additional gas chromatography on Poropak Q columns (at 230°). Mass spectral analysis of the mixed alcohol fraction gave ions consistent with the structures of the two components, thus ions at m/e 85 $(M - CH_3)^+$, 59 $(C_3H_7O)^+$, 43 $(C_3H_7)^+$, and 31 $(CH_3O)^+$ associated with 2-methylpent-4-en-2-ol and ions at 87 $(M - CH_3)^+$, 69 $(C_5H_9)^+$, 59 $(C_3H_7O)^+$, 45 $(C_2H_5O)^+$, 43 $(C_3H_7)^+$, and 31 $(CH_3O)^+$ associated with 2-methylpentan-2-ol.

Mass spectra of the reference alcohols (Aldrich Chemical Co. Inc., Milwaukee, Wis.) are given for comparison (with per cents in parentheses): 2-methylpent-4-en-2-ol m/e 85 (5), 83 (3), 59 (100), 55 (8), 43 (82), 41 (42), 39 (55), 31 (35), 29 (9), 27 (24); 2-methylpentan-2-ol 87 (21), 85 (3), 69 (7), 59 (94), 45 (37), 43 (100), 41 (30), 39 (28), 31 (20), 29 (15), 27 (38).

Registry No.—Cholesterol, 57-88-5; **3a**, 23652-97-3; **3b**, 23652-98-4; **4a**, 2140-46-7; **4c**, 10525-22-1; **5a**, 23653-01-2; **5b**, 23653-02-3; **6a**, 516-72-3; **6b**, 7484-20-0; **7a**, 5255-15-2; **7b**, 23653-06-7; **8a**, 2862-58-0; **8b**, 3090-79-7; **9a**, 901-56-4; **9b**, 1913-47-9; **10a**, 145-13-1; **10b**, 1778-02-5; **11a**, 1476-64-8; **11b**, 13067-44-2; **12a**, 521-17-5; **12b**, 2099-26-5; **13a**, 53-43-0; **13b**, 853-23-6.

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A Study of Amine-Catalyzed Epimerization of 2β-Methylcholestan-3-one[1]

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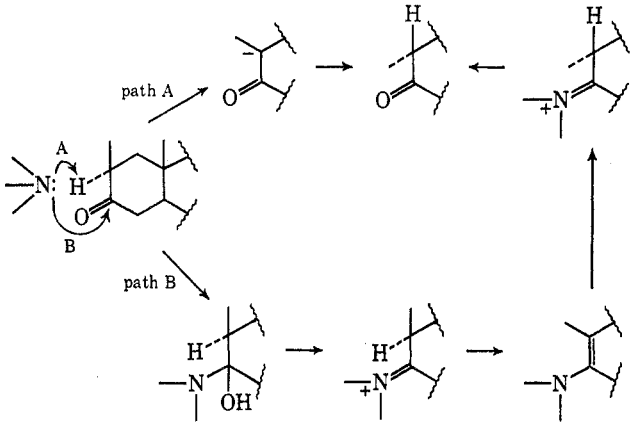
The epimerization of 2β-methylcholestan-3-one (1) to 2α-methylcholestan-3-one (2) in dioxane solution at 45° in the presence of an excess of various amines has been followed by optical rotation measurements. The results contrast with those previously found for the conversions **3** → **5** and **4** → **5**; piperidine was about as catalytically effective as pyrrolidine and hexamethylenimine, and the unhindered tertiary amine quinuclidine was only slightly less effective. These observations suggest that nucleophilic catalysis is less important in the conversion **1** → **2**, presumably because the 2β-methyl group inhibits enamine formation.

The primary question one seeks to answer in any investigation of the mechanism of an amine-catalyzed carbonyl compound reaction is whether the amine acts as a general base to remove a proton directly (as in path A below), or as a nucleophile to form an enamine which can react analogously to the enolate anion and then be reconverted to the carbonyl compound by hydrolysis (path B). Although the latter pathway was proposed many years ago,[2,3] systematic studies of this type of catalysis have appeared only within the last decade.[4-7] Most of these studies were presumably inspired by the increasing evidence of nucleophilic catalysis by amines in certain biochemical reactions.[8]

Much of this evidence comes from trapping substrate–enzyme imine intermediates by borohydride reduction.[9] However, these experiments do not prove that the imine is necessarily an intermediate and do not provide quantitative information about catalytic effectiveness. Kinetic investigations of model systems[2-7] designed to elucidate these matters by comparison of the catalytic rate constants for different amines have largely relied on relative inactivity of tertiary amines[3] and other deviations from the Brønsted catalysis law[6] as criteria for nucleophilic catalysis.



This paper describes our investigation of the epimerization of 2β-methylcholestan-3-one (1) to 2α-methylcholestan-3-one (2). This reaction was selected in order to provide a contrast to our previous study[10] of the aldol condensation–ketol dehydration sequence **3** → **4** → **5**, in which nucleophilic catalysis was inferred not only from the relative inefficiency of tertiary amines, but also from a comparison of the rates of reactions catalyzed by the three cyclic secondary amines pyrrolidine, piperidine, and hexamethylenimine. These amines are of similar base strength and steric bulk, and their kinetic basicity with respect to a given weak car-

(1) This research was presented at the Fifth Caribbean Chemical Symposium, University of the West Indies, Cave Hill, Barbados, Jan 1969.

(2) K. J. Pedersen, *J. Phys. Chem.* **38**, 559 (1934).

(3) F. H. Westheimer and H. Cohen, *J. Amer. Chem. Soc.*, **60**, 90 (1938); F. H. Westheimer, *Ann. N. Y. Acad. Sci.*, **39**, 401 (1940); F. H. Westheimer and W. A. Jones, *J. Amer. Chem. Soc.*, **63**, 3283 (1941).

(4) J. Hine, F. E. Rogers, and R. E. Notari, *ibid.*, **90**, 3279 (1968), and previous papers in this series.

(5) L. P. Koshechkina, E. A. Shilov, and A. A. Yasnikov, *Ukr. Khim. Zh.*, **35**, 55 (1969), and previous papers in this series. These extensive reports by Yasnikov and coworkers contain many arguable mechanistic suggestions. Discussion of these papers has been promised by Hine [J. Hine, B. C. Menon, J. H. Jensen, and J. Mulders, *J. Amer. Chem. Soc.*, **88**, 3367 (1966)].

(6) M. L. Bender and A. Williams, *ibid.*, **88**, 2502 (1966).

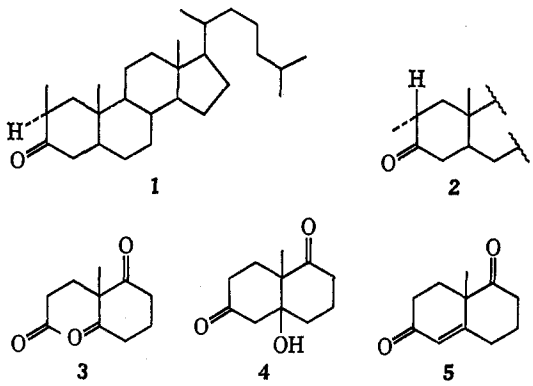
(7) G. E. Lienhard and T-C. Wang, *ibid.*, **90**, 3781 (1968).

(8) See W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, Chapter 2, especially pp 116–146, for a review and specific references.

(9) For example: (a) S. Warren, B. Zerner, and F. H. Westheimer, *Biochemistry*, **5**, 817 (1966); (b) J. C. Speck, Jr., P. T. Rowley, and B. L. Horecker, *J. Amer. Chem. Soc.*, **85**, 1012 (1963), and B. L. Horecker, T. Cheng, E. Grazi, C. Y. Lai, P. Rowley, and O. Tchola, *Fed. Proc.*, **21**, 1023 (1962); (c) D. Portsmouth, A. C. Stoolmiller, and R. H. Abeles, *J. Biol. Chem.*, **242**, 2751 (1967).

(10) T. A. Spencer, H. S. Neel, T. W. Flechtner, and R. A. Zayle, *Tetrahedron Lett.*, 3889 (1965).

bon acid (such as a ketone) should be similar. They differ, however, in the ease with which they will form enamines.[11] It is less easy to make an atom of a six-membered ring trigonal than an atom of a five- or seven-membered ring, as has been shown in several differing kinds of reactions.[12] Formation of an iminium ion en route to an enamine (as in path B) will thus be least favorable with a six-membered-ring catalyst, and piperidine would be expected to be the least effective catalyst of the three amines, as observed in our earlier studies.[10]



However, before a conclusion was reached that a minimum in rate constant for piperidine is diagnostic of nucleophilic catalysis, it was desirable to show that a reaction which would *not* be expected to be nucleophilically catalyzed did not show such a minimum. A reaction involving proton abstraction from the 2′ position of a carbonyl compound bearing a 2 substituent seemed appropriate for this study, since a sizable 2 substituent will tend to impede nucleophilic addition to the carbonyl group more than it will proton abstraction.[13]

In a study very relevant to our choice of a system, Malhotra and Johnson have presented convincing evidence that the proton in the 2′ position of 2-methylcyclohexanone was not detectably removed during treatment with pyrrolidine which effected substantial deuterium incorporation at the 6 positions.[14] Although such data are not available for other amines, and despite the fact that Gurowitz has shown[15] that amines other than pyrrolidine do not to the same degree avoid formation of 2-methyl-$\Delta^{1,2}$-enamines, use of a 2-methyl ketone as substrate should *at least* eliminate the previously observed[10] unusually effective catalysis by pyrrolidine. We therefore chose to study the epimerization of **1**, which is a relatively simple reaction involving in essence only removal of the 2α proton and reprotonation from the β side.[16]

The same seven amines were used as in the previous studies:[10] the three discussed above, plus morpholine (similar in structure, but a weaker base), *n*-butylamine (a primary amine), triethylamine (a tertiary amine), and quinuclidine (an unhindered tertiary amine). The same solvent, dioxane, was also chosen. This is convenient from the standpoint of solubility of substrate, but has the disadvantage that the relative base strengths of the amines are uncertain. It is not safe to assume that the relationships among pK_a's determined in water will hold in other solvents.[17] It would be meaningless to attempt to construct a Brønsted plot, for example, unless the base strengths of the amines in dioxane were determined. However, the similarity in structure of many of the amines used in this study probably minimizes differences among them in the dependence of base strength upon medium.

The required substrate, 2β-methylcholestan-3-one (**1**), can be readily prepared in large quantity by a synthetic sequence developed by Nickon and DiGiorgio.[18] The epimerization of **1** to **2** was followed by measurement of the accompanying change in optical rotation. Solutions of **1** in dioxane were indefinitely stable without added amine. Relatively large concentrations of amine were necessary to effect the conversion of **1** to **2** at conveniently measurable rates, even at 45°. In the presence of amines the optical rotation of solutions of **1**, measured at 365 mμ (where the difference in rotation between **1** and **2** is much larger than at 589 mμ), decreased until it corresponded to a mixture of *ca.* 90% **2** and 10% **1**, in those cases where the reaction was followed that far. Evaporation of such a product mixture (from a pyrrolidine-catalyzed epimerization) afforded 89% crude and 22% pure **2**.

Good pseudo-first-order kinetic plots were obtained using the observed final rotation or the value calculated for 90% epimerization in reactions which were too slow to be followed to completion. A typical plot is shown in Figure 1. It was not determined whether the approximately 9:1 mixture of **2** and **1** represented an equilibrium mixture.[19] If this were the case, the rate constants discussed below are the sum of the rate for **1** → **2** and the smaller rate for **2** → **1**.[20] In view of the uncertainties involved and the relatively small potential correction for the rate of **2** → **1**, no adjustment of

(11) Quantitative comparisons of the facility of various amines for enamine formation are lacking, but the assertion that pyrrolidine, piperidine, and hexamethylenimine differ is substantiated by the discussion and experimental procedures given by (a) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963); (b) A. A. Brizzolara, Jr., Ph.D. Dissertation, Columbia University, 1960.

(12) H. C. Brown, *J. Org. Chem.*, **22**, 439 (1957); H. C. Brown, *J. Chem. Soc.*, 1248 (1956); H. C. Brown, J. H. Brewster, and H. Schecter, *J. Amer. Chem. Soc.*, **76**, 467 (1954). These ideas were first applied to enamine formation by G. Stork, *et al.*[11a]

(13) (a) W. P. Jencks, ref 8, p 96; (b) also, it can be inferred from experimental procedures given in ref 11a and 11b that the overall rate of enamine formation from 2-methylcyclohexanone is slower than from cyclohexanone.

(14) S. K. Malhotra and F. Johnson, *Tetrahedron Lett.*, 4027 (1965).

(15) W. D. Gurowitz and M. A. Joseph, *ibid.*, 4433 (1965).

(16) It is assumed in this study that all amines have approximately the same *ratio* for α *vs.* β deprotonation or reprotonation of a given species. In this connection it should also be noted that **1** probably has ring A predominantly in the twist conformation [K. L. Williamson and W. S. Johnson, *J. Amer. Chem. Soc.*, **83**, 4623 (1961)], which is favorable for removal of the 2α proton *via* the stereoelectronically favored pathway [see ref 14 and F. Johnson, *Chem. Rev.*, **68**, 375 (1968), for pertinent discussions of the subtleties of a very closely analogous situation].

(17) See F. M. Menger and J. H. Smith, *J. Amer. Chem. Soc.*, **91**, 5346 (1969), for considertion of the importance of the effect of solvent on base strength in kinetic studies.

(18) J. DiGiorgio, Ph.D. Dissertation, Johns Hopkins University, 1960.

(19) A. Nickon and J. DiGiorgio (ref 18) have determined that the equilibrium composition of these epimers in chloroform containing hydrogen chloride at room temperature is *ca.* 96% **2** and 4% **1**. Thus a 9:1 mixture is not unreasonable for the equilibrium composition in dioxane containing amines at 45°. However, experimental determination of the equilibrium composition of **1** and **2** under these conditions might not be straightforward owing to the presence at equilibrium of some enamine or carbinolamine species of different rotation.

(20) For discussions of the kinetics of first-order reversible reactions, and derivation of the expression $k_{obsd} = k_{forward} + k_{reverse}$, see W. P. Jencks, ref 8, p 586; A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, 2nd ed, New York, N. Y., 1961, p 185.

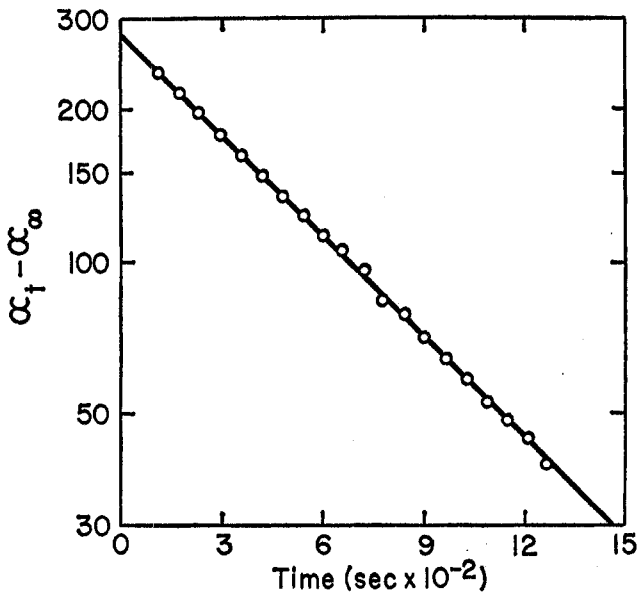


Figure 1.—Semilogarithmic plot of the change in optical rotation at 365 mμ of a solution of 2β-methylcholestan-3-one (1) (2.3×10^{-2} *M*) in dioxane containing pyrrolidine (5.7 *M*) at 45°.

the observed rates has been made in the following discussion.

In Table I are shown the specific second-order rate constants (k_2) obtained by dividing k_{obsd} by the appropriate amine concentration. In the case of pyrrolidine the concentration of amine was varied 60-fold from 0.1 to 6.0 *M*. Over this concentration range k_2 for pyrrolidine increased about threefold. Although from our data we cannot exclude a small incursion of a catalytic term greater than first order in amine, it seems reasonable that this increase is due instead to the changing nature of the medium, which contains *ca.* 1% amine at 0.1 *M*, as opposed to *ca.* 50% amine at 6 *M*.

TABLE I

EFFECTIVENESS OF AMINES IN CATALYZING THE EPIMERIZATION OF 1 TO 2 IN DIOXANE SOLUTION AT 45°

Amine	Structure	pK_a[a]	Amine concn, *M*	$k_2 \times 10^5$ (M^{-1} sec^{-1})
Pyrrolidine	$(CH_2)_4NH$	11.32	5.7	25
Piperidine	$(CH_2)_5NH$	11.20	6.6	10
Hexamethylenimine	$(CH_2)_6NH$	11.10	5.3	4.4
n-Butylamine	$CH_3CH_2CH_2CH_2NH$	10.61	7.2	11
Morpholine	$O(CH_2CH_2)_2NH$	8.36	6.2	0.44
Quinuclidine	$HC(CH_2CH_2)_3N$	10.95	0.25	1.0
Triethylamine	$(CH_3CH_2)_3N$	10.75	3.5	0.01

[a] The pK_a's are literature values for aqueous solution at 25°.

Accordingly, it is important to compare rate constants obtained at approximately the same concentration of catalyst. This is done in Table I with the exception of quinuclidine, which was run only at a much lower amine concentration. The value of k_2 for quinuclidine thus is almost certainly somewhat lower than it should be for comparison with the other rate constants.

In Table II these relative rates are compared with those previously reported for the conversions **3** → **5** and **4** → **5**.[10] Clearly different trends appear. There is less difference among the amines in the epimerization of

TABLE II

COMPARISON OF AMINE CATALYSIS OF CONVERSIONS **1** → **2**, **3** → **5**, AND **4** → **5**

Amine	**1** → **2**, k_{rel}	**3** → **5**,[a] k_{rel}	**4** → **5**,[a] k_{rel}
Pyrrolidine	2.5	120	1000
Piperidine	1.0	1	1
Hexamethylenimine	0.44	5	15
n-Butylamine	1.1	50	50
Morpholine	0.044	0.4	1
Quinuclidine	0.1	0.03	0.02
Triethylamine	0.001	0.005	0.02

[a] See ref 2.

1. Quinuclidine, the unhindered tertiary amine, does not differ markedly from the secondary and primary amines in catalytic effectiveness. The low epimerization rate with triethylamine can be ascribed to steric hindrance to proton abstraction.[21] Most significantly for our purposes, there is no minimum in the rate of epimerization of **1** with piperidine, compared with pyrrolidine and hexamethylenimine. The rate constants for these three homologs simply decrease slightly as the ring becomes larger.

These contrasts between amine catalysis of **1** → **2** and the earlier results[10] can be explained, as discussed above, on the basis of steric hindrance to the formation of the appropriate enamine from **1**, making nucleophilic catalysis less important relative to direct proton abstraction. These results lend validity to the use of a comparison of catalytic effectiveness *vs.* amine ring size as a criterion for nucleophilic catalysis. Further studies of amine catalysis, using this and other criteria, are in progress.[22]

Experimental Section[23]

2β-Methylcholestan-3-one (1).—The preparation of 2β-methylcholestan-3-one (**1**) was carried out by the procedures described by DiGiorgio.[18] Cholestan-3-one was converted to 2-hydroxymethylenecholestan-3-one, which was reduced with lithium aluminum hydride to 2-methylenecholestan-3β-ol (48%). Rearrangement of 2-methylenecholestan-3β-ol in ethyl acetate solution in the presence of palladium on carbon in a hydrogen atmosphere afforded 96% 2β-methylcholestan-3-one (**1**), mp 83–86°. When the reaction was run without hydrogen the rearrangement did not take place. Recrystallization of **1** from ether–methanol raised this to mp 99.5–100° (lit.[18] mp 98–99°; lit.[24] mp 96–97°): ir (KBr) 5.83 μ; $[\alpha]_{365}^{\text{dioxane, 45}}$ +470°; $[\alpha]_{578}^{\text{dioxane, 45}}$ +118°; (lit.[18] $[\alpha]_{589}^{\text{CHCl}_3,25}$ +122°; lit.[24] $[\alpha]_{589}^{\text{CHCl}_3,25}$ +86°).

2α-Methylcholestan-3-one (2).—Preparation of **2** was accomplished by epimerization of **1**, both with sulfuric acid and with pyrrolidine as catalyst. A solution of 0.566 g (1.4×10^{-3} mol) of **1** in a mixture of 45 ml of 95% ethanol and 1.5 ml of 20% aqueous sulfuric acid was refluxed for 4 hr. The mixture was partitioned between ether and water, and the ether layer was dried and evaporated to afford 0.426 g of **2**, mp 108–112°. Repeated recrystallization from methanol raised this to mp 116.5–117° (lit.[18] mp 119.5–120.5°; lit.[24] mp 119–120°): ir

(21) For a general discussion of steric hindrance to general base catalysis and references, see (a) F. Covitz and F. H. Westheimer, *J. Amer. Chem. Soc.*, **85**, 1773 (1963). For examples of relative ineffectiveness of triethylamine in reactions involving abstraction of a weakly acidic proton, see (a) J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *ibid.*, **87**, 5050 (1965); (b) L. R. Fedor, *ibid.*, **89**, 4479 (1967); (c) J. Weinstock, R. G. Pearson, and F. G. Bordwell, *ibid.*, **78**, 3473 (1956).

(22) See, *e.g.*, G. T. Sinner and T. A. Spencer, Abstract P-116, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968.

(23) Melting points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 137 spectrophotometer. Specific rotations listed for pure substances are the average value from two separate determinations.

(24) Y. Mazur and F. Sondheimer, *J. Amer. Chem. Soc.*, **80**, 5220 (1949).

(KBr) 5.84 μ; $[\alpha]_{365}^{\text{dioxane, 45}}$ +118°; $[\alpha]_{578}^{\text{dioxane, 45}}$ +28° (lit.[18] $[\alpha]_{589}^{\text{CHCl}_3, 25}$ +36°; lit.[24] $[\alpha]_{589}^{\text{CHCl}_3, 25}$ +32°). This material showed one spot upon tlc on silica gel using 3:2 ether–benzene.

Preparative epimerization of **2** was also accomplished by allowing a mixture of 0.083 g (2.1×10^{-4} mol) of **1**, 3.62 g (0.051 mol) of pyrrolidine, and 6.2 ml of dioxane to stand at 45°. After 60 min (*ca.* $8 \times t_{1/2}$), the optical rotation corresponded to a mixture of 89% **2** and 11% **1**. No further change in rotation was observed for 54 hr. The mixture was evaporated to dryness *in vacuo*, affording 0.077 g (89%) of yellowish solid, mp 92–103°. Three recrystallizations from methanol afforded 0.019 g (22%) of **2**, mp 115–116.5°, which had an ir spectrum identical with that of the material prepared by acid-catalyzed epimerization.

Other Materials.—All amines except quinuclidine were purchased from the Aldrich Chemical Company and were redistilled twice from barium oxide, the last time directly before use. Purity of each amine was checked by vpc once, but not routinely. Quinuclidine was prepared by reduction of 3-quinuclidone (derived from Aldrich 3-quinuclidone hydrochloride) by the Huang-Minlon procedure,[25] with a careful work-up to avoid evaporation of the product, and was purified by sublimation at aspirator pressure at 70°. The sublimed material had mp 155–158° (sealed tube) (lit.[26] mp 158°). Matheson Coleman and Bell spectroquality reagent dioxane was used as supplied from freshly opened bottles.

Kinetic Measurements.—The conversion **1** → **2** was monitored by following the change in optical rotation of solution of **1** in dioxane on a Perkin-Elmer Model 141 automatic digital readout polarimeter. Temperature was controlled by a Haake water circulating thermostating unit at 45.0°. The polarimeter cell used was 1 decimeter in length with a volume of 0.85 ml. Polarized light of 365-mμ wavelength was chosen because the difference between the rotations of **1** and **2** is greater at this wavelength than at the other, longer wavelengths available with the polarimeter.

Solutions of **1** in dioxane at 45° showed no change in rotation on standing for several hours. In many cases, mixing of amine with the dioxane solution of **1** was done at room temperature and not on materials preheated to 45°, but the mixtures were quickly inserted into the thermostated polarimeter. Good pseudo-first-order kinetic plots were obtained in all cases, for over 80% reaction in some cases. Many of the reactions were too slow to be followed conveniently to completion, and kinetic data were obtained for as little as 20% conversion.

The linear pseudo-first-order plots of log $(\alpha_t - \alpha_\infty)$ (specific rotation at time t minus specific rotation at the completion of reaction) *vs.* time were used to determine $t_{1/2}$ for the reactions, and k_2, the specific second-order rate constants (in $\text{sec}^{-1}\ M^{-1}$) were calculated by use of the expression $k_2 = k_{\text{obsd}}/[\text{amine}] = 0.693/[t_{1/2}][\text{amine}]$. In those cases where α_∞ was not observed experimentally, it was calculated using the assumption that α_∞ would correspond to 90% conversion of **1** to **2**. This method gave linear pseudo-first-order plots. As noted in the discussion, if the α_∞ at 90% conversion corresponds to the equilibrium composition of **1** and **2** under the prevailing conditions, then the k_2's derived are equal to the sum of the forward and reverse reaction rate constants.[20]

All amines except quinuclidine and triethylamine were run at several concentrations, and gave somewhat larger rate constants at higher amine concentrations as the proportion of amine in the mixture increased.

Acknowledgment.—The authors are indebted to Professor Alex Nickon for providing details of the preparation of **1**. Considerable earlier experimentation by Mr. H. A. Budd, Jr., and Mr. E. J. L. Wasserman on the epimerization of 2β-acetoxycholestan-3-one served both to demonstrate the need for a better substrate and to familiarize us with the techniques used in the optical rotation kinetics study. We are particularly grateful to Professor K. L. Williamson and his colleagues at Mount Holyoke College, who graciously allowed us unlimited access to their polarimeter and afforded patient guidance in its use. Financial support was provided by PHS Research Grant AM11815, from the National Institute of Arthritis and Metabolic Diseases.

Registry No.—**1**, 14528-10-0; **2**, 2097-78-1.

(25) Huang-Minlon, *J. Amer. Chem. Soc.*, **71**, 3301 (1949).
(26) J. Meisenheimer, *Justus Liebigs Ann. Chem.*, **420**, 190 (1920).

The Chemical Synthesis of the 1,2,4-Triazole Nucleosides Related to Uridine, 2′-Deoxyuridine, Thymidine, and Cytidine[1]

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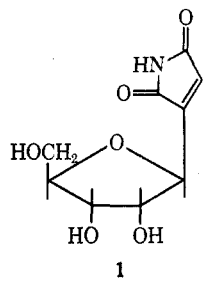
The synthesis of 1-(β-D-ribofuranosyl)urazole (**3**), 1-(2-deoxy-β-D-ribofuranosyl)urazole (**14**), and 1-(2-deoxy-β-D-ribofuranosyl)-2-methylurazole (**13**) has been accomplished *via* the trimethylsilyl derivatives of urazole and 1-methylurazole. The synthesis of the corresponding nucleoside related to cytidine, 3-amino-1-(β-D-ribofuranosyl)-1,2,4-triazolin-5-one (**26**), was accomplished in a lengthy procedure involving 3-bromo-5-nitro-1,2,4-triazole in the fusion process. Evidence in support of the site of glycosylation has been presented. The reaction mechanism involved in the various glycosylation procedures of the 1,2,4-triazole ring has been discussed.

The nucleoside antibiotic showdomycin, isolated from cultures of *Streptomyces showdoensis*,[3] has been shown by these laboratories[4] to possess structure **1**. Another antibiotic, pyrazomycin, has been shown[5] to possess the nucleoside structure **2**. It is thus quite clear that nucleoside derivatives of five-membered heterocyclic rings



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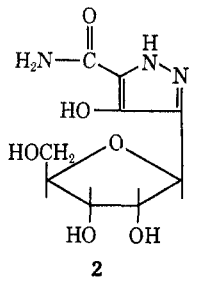

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(1) Supported in part by a NASA Traineeship to J. T. Witkowski.
(2) ICN Nucleic Acid Research Institute, 2727 Campus Drive, Irvine, Calif. 92664.
(3) H. Nishimura, M. Mayama, Y. Komatsu, H. Kato, N. Shimaoka, and Y. Tanaka, *J. Antibiot.*, **17A**, 148 (1964).
(4) K. R. Darnall, L. B. Townsend, and R. K. Robins, *Proc. Nat. Acad. Sci. U. S.*, **57**, 548 (1967).
(5) R. H. Williams, K. Gerzon, M. Hoehn, M. Gorman, and D. C. DeLong, Abstracts, 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, No. MICR 38.