[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Interaction of Certain Grignard Reagents with Nitriles Containing an α-Morpholinyl Substituent[1]

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The interaction of certain Grignard reagents with 4-morpholineacetonitrile, α-methyl-4-morpholineacetonitrile and α,α-dimethyl-4-morpholineacetonitrile has been studied.

Although the interaction of Grignard reagents with nitriles has been studied[2-4] frequently since the first example of ketone formation was reported in 1901,[5] relatively little attention has been devoted to the behavior of such reagents with amino nitriles. In the case of α-amino nitriles of the type R'_2NCR_2CN, products other than substituted α-amino ketones are possible, due to replacement of the cyano group by the organic radical of the Grignard reagent. Moreover, Bruylants[6] and Velghe[7] have reported that in some cases dimeric products, $(R'_2N)CR_2-CR_2(NR'_2)$, were obtained.

Stevens, *et al.*,[8] carried out an investigation of considerable extent which was summarized in an article published in 1932. On the basis of Bruylants' work and of their own results, some general conclusions were drawn concerning the kind of product obtained from interaction of the various types of α-amino nitriles with Grignard reagents. Since this review by Stevens there have been reported but two additional cases of reactions between α-(N-substituted)-amino nitriles and Grignard reagents. Thus, this reaction was utilized[9] in the synthesis of N,N-diethyltridecylamine from dodecylmagnesium chloride and diethylaminoacetonitrile. Likewise, more recently there has been reported[10] that the interaction of α-(disubstituted-amino)-phenylacetonitriles with benzylmagnesium chloride led to the production of amines in all cases except where the $-NR'_2$ portion was morpholinyl or di-(2-hydroxypropyl)-amino, in which instances ketone formation was exclusive.

We have now investigated the behavior of certain Grignard reagents with 4-morpholineacetonitrile (I), α-methyl-4-morpholineacetonitrile (II) and α,α-dimethyl-4-morpholineacetonitrile (III), respectively. In the few cases studied, compound I behaves as anticipated in that alkylmagnesium bromides react to yield ketones, whereas allylmagnesium bromide produced the expected carbinamine. Substitution of one (II) or two (III) methyl groups at the α-position of I changed the reactivity of the cyano group. Although, in general, primary or secondary alkyl Grignard reagents reacted with II or III to replace the cyano grouping with the corresponding alkyl group, *t*-alkylmagnesium reagents (*t*-butyl- or *t*-amyl) reacted with II and III to cause replacement of the cyano grouping with hydrogen. With both II and III, allylmagnesium bromide reacted to form an allylketimine. Phenylmagnesium bromide reacted similarly to the primary and secondary alkyl reagents, but the benzyl reagent behaved differently in that it produced a ketone from reaction with II. Alkyl substitution in the benzyl group led to behavior analogous to most alkyls, whereas *p*-substitution in the aryl nucleus resulted in both substitution for and reaction with the cyano grouping.

It was of considerable interest to contrast the behavior of α-methyl-4-morpholineacetonitrile (II) toward organolithium compounds with that of II and Grignard reagents, therefore, *n*-butyl-, *sec*-butyl- and phenyllithium were prepared and allowed to react with II. From the use of these lithium reagents, production only of morpholinyl ketones was realized; this result is in sharp contrast to the formation of N-alkyl- (or phenyl)-morpholines from II and the Grignard reagents.

Since it has been shown[11] that hydantoin formation is a useful means of characterizing ketones, an attempt was made to convert certain of these α-(4-morpholinyl)-ethyl ketones into hydantoins; only the *n*-butyl ketone was converted into the anticipated 5-butyl-5-(α-(4-morpholinylethyl)-hydantoin. In the case of three others of the $OC_4H_8NCH(CH_3)COR$ series of ketones, (where R = benzyl, *p*-ethylbenzyl- or *p*-isopropylbenzyl), cleavage occurred and the product isolated was the corresponding 5-aralkylhydantoin.

Experimental

Preparation of Acetonitrile Derivatives. A. 4-Morpholineacetonitrile[12] was obtained in 66% yield through interaction of the sodium bisulfite addition product of formaldehyde with excess morpholine and an aqueous solution of potassium cyanide; b.p. 232° (750 mm.) and 123° (24 mm.), m.p. 61–62°.

Anal. Calcd. for $C_6H_{10}N_2O$: mol. wt., 126.2; C, 57.12; H, 7.99. Found: mol. wt. (ebulliometric in acetone), 132; C, 57.02; H, 8.07.

B. **α-Methyl-4-morpholineacetonitrile** was obtained from the interaction of the sodium bisulfite addition product of acetaldehyde, morpholine and potassium cyanide solution, yield 40–50%. However, by mixing an aqueous solution of

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[1] From the Ph.D. dissertations of George L. Sutherland and George B. Roberts, the University of Texas, 1950.

[2] See S. T. Yoffe and A. N. Nesmeyanov, "Handbook of Magnesium-Organic Compounds," 3 Vols., Pergamon Press, New York, N. Y., 1956.

[3] M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Compounds," Prentice-Hall, Inc., New York, N. Y., 1954, Chapter X.

[4] V. Migrdichian, "The Chemistry of Organic Cyanogen Compounds," Reinhold Publishing Corp., New York, N. Y., 1947, Chapter 14.

[5] E. E. Blaise, *Compt. rend.*, **132**, 38 (1901).

[6] P. Bruylants, *Bull. soc. chim. Belg.*, **33**, 467 (1924); *C. A.*, **19**, 288 (1925); *Bull. sci. acad. roy. Belg.*, [5] **11**, 261 (1925); *C. A.*, **20**, 1053 (1926).

[7] M. Velghe, *Bull. sci. acad. roy. Belg.*, [5] **11**, 301 (1925); *C. A.*, **20**, 1053 (1926).

[8] T. Thomson and T. S. Stevens, *J. Chem. Soc.*, 2607 (1932).

[9] O. Westphal, *Ber.*, **74**, 1356 (1941).

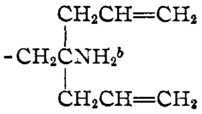
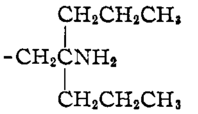
[10] L. H. Goodson and H. Christopher, THIS JOURNAL, **72**, 358 (1950).

[11] H. R. Henze and R. J. Speer, *ibid.*, **64**, 522 (1942).

[12] After this compound had been prepared and used in this study, its synthesis was reported by R. A. Henry and W. M. Dehn [*ibid.*, **72**, 2805 (1950)], m.p. 60–61°.

TABLE I

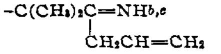
PRODUCTS FORMED FROM INTERACTION OF 4-MORPHOLINEACETONITRILE AND GRIGNARD REAGENTS

R-MgBr, R =	Product $O(CH_2CH_2)_2N-R'$, R' =	B.p. °C.	Mm.	Yield, %	$n^{20}D$	d^{20}_4	Molecular refraction Summation	Calcd.	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
$-C_2H_5$	$-CH_2COC_2H_5$[a]	86–89	3	26	1.4620	1.0117	42.55	42.73	61.12	60.83	9.62	9.91
$-(CH_2)_3CH_3$	$-CH_2COC_4H_9$	97–100	1	54	1.4615	0.9810	51.79	51.87	64.82	64.87	10.34	10.61
$-CH_2CH{=}CH_2$	 $-CH_2\underset{CH_2CH=CH_2}{\overset{CH_2CH=CH_2}{C}}NH_2$[b]	116	2	22	1.4925	0.9636	63.63	63.38	68.53	67.89	10.54	10.66
	 $-CH_2\underset{CH_2CH_2CH_3}{\overset{CH_2CH_2CH_3}{C}}NH_2$	112	2	75	1.4683	0.9286	64.57	64.20	67.24	66.69	12.22	12.49

[a] M.p. of picrate 130-131°; J. P. Mason and S. D. Ross [THIS JOURNAL, 62, 1448 (1940)] reported m.p. 127-129° for picrate. [b] The diallylcarbinamine was reduced catalytically to yield the dipropylcarbinamine, whose physical properties are listed in Table I.

TABLE II

PRODUCTS FORMED FROM INTERACTION OF α,α-DIMETHYL-4-MORPHOLINEACETONITRILE AND GRIGNARD REAGENTS

R-MgBr, R =	Product $O(CH_2CH_2)_2N-R'$, R' =	B.p., °C.	Mm.	Yield, %	$n^{20}D$	d^{20}_4	Molecular refraction Summation	Calcd.	Carbon, % Calcd.	Found	Hydrogen % Calcd.	Found
$-C_2H_5$	$-C(CH_3)_2C_2H_5$	64–67	11	46	1,4553	0,9103	47.32	46.89	68.75	68.48	12.18	11.93
$-(CH_2)_3CH_3$	$-C(CH_3)_2C_4H_9$	122–125	30	46	1,4592	0,9085	56.40	55.78	71.30	71.48	12.48	12.36
$-C(CH_3)_3$	$-CH(CH_3)_2$	155–156	751	55	1,4450[a]							
$-CH_2CH{=}CH_2$	 $-C(CH_3)_2\underset{CH_2CH=CH_2}{C}{=}NH$[b,c]			61					67.30	67.29	10.27	10.62
$-C_6H_5$	$-C(CH_3)_2C_6H_5$	122–126	6	40	1,5278	1.028	62.01	61,39	76.95	76.48	9.33	9.21

[a] At 25°; for additional data concerning 4-(1-methylethyl)-morpholine, see Table III. [b] Calcd. for $C_{11}H_{20}N_2O$: mol. wt., 196.3. Found: mol. wt. (ebulliometric in acetone), 710. [c] Calcd. for $C_{11}H_{20}N_2O$: N, 14.27. Found: N, 14.38.

morpholine sulfate, acetaldehyde and potassium cyanide, yields of 51–57% were obtained, b.p. 97–98° (5 mm.) and 128–129° (25 mm.),[13] $n^{25}D$ 1.4621, d^{25}_4 1.030; ΣMR 37.66, MR calcd. 37.44. The picrate melted at 115–118°, but after recrystallization from boiling alcohol, from which the odor of hydrogen cyanide was pronounced, the m.p. was 148.5–149.5° (the latter is the m.p. of morpholine picrate).

Anal. Calcd. for $C_7H_{12}N_2O$: C, 59.93; H, 8.63. Found: C, 59.97; H, 8.63.

C. **α,α-Dimethyl-4-morpholineacetonitrile**[14] was produced from the interaction of morpholine sulfate, acetone and potassium cyanide solution; 63% yield, b.p. 123–124° (20 mm.),[15] $n^{20}D$ 1.4650 d^{20}_4 1.0072; ΣMR 42.28, MR calcd. 43.32.

Anal. Calcd. for $C_8H_{14}N_2O$: C, 62.31; H, 9.15. Found: C, 62.49; H, 9.39.

The crude picrate melted at 118–120° with decomposition and evolution of gas; attempts to purify the picrate converted it into morpholine picrate.

Interaction of Grignard Reagents with these Acetonitriles.—In general, an excess of the appropriate Grignard reagent in very dilute, anhydrous ether solution was prepared and treated with a dilute solution of the nitrile; in the case of 4-morpholineacetonitrile, because of its limited solubility in ether, benzene was used as its solvent. The adduct was hydrolyzed (either with ice-water, 5 *N* hydrochloric acid or concd. hydrochloric acid), and the products were extracted, dried and fractionated in the usual manner. In certain experiments, it proved advantageous to filter the adduct (A) from the ether solution (filtrate B). Fraction A was added slowly to ice-water, forming an ether layer and slurry of magnesium compounds; the latter was extracted with ether and discarded. The initial filtrate (B) was treated with concd. acid, extracted with ether, made basic by addition of sodium carbonate and again ether extracted. The products isolated from the several adducts are listed, together with pertinent data for their properties, in Tables I–III.

Reduction of 4-(2-Allyl-2-amino-4-pentenyl)-morpholine. Four grams of this amine, produced from interaction of allylmagnesium bromide and 4-morpholineacetonitrile, was dissolved in 100 ml. of alcohol and made barely acidic with hydrochloric acid. About 0.1 g. of Adams platinum catalyst was added and the mixture was shaken under an atmosphere of hydrogen. After filtration from the catalyst, alcohol was removed under diminished pressure, the residue was treated with 50% potassium hydroxide solution and the organic material was removed and fractionated *in vacuo;* 3 g., b.p. 112° (2 mm.), $n^{20}D$ 1.4683, d^{20}_4 0.9286; ΣMR 64.57, MR calcd. 64.20.

Anal. Calcd. for $C_{12}H_{26}N_2O$: C, 67.24; H, 12.22. Found: C, 66.69; H, 12.49.

Product from Interaction of Allylmagnesium Bromide and α,α-Dimethyl-4-morpholineacetonitrile.—Allylmagnesium bromide (1 mole) in ether solution was treated with an ether solution of α,α-dimethylamino-4-morpholineacetonitrile (0.25 mole), and the adduct was decomposed with ice-water. The reaction product was extremely viscous and difficult to purify. After exposure to a vacuum of 1 mm. for several hours, the product (61% yield) dissolved slowly in acid, formed a picrate but did not yield an acetyl or benzoyl derivative. The amine was boiled for 1 hr. with 20% sulfuric acid and, subsequently, with 10% sodium hydroxide solution without causing evolution of ammonia or other chemical change. Solutions of bromine in carbon tetrachloride and of potassium permanganate in acetone were decolorized by the product which, apparently, was the polymer of 4-(2′-amino-1′,1′-dimethyl-4′-pentenyl)-morpholine.

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(13) Henry and Dehn, ref. 11, reported b.p. 127° (26 mm.) but did not record analytical data for this nitrile.

(14) It may be noted that when this nitrile is subjected to treatment with inorganic acids, under conditions which ordinarily effect hydrolysis, it decomposes slowly with evolution of hydrogen cyanide. None of the anticipated amide or amino acid could be isolated, although a small amount of the nitrile was recovered.

(15) Henry and Dehn, ref. 12, reported b.p. 123–125° (21 mm.).

TABLE III

PRODUCTS FORMED FROM α-METHYL-4-MORPHOLINEACETONITRILE AND GRIGNARD REAGENTS

Grignard reagent R-Mg-X R =	Product $O(CH_2CH_2)_2N$-R, R =	B.p., °C.	Mm.	Yield, %	$n^{25}D$	d^{25}_4	Molecular refraction Summation	Molecular refraction Calcd.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Neut. equiv. Calcd.	Neut. equiv. Found
$-CH_3$	$-CH(CH_3)_2$	154.0–155.5	743	42	1.4450	0.9127	37.91	37.82	65.07	64.84	11.70	11.96	129	130
$-C_2H_5$	$-CH(CH_3)C_2H_5$	176–177	745	53	1.4461	.9058	42.53	42.17	67.09	67.37	11.97	12.24	143	145
$-C_3H_7$	$-CH(CH_3)C_3H_7$	193–194	744	57	1.4475	.8982	47.15	46.82	68.74	69.02	12.18	12.38	157	160
$-CH(CH_3)_2$	$-CH(CH_3)CH(CH_3)_2$	192–193	745	31	1.4466	.8962	47.15	46.85	68.74	68.64	12.18	12.34	157	160
$-C_4H_9$	$-CH(CH_3)C_4H_9$	83	7	67	1.4498	.8926	51.76	51.54	70.12	69.94	12.36	12.33	171	173
$-CH(CH_3)C_2H_5$	$-CH(CH_3)CH(CH_3)C_2H_5$	109–110	31	17	1.4635	.9080	51.76	51.03	70.12	69.99	12.36	12.40	171	175
$-CH_2CH(CH_3)_2$	$-CH(CH_3)CH_2CH(CH_3)_2$	104.0–104.5	30	36	1.4469	.8908	51.76	51.36	70.12	70.15	12.36	12.43	171	175
$-C(CH_3)_3$	$-C_2H_5$[b]	138–139	752	47	1.4391	.9103	33.29	33.20	62.57	62.44	11.38	11.68		
$-C(CH_3)_2C_2H_5$	$-C_2H_5$			18	1.4394									
$-CH_2CH{=}CH_2$	$-CH(CH_3)C({=}NH)(CH_2CH{=}CH_2)$[c]			68					65.89	65.51	9.95	10.13	182	368
$-C_6H_5$	$-CH(CH_3)C_6H_5$[d]	113–114	5	77	1.5273	1.023	57.40	57.49	75.35	75.44	8.96	8.89	191	194
$-CH_2C_6H_5$	$-CH(CH_3)COCH_2C_6H_5$[e]	155–156	3	52	1.5250	1.070	66.64	66.84	72.07	72.18	8.21	8.39	233	235
$-CH(CH_3)C_6H_5$	$-CH(CH_3)CH(CH_3)C_6H_5$	127–129	4	59	1.5187	1.000	66.63	66.52	76.67	76.26	9.65	9.84	219	222
$-CH_2C_6H_4(C_2H_5\text{-}p)$	$-CH(CH_3)CH_2C_6H_4C_2H_5\text{-}p$	135–137	2	17	1.5201	0.9943	71.25	71.36	75.45	75.76	9.91	9.89	231	235
$-CH_2C_6H_4(C_2H_5\text{-}p)$	$-CH(CH_3)COCH_2C_6H_4C_2H_5\text{-}p$[f]	160–161	2	32	1.5210	1.043	75.88	76.26	73.52	73.15	8.87	9.11	261	264
$-C_6H_4CH(CH_3)_2\text{-}p$	$-CH(CH_3)CH_2C_6H_4CH(CH_3)\text{-}p$	145–147	2	25	1.5164	0.9825	75.87	76.09	77.68	77.79	10.18	10.30	247	251
$-C_6H_4CH(CH_3)_2\text{-}p$	$-CH(CH_3)COCH_2C_6H_4CH(CH_3)_2$[g]	174–175	3	15	1.5166	1.032	80.50	80.66	74.14	73.99	9.15	9.45	275	279

[a] This amine was prepared also by heating 0.25 mole of morpholine and 0.5 mole of isopropyl bromide on a steam-bath for 18 hr. After filtration from morpholine hydrobromide, fractionation of the filtrate gave 4-(methylethyl)-morpholine (22% yield), b.p. 155–156° (745 mm.), $n^{25}D$ 1.4450, d^{25}_4 0.9110, *MR* calcd. 37.74; picrate, m.p. 187–189°, m.p. not depressed by admixture of picrate of the amine resultant from the Grignard reaction. [b] L. Knorr [*Ann.*, **301,** 14 (1898)] reported b.p. 138–139° (751 mm.), d^{20}_4 0.8996, $n^{20}D$ 1.4400. H. T. Clarke [*J. Chem. Soc.*, **101,** 1808 (1912)] recorded b.p. 138–139°, d^{20}_4 0.9115. [c] This material did not distil at 150° under 1 mm. pressure. *Anal.* Calcd. for $(C_{10}H_{18}N_2O)_2$: mol. wt., 364; C, 65.89; H, 9.95. Found: mol. wt., 366; C, 65.40; H, 10.21. [d] M. T. Leffler and E. H. Volwiler [THIS JOURNAL, **60,** 896 (1938)] reported preparation of the hydrochloride of this compound, m.p. 211–212°. [e] The ketone yielded a semicarbazone, m.p. 158–159°. *Anal.* Calcd. for $C_{15}H_{22}N_4O_2$: N, 19.30. Found: N, 19.36. [f] The semicarbazone formed readily, softening temp. 59°. *Anal.* Calcd. for $C_{17}H_{26}N_4O_2$: N, 17.60. Found: N, 17.81. [g] *Anal.* Calcd. for $C_{23}H_{28}N_4O_9$ (picrate): N, 8.99. Found: N, 9.10.

TABLE IV

PRODUCTS FORMED FROM α-METHYL-4-MORPHOLINEACETONITRILE AND ORGANOLITHIUM REAGENTS

Reagent RLi, R =	Product $O(CH_2CH_2)_2NCH(CH_3)COR$, R′ =	B.p., °C.	Mm.	Yield, %	$n^{20}D$	d^{20}_4	Molecular refraction Summation	Molecular refraction Calcd.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
$-(CH_2)_2CH_3$	$-(CH_2)_3CH_3$[a]	122–124	7	65	1.4589	0.9686	56.39	56.24	66.24	66.12	10.62	10.64
$-CH(CH_3)C_2H_5$	$-CH(CH_3)C_2H_5$[b]	113–114	6	48	1.4600	.9753	56.39	55.96	66.24	66.08	10.62	10.59
$-C_6H_5$	$-C_6H_5$[c]	162–163	9	58	1.5390							

[a] Semicarbazone, m.p. 127–128°; picrate, m.p. 127.5–129.0°. Calcd. for $C_{12}H_{24}N_4O_2$: N, 21.86. Found: N, 21.91. [b] Semicarbazone, m.p. 174–176°. Calcd. for $C_{12}H_{24}N_4O_2$: N, 21.86. Found: N, 21.98. [c] Semicarbazone, m.p. 205–206°; hydrochloride, m.p. 238.5–240.0° dec.; H. R. Henze and W. C. Craig [*J. Org. Chem.*, **10,** 2 (1945)] reported for this compound: $n^{25}D$ 1.5393; semicarbazone, m.p. 206–207°; hydrochloride, m.p. 239–240°.

TABLE V

HYDANTOINS OBTAINED FROM CERTAIN MORPHOLINYL KETONES

Ketone $OC_4H_8N-CH(CH_3)COR$, R =	5-R'-5, R' =	Hydantoin R =	Yield, %	Nitrogen, % Calcd.	Found
$-CH_2C_6H_5$	H	$-CH_2C_6H_5$	189–190[a]	14.73	14.78
$-CH_2C_6H_4C_2H_5$-*p*	H	$-CH_2C_6H_4C_2H_5$-*p*	177–178	12.86	12.98
$-CH_2C_6H_4CH(CH_3)_2$-*p*	H	$-CH_2C_6H_4CH(CH_3)_2$-*p*	186–187	12.12	12.15
$-CH_2CH_2CH_2CH_3$	C_4H_9	$-CH(CH_3)NC_4H_8O$	218–220 d.	15.72	15.70

[a] H. T. Bucherer and V. A. Lieb [*J. prakt. Chem.*, [2] **141,** 5 (1934)] reported m.p. 190°. The m.p. of the product here reported was not depressed when mixed with an authentic sample of 5-benzylhydantoin.

Anal. Calcd. for $C_{11}H_{20}N_2O$: C, 67.30; H, 10.27; N, 14.27; mol. wt., 196.3. Found: C, 67.29; H, 10.62; N, 14.38; mol. wt. (ebulliometric), 710.

Interaction of Organolithium Reagents with α-Methyl-4-morpholineacetonitrile.—Three organolithium compounds (*n*-butyl, *sec*-butyl and phenyl) were allowed to react with this substituted nitrile in 0.15:0.5 mole ratio; hydrolysis was accomplished by the use of 50 ml. of water. The ether layer was separated and made acidic by addition of hydrochloric acid (6 *N*). After standing for 15 min., sodium carbonate was added until the aqueous phase was alkaline, then the ether layer was recovered, dried over anhydrous sodium sulfate and fractionated. In all three cases, the sole product was a ketone; certain properties of the latter are collected in Table IV.

Conversion of α-(4-Morpholinyl)-ethyl Ketones into Hydantoins.—An attempt was made to convert certain of these ketones with potassium cyanide and ammonium carbonate. After about 12 hr., the reaction mixture was concentrated to about one-third of its original volume and was acidified to *p*H 7 to precipitate the hydantoin. Purification was achieved through re-solution in alkali, with subsequent acidification, and by crystallization from ethyl alcohol. The formulas and certain physical properties of the hydantoins produced from these ketones are listed in Table V.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY]

Stereochemistry of the Primary Carbon. VIII. Acetolysis of Optically Active 1-Butyl-1-*d* *p*-Nitrobenzenesulfonate[1-3]

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The reaction of 1-butyl-1-*d* *p*-nitrobenzenesulfonate with acetic acid at 114° gives butyl-1-*d* acetate with 85% net inversion of configuration (15% racemization). The ester is shown to be optically stable to the reaction conditions; consequently, a primary carbonium ion or its solvated equivalent is demonstrated to be involved to a significant extent. Addition of nitrobenzene or dioxane but not *o*-dichlorobenzene to the solvent causes a marked increase in the amount of racemization. These results are explained in terms of "covalently solvated" carbonium ions.

Previous results[5] on the acetolysis and formolysis of optically active 1-butyl-1-*d* brosylate demonstrated that the solvolyses proceeded with 96 ± 8% and 98 ± 5%, respectively, of net inversion of configuration. The relatively large experimental uncertainties were due to systematic and nonsystematic errors associated with the polarimetric measurement in narrow bore tubes of the small quantities of deuterated materials available at that time. With the preparation of a relatively large quantity of optically active 1-butanol-1-*d*[6] (I) a more extensive and precise investigation of the stereochemistry of solvolysis reactions of primary compounds was undertaken.

The optically active alcohol I was converted to the *p*-nitrobenzenesulfonate II which had a higher melting point than the brosylate and which could be purified more readily by crystallization. In the solvolysis experiments, it is obviously important to use sulfonate esters free from alcohol, for the presence of such alcohol would give rise to a corresponding amount of product ester of retained configuration. A 0.3 *M* solution of II in acetic acid was maintained at 114.4° for 24 hr. and produced 1-butyl-1-*d* acetate (III) having an optical rotation of $\alpha^{25}D$ −0.171 ± 0.003° (*l* 2). III prepared directly from I with acetyl chloride and pyridine had $\alpha^{25}D$ +0.200 ± 0.003° (*l* 2); therefore, the acetolysis product shows 85 ± 2% net inversion of configuration. Optically active III was maintained in acetic acid 0.45 *M* in *p*-toluenesulfonic acid for 24 hr. at 114.4°. It was recovered with 98 ± 10% of retention of its optical activity. Racemization of III under these conditions is undoubtedly acid catalyzed. At the completion of the solvolysis reaction of II, the medium is only 0.3 *M* in strong acid; hence, III produced in the solvolysis reaction could have suffered only 1 ± 7% racemization by an acid-catalyzed reaction after its formation. In similar solvolyses described below, II recovered from a partial solvolysis was found to have essentially no loss in optical activity. Thus, at least part of the 15% racemization described above is due neither to racemization of the starting II nor of the product III but must be a property of the solvolytic displacement reaction itself. The demonstration of racemization is an accepted and sensitive criterion for the production of symmetrically solvated carbonium ions in solvolytic reactions. The present results demonstrate unequivocally the

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[1] Paper VII, THIS JOURNAL, **79**, 2893 (1957).

[2] Taken from the Ph.D. dissertation of W.D.S., June, 1956.

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[4] General Electric Fellow, 1955–1956.

[5] A. Streitwieser, Jr., THIS JOURNAL, **77**, 1117 (1955).

[6] A. Streitwieser, Jr., and W. D. Schaeffer, *ibid.*, **78**, 5596 (1956).