*[d]	206 q		240 q	~260 m	348 d (5.2)		
5	OH	$NHCH_3$	*cis*[b]		174[c] m		~193 m	289 d (5.5)	CH_3	145
	OH	$NHCH_3 \cdot HCl$	*cis*[d]		218[c] m		254 m	341 d (5.4)	CH_3	198
8	OH	$N(CH_3)_2$	*cis*[b]		~173[c] m		~173 m	290 d (5.0)	CH_3	140
									OH	241
	OH	$N^+(CH_3)_2H$	*cis*[d]		~222 m		~252 m	342 d (4.9)	CH_3	206, 211
13	OH	$N(CH_3)_2$	*trans*[b]		~167[c] m		~167 m	302[e] t[i]	CH_3	135
									OH	331
	OH	$N^+(CH_3)_2H$	*trans*[f]		~238 m		~238 m	354 d (6.0)	CH_3	202, 208
	OH	$N^+(CH_3)_3I^-$	*cis*[d]				~263 m	354 d (5.0)	CH_3	229
	$OCOCH_3$	$N(CH_3)_2$	*cis*[b]		~182 m		~182 m	368 d (4.9)	CH_3	141
									$COCH_3$	122
	$OCOCH_3$	$N^+(CH_3)_2H$	*cis*[f]		~227 d		~260 m	398 d (5.0)	CH_3	207, 209
									$COCH_3$	148
14	$OCOCF_3$	$N^+(CH_3)_2H$	*cis*[g]		209[c] m		252 m	392 d (4.7)	CH_3	196
15	$OCOCF_3$	$N^+(CH_3)_2H$	*trans*[g]		~210[i]		260 m	401 d (4.3)	CH_3	185
17	$OCOCH_3$	$NHCOCH_3$	*cis*[b]		184[c] m		290 m	365 d (6.1)	CH_3	120, 122
20	$OCOCH_3$	$NHCOCH_3$	*trans*[b]	162 q		210 q	273 m	369 d (6.0)	CH_3	117, 126
18	OH	$NHCOC_6H_5$	*cis*[h]		186[c] m		278 m	300 d (6.0)		
19	OH	$NHCOC_6H_5$	*trans*[h]	166 q		194 q	264 m	311 d (7.0)		
16	OH	$N(COOC_2H_5)(NHCOOC_2H_5)$	*cis*[d]		180[c] m		284 m	315 q[i] (8.5)	CH_3 t	77 (6.8)
									CH_2 q	253
	OH	NHCHO	*trans*[h]	164 q		193 q	250 m	296 d (6)	CHO	488
21	$OCOC_6H_5$	$NH_2 \cdot HCl$	*cis*[d]		~221[c] m		~274 m	401 d (5.5)		
4	OH	$N(CH_3)(NHCH_3)$	*cis*[b]		~180[c] m		~180 m	300 d (4.4)	CH_3	152, 154
3			*cis*[b]		193[c] m		301 m	327 d (4.5)	CH_3	79 t (7.0)
										83 t (7.0)
									CH_2	260 q
										264 q
10			*cis*[h]		183[c] m		274 m	354 d (7.5)		

[a] The spectra were obtained with a Varian A-60 spectrometer. All data reported in cycles per second (cps) from tetramethylsilane as internal standard. d = doublet, t = triplet, q = quartet, m = multiplet, and values in parentheses are coupling constant in cps obtained by first-order analysis. The symbol ~ indicates the values are approximate due to overlapping bands from other protons. [b] Chloroform-*d*. [c] See text for interpretation. [d] Deuterium oxide. [e] The observed triplet is most likely a quartet. H_1 is coupled (4.3) to H_2 and each band split (3.5) by the H_3 proton which forms a figure W with the C_1 [S. Sternhell, *Rev. Pure Appl. Chem.*, 14, 15 (1964)]. [f] Sulfuric acid-d_2. [g] Trifluoroacetic acid. [h] Dimethyl sulfoxide-d_6. [i] Assignment of the respective protons was difficult; however, they have the general appearance of an octet with a spread of at least 50 cps. [j] Coupling of H_1 with OH is removed by addition of D_2O.

appeared to be an octet, it was assigned the *trans* stereochemistry. We have listed (Table I) the spectral data for a number of *cis* and *trans* compounds whose stereochemistry now has been established unequivocally.

Three types of spectra can be observed for our series of 1,2-disubstituted indanes. Provided an electronegative group is present at C-2 producing an appreciable chemical shift difference between the protons at C-2 and C-3, the *trans* series always gives AMX-type spectra. *cis* compounds have ABX spectra in which the differences in chemical shift between the C-3 methylene protons vary, but are always smaller than those of the related *trans* compound. These ABX spectra may vary. For example, the *cis* amino alcohol **7** shows four strong bands of irregular intensity in a central cluster with very weak wings. The diacetate **17** exhibits three bands. An irregular doublet is seen for **16** and **17**. The oxadiazene **3** exhibits seven bands. In general, the AB bands overlap. Since AMX and ABX spectra merge as the difference in chemical shift between the C-3 protons decreases, it is advisable to examine the spectra of both the *cis* and *trans* compound when using nmr data in assigning



stereochemical configuration. A third type of spectrum, the ABC type in which the difference in chemical shift between C-2 and C-3 is small, is of no help in determining stereochemistry. The methylated amino alcohols **4**, **8**, and **13** fall into this class.

The vicinal coupling constants of the C-1 and C-2 protons cannot be used to determine stereochemistry. If the five-membered ring were planar, *cis* compounds with a vicinal angle of 0° should have a larger coupling constant than *trans* compounds. However, the five-membered ring in 1,2-dihydroxyindane is known to be puckered,[19] and the extent of puckering will be dependent on the type of substitution at C-1 and C-2. Thus, even if the Karplus values were to hold rigidly, coupling constants would not unerringly give correct stereochemistry since the degree of distortion from planarity is not known beforehand. For example, $J_{1,2}$ is larger for the *trans* amino alcohol **9** than for the *cis* **7**, while the reverse is true for their respective hydrochlorides. Similarly, the *trans* N-benzoate **19** has a larger $J_{1,2}$ than does the *cis* stereoisomer **18**. A similar situation has been encountered in some 2,3-disubstituted dihydrobenzofurans.[20]

Experimental Section[21]

2-(1,2-Dimethylhydrazino)-1-indanol (4).—A solution of 5.1 g of the oxadiazine **3** in 175 ml of anhydrous ether was added dropwise with stirring to a suspension of 3 g of lithium aluminum hydride in 20 ml of ether. The reaction mixture was refluxed for 2 hr then decomposed by the cautious addition of 15 ml of ethyl acetate, followed by 3 ml of water, 6 ml of 12% sodium hydroxide solution, and finally 9 ml of water. The inorganic solids were filtered and the filtrate extracted with 5% hydrochloric acid. The aqueous layer was made basic with ammonium hydroxide and the organic material extracted into ether. The ether was dried ($MgSO_4$) and evaporated. The solid residue was triturated with petroleum ether (bp 30–60°), giving 1.4 g of product **4**, mp 70–73°.

Anal. Calcd for $C_{11}H_{16}N_2O$: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.82; H, 8.34; N, 14.39.

2-(2-Acetyl-1,2-dimethylhydrazino)-1-indanyl Acetate.—A solution of 250 mg of **4** in 0.25 ml of pyridine and 0.25 ml of acetic anhydride was allowed to stand at room temperature for 1 week, then poured into ice–water and shaken for 15 min. The reaction mixture was made basic with ammonium hydroxide and the organic material extracted into chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and evaporated *in vacuo*. The residue, which slowly solidified was recrystallized from benzene–petroleum ether (bp 30–60°), mp 84–86°.

Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.19; H, 7.30; N, 10.14. Found: C, 65.51; H, 7.43; N, 10.38.

Reductions of 4 to *cis*-2-Methylamino-1-indanol (5).—A solution of 0.6 g of **4** in 10 ml of 90% acetic acid was reduced over 40 mg of platinum oxide at atmospheric pressure. After the uptake of one molar equivalent of hydrogen, the catalyst was filtered off and the solvent evaporated *in vacuo*. The residue after treatment with excess 50% potassium hydroxide was extracted with ethyl acetate. Evaporation of the solvent left a crystalline residue (mp 70–72°) which by analysis appeared to be essentially **5**.

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 72.61; H, 8.16; N, 8.75.

The **picrate** melted at 170–171° after recrystallization from ethanol.

Anal. Calcd for $C_{10}H_{13}NO \cdot C_6H_3N_3O_7$: C, 48.98; H, 4.11; N, 14.28. Found: C, 48.71; H, 4.18; N, 13.98.

Braun[22] reported a trace amount of a methylamino indanol formed at the end of a reaction sequence beginning with 1-bromo-2-indanol melting at 77–79° and a picrate melting at 171° which is undoubtedly **5**. The **hydrochloride** of **8** prepared with ethanolic hydrogen chloride and recrystallized from ethanol–ether melted at 168–170°. A sample of **5** obtained from Dr. Heinzelmann[17] melted at 160–162° (mixture melting point with our sample 161–163°). Infrared absorption spectra of the two samples were identical.

Anal. Calcd for $C_{10}H_{13}NO \cdot HCl$: C, 60.12; H, 7.07; N, 7.01. Found: C, 60.31; H, 6.89; N, 7.36.

***cis*-2-Dimethylamino-1-indanol (8) from 5 and *cis*-2-Amino-1-indanol (7).**—A solution of 0.6 g of **5** was refluxed in 8 ml of propanol with 0.7 ml of 36% formaldehyde solution and 0.55 ml of formic acid for 6 hr. After evaporation *in vacuo* the residue was treated with excess 50% potassium hydroxide and extracted with ethyl acetate. Evaporation of the solvent and recrystallization of the residue from methanol yielded 0.4 g of **8**, mp 124–126°.

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.99. Found: C, 74.30; H, 8.46; N, 7.80.

The **hydrochloride** (recrystallized from ethanol–ethyl acetate) melted at 175–176°.

Anal. Calcd for $C_{11}H_{15}NO \cdot HCl$: C, 61.81; H, 7.52; N, 6.56. Found: C, 61.81; H, 7.79; N, 6.47.

Similar methylation of **7**[8] gave a sample of the dimethyl derivative **8** which by mixture melting point, nmr, and infrared spectra proved to be identical with the sample of **8** derived by the monomethylation of **5** described above.

***cis*-2-Dimethylamino-1-indanol Methiodide from 5 and 7.**—A mixture of 0.15 g of **5**, 0.18 ml of methyl iodide, and 0.7 g of potassium carbonate in 5 ml of acetonitrile was refluxed for 6 hr. The inorganic salts were filtered off hot, and cooling the filtrate yielded 0.20 g of the methiodide of **8**, melting point after recrystallization from ethanol 227–230° dec.

Anal. Calcd for $C_{12}H_{18}INO$: C, 45.14; H, 5.68; N, 4.39. Found: C, 45.16; H, 5.77; N, 4.42.

Similar methylation of **7** or treatment of the dimethyl derivative **8** with methyl iodide gave methiodides shown to be identical by mixture melting point and infrared spectra with the sample described above.

***trans*-2-Amino-1-indanol (9) Hydrochloride and Base.**—A solution of 3.7 g of 2-hydroxyimino-1-indanone (**6**) and 13.5 ml of 6.1 *N* ethanolic hydrogen chloride in 230 ml of ethanol in the presence of 600 mg of 20% palladium on carbon was hydrogenated at 40 psi pressure. The absorption of hydrogen ceased after 30 min, during which time approximately 3 mol of hydrogen was absorbed. The catalyst was filtered and the filtrate evaporated *in vacuo*. The solid residue was washed well with ether and recrystallized three times from ethanol–ether, mp 222–224°.

Anal. Calcd for $C_9H_{11}NO \cdot HCl$: C, 58.12; H, 6.52; N, 7.54. Found: C, 58.28; H, 6.27; N, 7.32.

The corresponding base was prepared by dissolving the hydrochloride in a minimum amount of water, making it strongly basic with ammonium hydroxide, and extracting into ether. The ether solution was dried ($MgSO_4$) and concentrated and the solid residue recrystallized from benzene, mp 100–103°.

Anal. Calcd for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.39. Found: C, 72.42; H, 7.66; N, 9.11.

3,3a,4,8b-Tetrahydroindeno[2,1-*d*]oxazol-2-one (10).—A mixture of 0.15 g of **7** and 0.15 g of urea in 5 ml of ethanol was acidified with 6 *N* ethanolic hydrogen chloride, evaporated to dryness, and heated in an oil bath at 170° for 0.5 hr and at 200° for 1 hr. The residue was washed with water and recrystallized from ethanol yielding **10**, mp 205–206°.

Anal. Calcd for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.26; H, 5.07; N, 8.06.

Heating of **9** hydrochloride with urea at various temperatures yielded only starting material or an intractable tar.

***cis*-N-(1-Hydroxy-2-indanyl)benzamide (18).**—A mixture of 300 mg of the *cis* amino alcohol **7** and 337 mg of benzoyl chloride was react under the usual Schotten–Baumann conditions. The product was recrystallized from ethanol: mp 200–202°; yield, 250 mg; infrared 1630 cm^{-1} (amide I), 1560 cm^{-1} (amide II).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.90; H, 6.13; N, 5.31.

***trans*-N-(1-Hydroxy-2-indanyl)benzamide (19).**—Similarly 500 mg of the *trans* amino alcohol **9** was benzoylated. After recrystallization from ethanol–benzene the product melted at 229–230° dec: yield 580 mg; infrared 1630 cm^{-1} (amide I), 1560 cm^{-1} (amide II).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.79; H, 5.95; N, 5.60.

Rearrangement of 18 and 19 to Yield *cis*-2-Amino-1-indanol Benzoate Hydrochloride (21).—A solution of 250 mg of *cis*-N-(1-hydroxy-2-indanyl)benzamide in 10 ml of ethanol and 0.18 ml of

(19) F. V. Brutcher, Jr., and E. L. James, *Diss. Abstr.*, **24**, 1938 (1963).

(20) L. H. Zalkow and M. Ghosal, *Chem. Commun.*, 922 (1967).

(21) Nmr spectra were recorded on a Varian A-60 instrument using tetramethylsilane as an internal standard. Solvents are recorded in Table I. Infrared spectra were run as Nujol mulls on a Perkin-Elmer 521 spectrophotometer. Melting points were determined with a Thomas–Hoover apparatus.

(22) J. V. Braun and K. Weissbach, *Ber.*, **63**, 3052 (1930).

6.088 *N* ethanolic hydrogen chloride was refluxed on a steam bath for 15 min. The solvent was evaporated *in vacuo* and the residue was triturated with 10 ml of water and filtered. The filtrate was evaporated to dryness *in vacuo* and the solid residue was washed well with ether: yield of **21**, 70 mg; mp 122–123°; infrared 1715 cm^{-1} (ester C=O).

Anal. Calcd for $C_{16}H_{15}NO_2 \cdot HCl$: C, 66.31; H, 5.56; N, 4.83. Found: C, 66.31; H, 5.48; N, 4.65.

The water-insoluble precipitate, mp 185–186°, weighed 1 70 mg; infrared 1630 cm^{-1} (amide I), 1560 cm^{-1} (amide II).

Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.90; H, 6.13; N, 5.31.

Treatment of 200 mg of *trans*-N-(1-hydroxy-2-indanyl)benzamide with 0.15 ml of 6.088 *N* ethanolic hydrogen chloride in an analogous manner yielded 160 mg of unchanged N-benzamide and 30 mg of **21** whose infrared and nmr spectra were identical with that of the *cis* compound described above.

***cis*-2-Acetamidoindanyl Acetate (17).**—A solution of 250 mg of the *cis* amino alcohol (**7**) in 1 ml of pyridine and 1 ml of acetic anhydride was allowed to stand at room temperature for 5 days, then poured into 5 ml of ice and 10 ml of water. The reaction mixture was stirred for 1 hr, keeping the temperature below 25°, then made basic with ammonium hydroxide. The organic material was extracted into ether, washed with water, dried ($MgSO_4$), and evaporated. The solid residue was recrystallized from benzene–petroleum ether (bp 30–60°), mp 118–120°, yield 140 mg.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01. Found: C, 67.11; H, 6.53; N, 5.87.

***trans*-2-Acetamidoindanyl Acetate (20).**—The *trans* amino alcohol **9** (250 mg) was treated as described above, mp 210–212°, yield 230 mg.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01. Found: C, 67.05; H, 6.46; N, 5.92.

***cis*-1-Amino-2-indanol (7) Hydrochloride.**—The salt prepared from a purified sample of **7**[8] with ethanolic hydrogen chloride and recrystallized from 2-propanol melted at 206° rather than the 181–182° reported.[8]

Anal. Calcd for $C_9H_{11}NO \cdot HCl$: C, 58.12; H, 6.52; N, 7.54. Found: C, 58.00; H, 6.33; N, 7.39.

***trans*-2-Dimethylamino-1-indanol (13).**—A solution of 1.75 g of the *trans* amino alcohol **9**, 2.1 ml of 36% formaldehyde solution, and 1.65 ml of formic acid in 25 ml of propanol was reacted as described above. The solid residue was recrystallized from ethyl acetate–ether, mp 105–107°.

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.99. Found: C, 74.78; H, 8.65; N, 7.81.

***cis*- and *trans*-2-Dimethylamino-1-indanol Trifluoroacetates (14 and 15).**—Nmr spectra were run by dissolving 50 mg of **8** and **13** in 0.1 ml of trifluoroacetic acid and completing the spectra as quickly as possible. The whole operation was completed in 2 min. The probe temperature was 40°. The spectrum of **14** resulting from the solution of **8** and of **15** resulting from the solution of **13** were characterized by doublets at 392 and 401 cps, respectively, due to the protons at C-1. No detectable amount of the unesterified **8** or **13** were present. By 2 hr later, at room temperature, measureable amounts of the C-1 epimer were detectable in the spectra of both **14** and **15**. By 3 days later, both had reached the equilibrium value of 55–45% with **15** predominating. Infrared spectra were run on the noncrystalline powder obtained by quickly evaporating freshly made solutions of **8** and **13** in trifluoroacetic acid. The ester bands of **14** and **15** were seen at 1775 and 1770 cm^{-1}, respectively. When attempts were made to isolate the bases **14** and **15** obtained from the solutions of **8** or **13** in trifluoroacetic acid or anhydride by basification of the salts with ammonia or sodium hydroxide and rapid extraction into ether, mixtures containing largely alcohol (infrared) were obtained. Recrystallization was unsuccessful in separating in a pure state the minor amount of unsaponified ester.

Esterification of Benzyl Alcohol with Trifluoroacetic Acid.—Benzyl alcohol (150 mg) was added to 0.4 ml of trifluoroacetic acid at 42° in a nmr probe. It was placed in the spectrometer, with the probe kept at 42°, and integrated between 250 and 350 cps at 1-min intervals. Integration of the singlet due to the methylene protons of benzyl alcohol at 282 cps and that due to the corresponding protons of the esterified alcohol at 319 cps was used to measure the rate of esterification. At 2 min esterification was 10% complete and at 12 min half complete.

Epimerization of *cis*-2-Dimethylamino-1-indanol (8).—A solution of 0.6 g of **8** in 6.3 ml of 1.6 *N* hydrochloric acid (3 molar equivalents) was refluxed for 16 hr. Addition of potassium hydroxide pellets and extraction with ethyl acetate gave a crude base which by nmr spectral analysis of the C-1 proton region was shown to be 62% *cis* (**8**) and 38% *trans* alcohol (**13**). (See Table I for nmr data.) Repetition of the acid treatment for an additional 36 hr gave a 50–50% mixture of the two alcohols.

Ethyl 2-(1-Hydroxy-2-indanyl)bicarbamate (16).—A solution of 4 g of the oxadiazine **3** in 10 ml of ethanol and 10 ml of water containing 1.25 ml of 8 *N* ethanolic HCl was refluxed for 1 hr. A small amount of flocculent material was filtered off, then the solvent was evaporated *in vacuo*. The organic material was taken up in ether and the ether solution washed with water, 10% sodium bicarbonate, and water, dried ($MgSO_4$), and evaporated. The oily residue, which slowly solidified, was recrystallized from benzene–petroleum ether (bp 30–60°), mp 128–129°.

Anal. Calcd for $C_{15}H_{20}N_2O_5$: C, 58.43; H, 6.54; N, 9.09. Found: C, 58.49; H, 6.52; N, 8.95.

Registry No.—**3**, 23337-75-9; **4** (*cis*), 23337-76-0; **5** (*cis*), 23337-77-1; **5** (HCl) (*cis*), 23337-78-2; **5** (picrate) (*cis*), 23337-79-3; **7** (*cis*), 23337-80-6; **7** (HCl) (*cis*), 23337-81-7; **8** (*cis*), 23359-90-2; **8** (cation H^+) (*cis*), 23335-56-0; **8** (HCl) (*cis*), 23337-82-8; **8** (methiodide) (*cis*), 23337-83-9; **9** (*trans*), 23359-91-3; **9** (HCl) (*trans*), 23337-84-0; **10**, 23337-85-1; **13** (*trans*), 23337-86-2; **13** (cation H^+) (*trans*), 23335-57-1; **13** (acetate) (*cis*), 23353-58-4; **13** (acetate) (cation H^+) (*cis*), 23335-58-2; **14** (cation H^+) (*cis*), 23335-59-3; **15** (cation H^+) (*trans*), 23355-56-8; **16** (*cis*), 23353-59-5; **16** (formylamine) (*trans*), 23353-60-8; **17** (*cis*), 23353-61-9; **18** (*cis*), 23353-62-0; **19** (*trans*), 23359-92-4; **20** (*trans*), 23359-93-5; **21** (*cis*), 23359-94-6; **21** (HCl) (*cis*), 23359-95-7; 2-(2-acetyl-1,2-dimethylhydrazino)-1-indanyl acetate, 23359-96-8; indene, 95-13-6.

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