TABLE III

INFRARED DATA FOR UNKNOWN MIXTURES

Run	D'	D''	D	$\Delta D'$	$\Delta D''$
1	0.218	0.126	0.018[a]	0.200	0.108
2	.268	.149	.014[a]	.254	.135
3	.319	.229	.028[a]	.291	.201
4	.305	.165	.041[a]	.264	.124
5	.328	.036	.027[b]	.301	.009
6	.114	.388	.022[b]	.092	.366
7	.360	.269	.143[a]	.217	.126
8	.229	.168	.012[b]	.217	.156
9	.078	.268	.008[b]	.070	.260
10	.108	.372	.004[b]	.104	.368
11	.568	.008	.003[a]	.565	.005
12	.261	.184	.004[b]	.257	.180
13	.292	.222	.004[b]	.288	.218
14	.202	.155	.000[b]	.202	.155
15	.244	.184	.002[b]	.242	.182
16	.301	.301	.008[b]	.293	.293
17	.261	.258	.006[b]	.255	.252
18	.245	.184	.008[b]	.237	.176
19	.095	.481	.000[b]	.095	.481
20	.131	.468	.008[b]	.123	.460

[a] Reference wave length = 12.40 μ. [b] Reference wave length = 13.89 μ.

and

$$F = \frac{C_c L_c}{C_t L_t}$$

$R_{c/t}$ is the ratio of *cis*-isomer to *trans*-isomer

$\Delta D'_c$ is the cor. optical density of pure *cis*-isomer at 9.80 μ
$\Delta D'_t$ is the cor. optical density of pure *trans*-isomer at 9.80 μ
$\Delta D'_m$ is the cor. optical density for the mixture of 9.80 μ
$\Delta D''_c$ is the cor. optical density of pure *cis*-isomer at 12.57 μ
$\Delta D''_t$ is the cor. optical density of pure *trans*-isomer at 12.57 μ
$\Delta D''_m$ is the cor. optical density for the mixture at 12.57 μ

All densities are corrected for errors in setting of zero density by subtraction of the optical density at a reference wave length, 12.40 μ.

C_{cm} is the concn. of the *cis*-isomer in the mixture
C_{tm} is the concn. of the *trans*-isomer in the mixture
C_c is the concn. of pure *cis*-isomer
C_t is the concn. of pure *trans*-isomer
L_c is the pellet thickness for pure *cis*-isomer
L_t is the pellet thickness for pure *trans*-isomer.

A large number of known mixtures were run in order to calibrate the method. For each of these runs the known value of $R_{c/t}$ and the determined values of the optical densities were inserted into equation 1, which was then solved for F. A plot of *F versus* per cent. *cis*-isomer (Fig. 1) was found to be linear in the range from 18–100%.

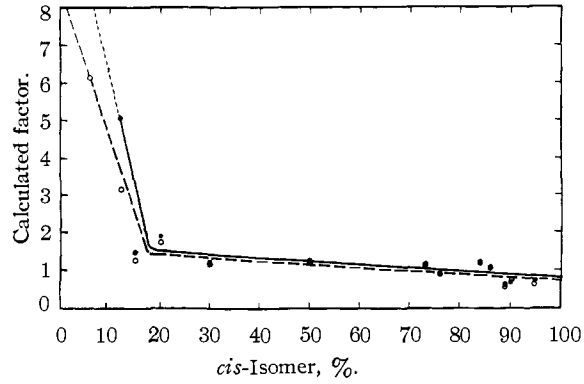


Fig. 1.—Calculated factor *vs.* % *cis*-isomer: ————, critical wave lengths = 12.57 and 9.80 μ, reference wave length = 12.40 μ; — — —, critical wave lengths 12.57 and 9.80 μ, reference wave length = 13.89 μ.

In the determination of unknown mixtures, F was assumed to be one as a first approximation. The per cent. *cis*-isomer obtained from equation 1 was used in conjunction with Chart II to obtain a more precise value of F and thus a more accurate per cent. *cis*-isomer. This procedure was continued until a limiting value of per cent. *cis*-isomer was obtained. Application of the method to further known mixtures indicated a probable accuracy of ±3 units of per cent. *cis*-isomer. Substitution of a different reference wave length (13.89 μ) gave substantially the same *F versus* per cent. *cis*-isomer curve.

Acknowledgments.—The authors are indebted to the Research Corporation for support of this research. H. J. G. also wishes to express his appreciation for a du Pont summer research fellowship.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA]

Duality of Mechanism in the Reactions of Naphthyl Halides with the Sodium Amide–Piperidine Reagent[1]

BY J. F. BUNNETT AND T. K. BROTHERTON[2]

RECEIVED JUNE 13, 1956

The reactions of seven of the eight monohalonaphthalenes with the sodium amide–piperidine reagent to form mixtures of III and IV go, to judge from product composition, entirely *via* "naphthalyne" intermediates (I and II). α-Fluoronaphthalene, however, reacts partly *via* α-naphthalyne (I) and partly by direct displacement of fluorine by a piperidino group. Direct displacement is also observed in the reactions of 1-fluoro-2-methylnaphthalene with sodium amide and piperidine to form 1-piperidino-2-methylnaphthalene, and of α- and β-naphthyl methyl sulfones with the same reagent to form III and IV, respectively. Thus this research is an exploration of the region of competition of the two mechanisms.

In a previous paper[3] it was shown that each of the two bromonaphthalenes reacts with sodium amide in refluxing piperidine to form a mixture of the two naphthylpiperidines in excellent yield. The mixture from α-bromonaphthalene contained 32% of α-naphthylpiperidine (III) and 68% of β-naphthylpiperidine (IV). The mixture from β-bromonaphthalene was 26% III and 74% IV. The formation of such product mixtures was explicable in terms of a

(1) Work supported in part by the Office of Ordnance Research, U. S. Army.

(2) American Enka Fellow, 1954–1955; R. J. Reynolds Fellow, 1955–1956.

(3) J. F. Bunnett and T. K. Brotherton, THIS JOURNAL, **78**, 155 (1956).

mechanism involving "naphthalyne" intermediates (see Chart I).

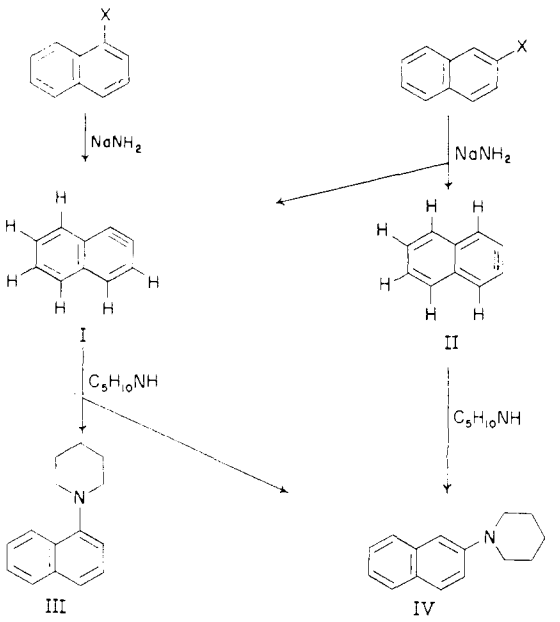


CHART I.

On the other hand, each bromonaphthalene reacts with piperidine at 230°, in the absence of sodium amide, to form the corresponding unrearranged naphthylpiperidine. The absence of isomeric products in these reactions indicates the non-participation of naphthalyne intermediates; the mechanism here is one of direct displacement. Thus in this system product structure is a criterion of mechanism: The formation of a mixture of III and IV indicates the "naphthalyne" mechanism, while the formation of a single, unrearranged product indicates a direct displacement.

In the earlier work,[3] it was clear that *most* of the mixture of III and IV obtained from the action of the sodium amide–piperidine reagent on either bromonaphthalene was generated *via* naphthalyne intermediates, but the possibility of a small percentage of direct displacement could not be excluded. It was reasoned that a decision on this point could be reached by studying the action of this reagent on the other halonaphthalenes. The reasoning was as follows: If two or more α-halonaphthalenes react wholly *via* α-naphthalyne (I), the same ratio of III to IV should be observed in each product mixture. On the other hand, if two or more α-halonaphthalenes react in part by the naphthalyne mechanism and in part by direct displacement, it would be unlikely that the same balance between the two mechanisms would be struck in each case and therefore one would expect the ratio of III to IV to vary in the several product mixtures. Similarly, the several β-halonaphthalenes would be expected to produce III and IV in variable ratio if the two mechanisms were competing, but in constant ratio[4] if only the naphthalyne mechanism were operative.

Largely for these reasons, we allow the sodium amide–piperidine reagent to act on the other six monohalonaphthalenes under the conditions previously used with the bromonaphthalenes. The two naphthyl methyl sulfones were also submitted to this treatment. The resulting mixtures of naphthylpiperidines were analyzed by chromatography on alumina and/or infrared spectrophotometry. Results are listed in Table I.

TABLE I

REACTIONS OF HALONAPHTHALENES AND NAPHTHYL METHYL SULFONES WITH THE SODIUM AMIDE–PIPERIDINE REAGENT

Naphthalene derivative	Total yield of III + IV, %	Composition of the mixture of III + IV	
		III, %	IV, %
2-F	54[a]	26	74
2-Cl	44	26	74
2-Br	94[b]	26	74
2-I	48[c]	22	78
2-SO_2CH_3	53[d]		100
1-F	57[e]	60	40
1-Cl	84	32	68
1-Br	92[b]	32	68
1-I	54[f]	35	65
1-SO_2CH_3	70[g]	100	

[a] A small amount of β-naphthylamine was also formed; see Experimental. [b] From reference 3. [c] Also, 41% of β-iodonaphthalene was recovered. [d] Also, 13% of β-naphthyl methyl sulfone was recovered. [e] Small amounts of both naphthylamines were formed; see Experimental. [f] Also, 6% of naphthalene was isolated. [g] Also, 4% of α-naphthyl methyl sulfone was recovered.

From the fact that all four β-halonaphthalenes furnished III and IV in constant proportion,[5] we conclude that all four reactions form naphthylpiperidines entirely by the naphthalyne mechanism. A subsidiary conclusion of some interest is that each β-halonaphthalene forms the two naphthalynes (I and II) in the same proportion, regardless of which halogen occupies the 2-position.

Because α-chloro-, α-bromo- and α-iodonaphthalene all formed III and IV in the same ratio,[5] we conclude that these reactions also proceed entirely by the naphthalyne mechanism. And from the fact that each naphthyl methyl sulfone gives the corresponding unrearranged naphthylpiperidine with no trace of a cine-substitution product, we deduce that the reaction with these two substrates goes wholly by a direct displacement mechanism.[6] This is the first definite indication that the sodium amide–piperidine reagent can effect the introduction of piperidino groups in a direct displacement process.

The behavior of α-fluoronaphthalene is of particular interest. The fact that a considerable amount of IV is produced shows that a large part of the reaction goes *via* α-naphthalyne (I). On the other hand, the fact that an unusually large proportion of

(4) This statement involves the assumption that the ratio of proton abstraction from the 1- *vs.* the 3-position (*i.e.*, the ratio of I to II) would not depend on the nature of the halogen in the 2-position.

(5) The result from the iodo compound is considered to be the same as the others within experimental error.

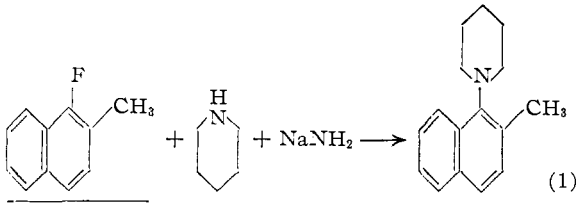
(6) In private conversation, Dr. Philip J. Hamrick, Jr. (Wake Forest College) has pointed out that substantial fractions of the naphthyl methyl sulfones may be converted to their conjugate bases by the reagent. Nevertheless, it is quite possible that the neutral sulfone molecules are the effective participants in the displacement reaction. W. Bradley, *J. Chem. Soc.*, 458 (1938), observed the cleavage of diphenyl sulfone by the sodium amide–piperidine reagent to form N-phenylpiperidine, and we have confirmed this observation. This reaction is probably also a direct displacement.

III is obtained indicates that a significant part of the reaction proceeds by direct displacement of the fluorine atom. Here the two mechanisms are competing for the same substrate. The yield figures indicate that 59% of the mixture of III and IV was produced *via* I and 41% by direct displacement.

It is interesting to compare our results with those of Urner and Bergstrom[7] who studied the reactions of all eight monohalonaphthalenes with potassium amide in liquid ammonia. These authors analyzed their product mixtures by a crystallization technique which is inherently less accurate than the techniques we used; nevertheless their work appears to have been done carefully. They found that six of the halonaphthalenes, excluding only the fluoronaphthalenes, gave about the same yields of two products: *circa* 46% of β-naphthylamine and 2% of α-naphthylamine. The fluoronaphthalenes each gave a single unrearranged naphthylamine: around 43% of α-naphthylamine from α-fluoronaphthalene and 10% of β-naphthylamine from β-fluoronaphthalene. The similarity to our results is striking: the chloro-, bromo- and iodonaphthalenes appear to react *via* naphthalyne intermediates (mostly *via* I) and α-fluoronaphthalene undergoes only direct displacement. Their result from β-fluoronaphthalene also suggests direct displacement but it is possible that a small amount of α-naphthylamine may have escaped detection.

In contrast to the results of Urner and Bergstrom, Gilman and co-workers[8] found that α-fluoronaphthalene with lithium diethylamide in ether formed exclusively a cine-substitution product: 40% of N,N-diethyl-β-naphthylamine. In view of our work, this contrast is no longer disturbing. We find direct displacement and naphthalyne formation to be closely balanced (2:3) in the reaction of α-fluoronaphthalene with the sodium amide–piperidine reagent. It is not surprising that changes in the reagent and conditions should tip the balance altogether one way in one case and altogether the other way in another.

As a further check on our conclusion that α-fluoronaphthalene reacted with the sodium amide–piperidine reagent to a considerable extent by direct displacement, we studied the action of this reagent on 1-fluoro-2-methylnaphthalene. This compound is structurally unable to give rise to a naphthalyne derivative since it does not possess any hydrogen atom *ortho* to its fluorine atom. The reaction furnished 1-piperidino-2-methylnaphthalene in 84% yield (equation 1). Thus it is confirmed that the sodium amide–piperidine reagent can effect the direct displacement of fluorine from an unactivated aryl fluoride.

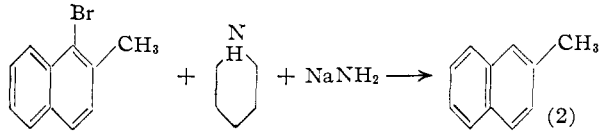


(1)

(7) R. S. Urner and F. W. Bergstrom, THIS JOURNAL, **67**, 2108 (1945); R. S. Urner, Ph.D. thesis, Stanford University, 1940.

(8) H. Gilman, N. N. Crounse, S. P. Massie, R. A. Benkeser and S. M. Spatz, *ibid.*, **67**, 2106 (1945).

The action of this reagent on 1-bromo-2-methylnaphthalene was next studied. The product, unexpectedly, was 2-methylnaphthalene in 81% yield (equation 2). Such reductive dehalogenation



(2)

through the action of amide reagents is not uncommon.[9] Indeed, we obtained 6% of naphthalene from α-iodonaphthalene (Table I). The mechanism is probably some sort of nucleophilic displacement on the halogen atom effecting the removal of "positive" halogen, the place of which is taken by a proton. Benkeser and DeBoer[9d] have proposed a mechanism of somewhat different character for dehalogenations induced by lithium dialkylamides in ether.

From the facts that α-fluoronaphthalene reacts to a considerable extent by direct displacement whereas α-bromonaphthalene reacts wholly *via* naphthalyne intermediates, and that 1-fluoro-2-methylnaphthalene gives an apparently normal substitution product whereas 1-bromo-2-methylnaphthalene gives a reduction product, one might be tempted to conclude that fluorine is more readily replaced than bromine in direct displacement reactions. This conclusion is not warranted, however, since what is observed is that the bromo compound in each case reacts in some other way. It is possible that the alternate mode of reaction is, in each case, faster for the bromo than for the corresponding fluoro compound. It is well established that bromobenzene forms benzyne rapidly under conditions that produce no over-all chemical change with fluorobenzene,[10] and therefore the fact that α-bromonaphthalene reacts solely *via* α-naphthalyne may be due to greater susceptibility of the bromo compound to dehydrohalogenation rather than to lesser reactivity in direct displacement. The reductive dehalogenation reaction may also go faster with aryl bromides than aryl fluorides.

Nevertheless, it is of interest that the fluoro compounds have been the ones to give direct displacement since unactivated aryl fluorides are commonly stated[3,11] to be less reactive toward nucleophilic reagents than the corresponding chlorides, bromides or iodides. This belief derives from two sources: observations by Bergstrom and co-workers[12] that aryl fluorides are especially unreactive with sodium or potassium amide in liquid ammonia, and by Tronov and Krueger[13] that phenyl halides have the order of reactivity I > Br > Cl > F with piperidine and with sodium methoxide. The

(9) (a) T. H. Vaughn, R. R. Vogt and J. A. Nieuwland, *ibid.*, **56**, 2121 (1934); (b) R. V. Paulson and W. S. MacGregor, *ibid.*, **73**, 679 (1951); (c) M. Bourguel, *Ann. chim.*, [10] **3**, 225, 343 (1925); (d) R. A. Benkeser and C. E. DeBoer, *J. Org. Chem.*, **21**, 281 (1956); (e) P. Wilder, Jr., and G. T. Youngblood, private communication.

(10) J. D. Roberts, D. A. Semenow, H. E. Simmons and L. A. Carlsmith, THIS JOURNAL, **78**, 601 (1956).

(11) E. Berliner, M. J. Quinn and P. J. Edgerton, *ibid.*, **72**, 5305 (1950).

(12) F. W. Bergstrom, R. E. Wright, C. Chandler and W. A. Gilkey, *J. Org. Chem.*, **1**, 170 (1936).

(13) B. Tronov and E. Krueger, *J. Russ. Phys.-Chem. Soc.*, **58**, 1270 (1926) [*C. A.*, **21**, 3887 (1927); *Chem. Zent.*, **98**, **II**, 1145 (1927)].

former reactions are now known to go *via* benzyne.[10] The position of fluorine in Tronov and Krueger's reactivity series has apparently not been checked,[14] nor has any similar study on the comparative reactivity of unactivated aryl fluorides been published. We therefore allowed α-fluoronaphthalene to react with piperidine (but not sodium amide) under conditions known[3] to give rise to the formation of III from α-bromonaphthalene in a direct displacement process. A 36% yield of III was obtained in 24 hours; this compares with 49% in 48 hours from α-bromonaphthalene. This experiment cannot be regarded as conclusive, but it does raise doubt as to whether the reactivity series of Tronov and Krueger is correct insofar as the position of fluorine is concerned. Further study of this matter is planned.

The present research constitutes an exploration of the region of conflict between the elimination–addition ("benzyne") mechanism and the direct displacement mechanism for substitution in unactivated aryl halides and sulfones induced by a strongly basic, powerfully nucleophilic reagent. No other comparable study has been reported, although competition between the two mechanisms has been detected by Roberts and co-workers[10] in the reaction of potassium amide with ^{14}C-labeled phenyltrimethylammonium bromide to form aniline. Competition between the two mechanisms is to be expected with yet other reagents, but the regions of dominance of the two mechanisms may not be the same with one reagent as with another.

Experimental

α-Fluoronaphthalene, f.p. −12.5° (lit.[15] −14°), $n^{25}D$ 1.5915, and **β-fluoronaphthalene**, m.p. 60–60.5° (lit.[15] 60°), were prepared from the corresponding amines by the Schiemann reaction.[16] **α-Chloronaphthalene**, f.p. −2.3° (lit.[17] −2.3°), was obtained by purification of a commercial product by the method of Jones and Lapworth.[18] **β-Chloronaphthalene**, m.p. 57.5–58.5° (lit.[17] 57.4–57.8°), was prepared by a Sandmeyer reaction. Eastman Kodak Co. **α-iodonaphthalene** was repurified by distillation; b.p. 100–101° (2 mm.). **β-Iodonaphthalene**, m.p. 54–54.5° (lit.[19] 54.5°), was prepared by treating the corresponding diazonium solution with potassium iodide.

α-Naphthyl methyl sulfone, m.p. 100.5–102° (lit.[20] 102–103°), was prepared from α-naphthalenesulfonyl chloride by the method of Oxley, Partridge, Robson and Short.[21] **β-Naphthyl methyl sulfone**, m.p.140–141° (lit.[20] 142–143°), was prepared by permanganate oxidation of the corresponding sulfide which in turn was obtained by methylation of Eastman Kodak Co. β-naphthalenethiol with dimethyl sulfate.

1-Fluoro-2-methylnaphthalene was prepared in 38% yield from 1-amino-2-methylnaphthalene as described by Willstaedt and Scheiber.[22] The product was a colorless liquid, b.p. 75° (4 mm.), $n^{18}D$ 1.5901.

Anal. Calcd. for $C_{11}H_9F$: C, 82.48; H, 5.66. Found[23]: C, 82.66; H, 5.77.

1-Bromo-2-methylnaphthalene, b.p. 154–154.5° (13 mm.), $n^{23}D$ 1.6480, was obtained by bromination of 2-methylnaphthalene.[24]

Commercial **piperidine** (mostly from Reilly Tar and Chemical Corp.) was refluxed over sodium for six hours and then distilled from sodium.

Reactions of Halonaphthalenes with Sodium Amide and Piperidine.—The reactions were run as described previously.[3] The products from α-chloronaphthalene were determined as in the earlier work,[3] but the products from β-chloronaphthalene, and from the fluoro- and iodonaphthalenes were isolated and analyzed by a somewhat different procedure owing to the larger proportion of by-products in these cases. The crude product was divided into neutral and basic fractions by a simple extraction technique. The basic fraction was distilled at reduced pressure and the total material distilling in the temperature region where the naphthylpiperidines distil was chromatographed on alumina with benzene as the eluting solvent. The first fractions to emerge from the column were oils rich in III but usually contaminated to some extent with IV; the composition was determined by the infrared method described previously.[3] Later fractions of pure IV, recognized by melting point and mixed melting point, usually were obtained. Still later fractions, in runs with the fluoronaphthalenes, contained small amounts of naphthylamines (see below), but naphthylamines were not detected amongst products from the chloro-, bromo- or iodonaphthalenes. Finally, methanol removed reddish, glassy oils of unknown nature. From the weights and analyses of the various fractions of III and/or IV, the total yield and distribution between the two was calculated. Several runs were made with α-fluoronaphthalene, and there was good agreement between them. We estimate the composition figures in Table I to be good to ±3%.

The neutral fraction was also examined in every case, but the only identifiable materials found among the frequently considerable tars were some unreacted starting material from β-iodonaphthalene, and some naphthalene (verified by mixed melting point) from α-iodonaphthalene (see Table I).

The basic product from one run from α-fluoronaphthalene was treated with acetic anhydride in the presence of aqueous sodium acetate, and the products were then separated by usual techniques of extraction and chromatography. Besides III and IV, both α- and β-naphthylacetamides were isolated, each in about 1% yield. N-(α-Naphthyl)-acetamide, m.p. 157–159° (lit.[25] 160°), failed to form an adduct with trinitrotoluene in agreement with Sudborough[26]; the mixed melting point with an authentic sample was not depressed, and the infrared spectrum was identical to that of an authentic sample. N-(β-Naphthyl)-acetamide, m.p. 130.5–132° (lit.[25] 132°) not depressed on admixture with an authentic sample, formed with trinitrotoluene an adduct of m.p. 106° as reported by Sudborough,[26] and its infrared spectrum was identical to that of an authentic sample.

The basic products from one run from β-fluoronaphthalene were treated in benzene solution with acetic anhydride. By standard techniques, a 12% yield of N-(β-naphthyl)-acetamide, m.p. 132° not depressed on admixture with an authentic sample, was isolated in addition to III and IV. N-(α-Naphthyl)-acetamide was not found in this case.

Reactions of Naphthyl Methyl Sulfones with Sodium Amide and Piperidine.—The reactions were run as described[3] for β-bromonaphthalene and the products were isolated by distillation and chromatography as described above. From 10.3 g. of α-naphthyl methyl sulfone, 7.4 g. of III was obtained as a blue-fluorescent oil, b.p. 120–130° (2 mm.), $n^{25}D$ 1.6129, identical in infrared spectrum to authentic III; 0.4 g. of the starting sulfone was recovered. No trace of IV could be found. From 10.3 g. of β-naphthyl methyl sulfone, 5.6 g. of IV was obtained as a white solid, m.p. 54–55.5° not depressed on admixture with authentic IV. No trace of III could be found, but 1.3 g. of the starting sulfone was recovered.

(14) Berliner, *et al.*,[11] verified the order I > Br > Cl for reactions of phenyl and naphthyl halides with piperidine, but apparently did not include fluorobenzene or the fluoronaphthalenes in their study.

(15) L. Klemm, W. Klemm and G. Schiemann, *Z. physik. Chem.*, **A165**, 379 (1933).

(16) A. Roe, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 193.

(17) G. U. Zilberman, S. T. Rashevskaya and S. S. Martyntseva, *J. Appl. Chem. (U.S.S.R.)*, **9**, 1832 (1936); *C. A.*, **31**, 2597 (1937).

(18) M. Jones and A. Lapworth, *J. Chem. Soc.*, **105**, 1804 (1914).

(19) P. Jacobson, *Ber.*, **14**, 804 (1881).

(20) R. Otto, A. Rössing and J. Traeger, *J. prakt. Chem.*, [2] **47**, 102 (1893).

(21) P. Oxley, M. W. Partridge, T. D. Robson and W. F. Short, *J. Chem. Soc.*, 767 (1946).

(22) H. Willstaedt and G. Scheiber, *Ber.*, **67**, 466 (1934).

(23) Analysis by Micro-Tech Laboratories, Skokie, Ill.

(24) R. Adams and L. O. Binder, THIS JOURNAL, **63**, 2773 (1941).

(25) A. Calm, *Ber.*, **15**, 609 (1882).

(26) J. J. Sudborough, *J. Chem. Soc.*, **79**, 522 (1901).

Reaction of 1-Fluoro-2-methylnaphthalene with Sodium Amide and Piperidine.—The reaction was run as described[3] for the bromonaphthalenes, and the basic products were purified by fractional distillation at reduced pressure. A colorless liquid, b.p. 134° (2 mm.), $n^{15}D$ 1.6060, was obtained in 84.5% yield (reckoned as 1-piperidino-2-methylnaphthalene).

Anal. Calcd. for $C_{16}H_{19}N$: C, 85.28; H, 8.50. Found[23]: C, 85.38; H, 8.82.

1-Piperidino-2-methylnaphthalene from 1-Bromo-2-methylnaphthalene.—As a check on the identity of the above product, 22.1 g. of 1-bromo-2-methylnaphthalene and 35 cc. of piperidine were heated in a sealed tube 82 hours at 200°. The basic products were isolated by standard procedures including distillation at reduced pressure. The liquid so obtained was treated with *p*-toluenesulfonyl chloride in pyridine to remove primary and/or secondary amines apparently derived solely from the piperidine,[3] and the remaining basic product was finally purified by distillation at reduced pressure. A clear oil (2.1 g., 9%), b.p. 137–141° (3–4 mm.), $n^{19}D$ 1.6051, was so obtained. Its infrared spectrum was identical to that of the product described immediately above.

The products of the two reactions are identical, and the substance is almost surely 1-piperidino-2-methylnaphthalene. If the piperidino group is anywhere but the 1-position, an unprecedented rearrangement has occurred in two separate instances.

Attempted Reaction of α-Naphthyl Methyl Sulfone with Piperidine.—This experiment was run to check on the unlikely possibility that the production of III from this sulfone and the sodium amide–piperidine reagent might have been due solely to the action of the piperidine in the reagent. The sulfone and piperidine were combined just as in the earlier experiment except that sodium amide was omitted. The mixture was refluxed two hours. No III was obtained, and 86% of the sulfone was recovered in a state of high purity.

CHAPEL HILL, N. C.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Stereoelectronic Control in Enolization–Ketonization Reactions[1]

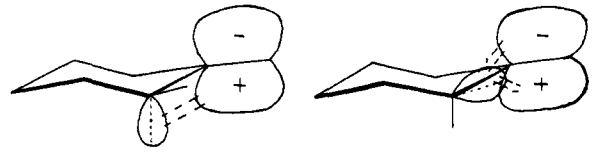
BY E. J. COREY AND R. A. SNEEN

RECEIVED MARCH 26, 1956

The stereochemistry of the enolization of 3β-acetoxycholestan-7-one to the Δ⁶-en-7-ol and of the ketonization of this enol have been studied using deuterium tracer. With hydrogen bromide as catalyst in chloroform solution the axial hydrogen at C_6 is lost in enolization 1.2 times as rapidly as the equatorial hydrogen (corrected for isotope effect); for the reverse reaction, ketonization, an axial hydrogen is gained *ca.* 1.5 times as rapidly as an equatorial hydrogen. These values, which in theory should be identical, are in reasonably good agreement and indicate that despite a strong steric retardation of the gain and loss of an axial hydrogen, axial attack is still at least as favorable as equatorial attack. Correction for this steric effect gives the result that stereoelectronic factors favor axial attack over equatorial attack by a factor of at least 12. The acetic acid catalyzed enolization–ketonization reaction is even more specific and axial attack is favored over equatorial attack by a total factor of at least 9 with a stereoelectronic component of at least 50. The kinetic isotope effect of deuterium in enolization of 7-ketosteroids has been found to be *ca.* 7.4, close to the theoretical maximum at 10°. A thermodynamic explanation is presented to explain the variation in degree of stereoelectronic control with reactivity of the reagent and supporting data are cited from a comparison of chlorination and bromination experiments. The occurrence of a high degree of stereoelectronic control is postulated to explain the exclusive axial attack observed in reactions of steroidal 4,5,6-allyl cations.

It has been shown previously[2] that the bromination of steroid ketones *via* the corresponding enols is characterized in several cases, and perhaps generally, by an effect which directs the incoming bromine substituent to the axial rather than the equatorial position. Opposing this effect is the classical steric effect, which directs a large substituent such as bromine to the less crowded equatorial orientation. The net result of these two effects, which influence the relative rates of formation of the epimers with axial and equatorial bromine, is clear in those cases where the bromoketone which is isolated is the unstable epimer, formed for kinetic rather than for steady-state reasons. In such instances the importance of the non-steric effect is apparent since the major product has invariably been found to be the epimer with axial bromine.[2]

It has been proposed that the orienting influence which is responsible for this stereochemical preference is stereochemical–electronic in nature and depends on the difference in degree of delocalization of electrons in perturbed axial and equatorial bonds which are alpha to an exocyclic π-orbital. Reference to Fig. 1 indicates the relationship between stereochemical orientation and the extent of delocalization of exocyclic σ-electrons to an adjacent exocyclic π-orbital. Since the transition state for enolization–ketonization type processes



axial interaction (bonding) equatorial interaction (non-bonding)

Fig. 1.

is stabilized by bonding between the alpha and carbonyl carbon atoms involving σ–π delocalization as shown in Fig. 1, there should be a preference for loss or gain of an axial α-substituent over an equatorial α-substituent. Or, in slightly different terms, there is better bonding in the transition state for enolization–ketonization when the entering or leaving α-substituent possesses the axial orientation than the alternative equatorial orientation. Because the structure of the transition state for such processes is intermediate between the structures of the enol and ketone or ketone conjugate acid, the bond being formed to or broken from C_α will not possess pure axial or equatorial character and the considerations expressed in Fig. 1 are extreme. However, as the transition

(1) Presented at the Fifth Conference on Organic Reaction Mechanisms, Durham, N. H., September, 1954. Taken from the Ph.D. thesis of Richard A. Sneen, University of Illinois, 1955.

(2) E. J. Corey, THIS JOURNAL, **76**, 175 (1954).