Additional Investigations of the *ortho* Claisen Rearrangement in Pyrimidines[1a]

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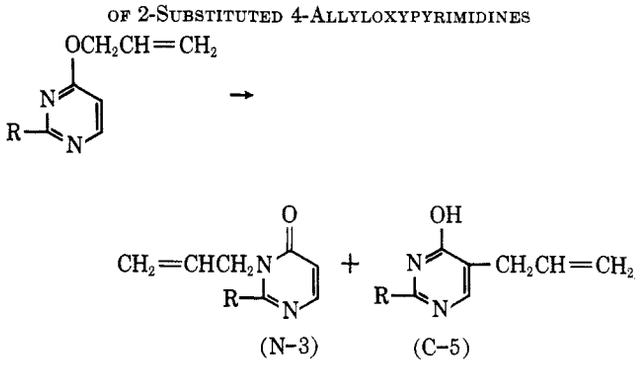
Product distribution studies for the Claisen rearrangement of several 2-substituted 4-allyloxypyrimidines were made under a variety of conditions. Thermal decomposition of products and apparent nucleophilic substitution on the allyl ethers by tertiary amine solvents were found to limit severely the utility of the reaction. 1-Substituted 4-allyloxy-2-pyrimidones give nearly quantitative rearrangement to nitrogen at advanced rates. 2-Substituted 4-allylthiopyrimidines and 2-substituted 4-allylaminopyrimidines do not give Claisen rearrangement products.

The discovery that 2-substituted 4-hydroxy-5-allylpyrimidines were products of the thermal rearrangement of several 2-substituted 4-allyloxypyrimidines was the first observation of a Claisen rearrangement to an *o*-carbon atom while the possibility existed for a competing rearrangement to an *o*-nitrogen atom.[2] This was shown to be a true Claisen rearrangement,[3] and subsequent investigations in this laboratory and elsewhere have since extended the generality of the reaction to the pyridine[4,5] ring system, where it has been demonstrated that the accompanying rearrangement to nitrogen also has the characteristics of the Claisen rearrangement.[4] More recently, analogous examples have been observed with quinolines.[6]

We wish to report the results of a more detailed examination of the scope and limitations of the rearrangement in pyrimidines. Vapor phase chromatography was used to follow product distributions during the rearrangement of the allyl pyrimidinyl ethers listed in Table I. Except for the 2-trifluoromethyl ether, the course of the reaction as a function of time under optimum conditions in N,N-diethyl-*m*-toluidine solvent is illustrated in Figure 1. Limited data were previously reported for some of these compounds.[2,3] 2-Phenyl-4-allyloxypyrimidine, not previously studied, was shown to give both *ortho*-rearrangement products and to be useful synthetically for the preparation of 2-phenyl-4-hydroxy-5-allylpyrimidine. Of interest was the observation that 2-methyl-4-allyloxypyrimidine does rearrange, although the products could not be isolated by convenient classical methods.[2] In contrast, 2-trifluoromethyl-4-allyloxypyrimidine gives no observable *ortho*-rearrangement products. In all cases of successful rearrangement the yield of 5-allyl product was greater than 3-allyl product. The former, however, decomposed more rapidly as was demonstrated by heating authentic samples individually under rearrangement conditions. The observation that 2-trifluoromethyl-4-hydroxy-5-allylpyrimidine decomposed at a rate comparable to the disappearance of the starting ether explains the absence of this isomer in rearrangement mixtures. For the other ethers, a balance between the rate of product formation and decomposition results when about 20–25% of starting material remains. Variations in temperature and ratio of solvent to pyrimidinyl ether had no effect on product distributions.

TABLE I

MAXIMUM YIELD AND RELATIVE RATES OF REARRANGEMENT OF 2-SUBSTITUTED 4-ALLYLOXYPYRIMIDINES



R	Solvent[a]	Max. yield, %[b] N-3	Max. yield, %[b] C-5	$t_{1/2}$, hr.[c] 233°	$t_{1/2}$, hr.[c] 240°	$t_{1/2}$, hr.[c] 250°
CH_3S–	DEMT	19	32	6.1	3.6	2.1
$C_6H_5CH_2S$–	DEMT	14	34	5.7	3.4	0.94
C_6H_5–	DEMT	14	36	15.0	9.4	4.6
CH_3–	DEA[d]	16	25	14.2	8.4	4.3
CF_3–[e]						

[a] DEMT = N,N-diethyl-*m*-toluidine, DEA = N,N-diethylaniline. [b] Yields are given for rearrangements at 240°. Comparable yields are obtained at the other temperatures. Maximum yields are obtained by heating 2–2.5 times the time given for $t_{1/2}$. [c] Time for one-half of the starting material to disappear. [d] DEA was used because DEMT covers the peak for the N-3 isomer during v.p.c. analysis. Otherwise, results for the two solvents were comparable. [e] See explanation in text.

Extensive variations in conditions and solvents, including the use of Lewis acids, were employed in this study in an effort to increase yields or introduce selectivity of product formation. Unlike the considerable effect of solvent on the rearrangement of certain allyl phenyl ethers,[7] the allyl pyrimidinyl ethers decomposed extensively or polymerized. The results clearly showed that tertiary amine solvents are necessary at the high temperatures required to effect rearrangement. The additional use of free-radical inhibitors and the use of an inert atmosphere had no beneficial effect.

The choice of tertiary amine solvent also was limited. When N,N-dimethylaniline was substituted for N,N-diethyl-*m*-toluidine at 240°, all yields were significantly reduced. In each instance (including the trifluoro-

(1) (a) This investigation was supported by the Public Health Service Research Grant No. CA-02857 from the National Cancer Institute. (b) Allied Chemical Corp. Fellow, 1960–1961.

(2) H. J. Minnemeyer, J. A. Egger, J. F. Holland, and H. Tieckelmann, *J. Org. Chem.*, **26**, 4425 (1961).

(3) F. J. Dinan, H. J. Minnemeyer, and H. Tieckelmann, *ibid.*, **28**, 1015 (1963).

(4) F. J. Dinan and H. Tieckelmann, *ibid.*, **29**, 892 (1964).

(5) R. B. Moffett, *ibid.*, **28**, 2885 (1963).

(6) (a) Y. Makisumi, *Tetrahedron Letters*, **No. 39**, 2833 (1964); (b) *J. Org. Chem.*, **30**, 1986 (1965); (c) *ibid.*, **30**, 1989 (1965).

(7) A. T. Shulgin and A. W. Baker, *ibid.*, **28**, 2468 (1963).

methyl ether) the major product, usually representing about 50% of starting material, was N-methyl-N-allylaniline. This originated from solvent and pyrimidinyl ether since it was not formed when individual samples of rearrangement products were heated with solvent under comparable conditions. The 2-benzylthio ether gave N-methyl-N-benzylaniline (47%) as an additional major product. 2-Trifluoromethyl-4-allyloxypyrimidine was exceptional in that it was the only ether studied which reacted significantly with N,N-diethylaniline or N,N-diethyl-*m*-toluidine, giving 2-trifluoromethyl-4-ethoxypyrimidine (33%) as the major reaction product. These compounds were isolated and identified because they were formed in considerable quantity. The isolation and identification of additional components present in smaller amounts was not pursued because of the complexity of the reaction mixtures.

The formation of N-methyl-N-allylaniline might be rationalized on the basis of an SN2′ attack of the amine on the allyl pyrimidinyl ether. Tertiary amines are known to react with allylic systems in this manner.[8] This choice of mechanism is supported by the observation here that the more sterically hindered N,N-diethylaniline and N,N-diethyl-*m*-toluidine do not give corresponding products.[9] On the basis of the available data, mechanisms for the formation of the other observed products remain open to speculation.

It is worth noting that in general the yields of Claisen rearrangement products decrease with the increasing ability of the heteroaromatic nucleus to delocalize a negative charge at oxygen. This generalization reflects in part the increased energy required for rearrangement in heteroaromatic compounds compared with allyl phenyl ethers,[10] and the activation of the heterocycle toward competing reactions. Allyl pyrimidinyl ethers of the type listed in Table I are directly in the region where competing reactions become predominant. Cleaner Claisen rearrangements are observed in nitrogen heterocycles less able to delocalize an incipient charge at oxygen (pyridines[4]), in cases where energy requirements have been decreased through substitution in the allyl group,[3,4] where a naphthalene-like structure (quinolines[6]) has been introduced, or where a combination of these factors are operative.

The relative importance of a change in the electronic structure of the pyrimidine substrate was demonstrated by an examination of the rearrangement of 1-methyl-4-allyloxy-2-pyrimidone (**2**). Although compounds of this type are commonly regarded as aromatic,[11] the presence of the locked lactam structure indicates enhanced double-bond character associated with the carbon–nitrogen bond adjacent to the ether linkage. By analogy to the rearrangement of allyl naphthyl ethers,[10] exclusive rearrangement of the allyl group of **2** to nitrogen might be expected. This is indeed what was observed.

For the study, 2,4-diallyloxypyrimidine (**1**) was prepared from 2,4-dichloropyrimidine, and this in turn

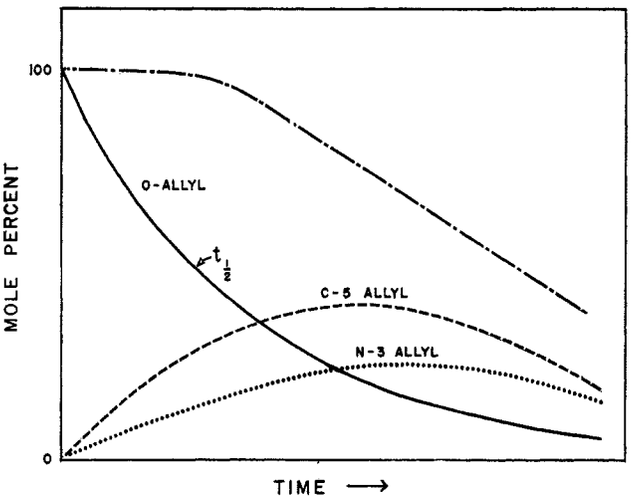
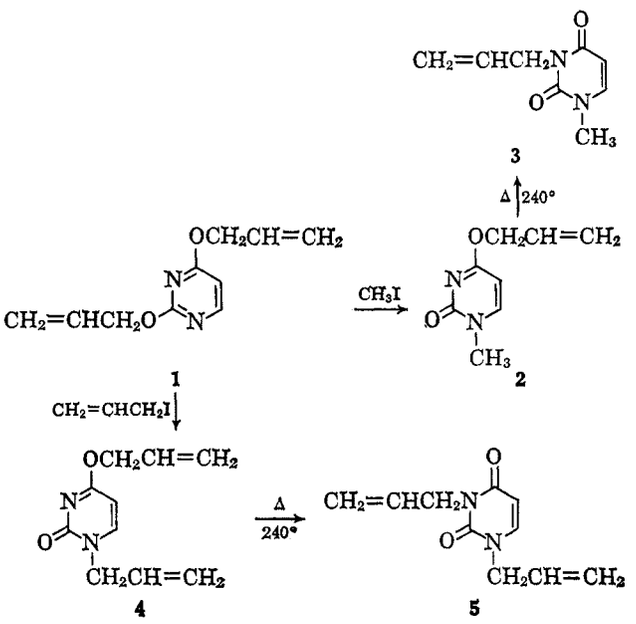


Figure 1.—Typical product distributions during the rearrangement of the allyl pyrimidinyl ethers listed in Table I. The top line represents the sum of starting material and the two major products.

was converted to **2** by treatment with methyl iodide according to the procedure of Hilbert.[12] When **2** was heated without solvent at 240° it rearranged in 90% yield to 1-methyl-3-allyl-2,4-pyrimidinedione (**3**) as indicated by quantitative infrared spectroscopy. Alumina column chromatography confirmed that no other major product was formed. Only 0.38 hr. was required for half of the starting material to rearrange, a rate much more rapid than that observed for any of the 2-substituted 4-allyloxypyrimidines.[13]

Treatment of **1** with allyl iodide gave 1-allyl-4-allyloxy-2-pyrimidone (**4**). When **4** was heated at 240° without solvent, it rearranged at a rate compar-



able with **2** to give 1,3-diallyl-2,4-pyrimidinedione (**5**) in 62% yield after alumina column chromatography. When **1** was heated at 240° without solvent, or with N,N-diethyl-*m*-toluidine, an initial indiscriminant re-

(8) W. G. Young, R. A. Clement, and C. Shih, *J. Am. Chem. Soc.*, **77**, 3061 (1955).

(9) A possible mechanism invoking ion formation in N,N-dimethylaniline is not indicated on the basis that crossover products were not detected in rearrangements conducted in N,N-diethyl-*m*-toluidine.[3]

(10) D. J. Tarbell, *Org. Reactions*, **2**, 1 (1944).

(11) F. Arndt, L. Loewe, and L. Ergener, *Rev. Fac. Sci. Univ. Istanbul*, **A13**, 103 (1948); *Chem. Abstr.*, **43**, 579 (1949).

(12) G. E. Hilbert and T. B. Johnson, *J. Am. Chem. Soc.*, **52**, 2001 (1930).

(13) These results are in close accord with data on allyl N-phenylformimidate, the allyl group of which rearranges about an isolated carbon–nitrogen double bond: R. M. Roberts and F. A. Hussein, *ibid.*, **82**, 1950 (1960).

TABLE II

PHYSICAL PROPERTIES OF 4-ALLYLTHIO- AND 4-ALLYLAMINOPYRIMIDINES

Pyrimidine	% yield	B.p. (mm.) or m.p., °C.	Formula	Calcd., % C	H	N	S	Found, % C	H	N	S
2-Methylthio-4-allylthio-	78	126 (1.3)	$C_8H_{10}N_2S_2$	48.45	5.08		32.34	48.73	5.01		32.60
2-Benzylthio-4-allylthio-	81	173 (0.9)	$C_{14}H_{14}N_2S_2$	61.28	5.14	10.21	23.37	61.16	5.26	10.48	23.06
2-Phenyl-4-allylthio-	76	129 (0.1)	$C_{13}H_{12}N_2S$	68.38	5.30		14.05	68.04	5.54		13.91
2-Methyl-4-allylthio-	66	67 (0.1)	$C_8H_{10}N_2S$	57.79	6.06		19.29	57.75	6.28		19.42
2-Amino-4-allylthio-	85[a]	117–125[a]	$C_7H_9N_3S$	50.27	5.42		19.18	50.10	5.44		19.36
	24[b]	133–135[b]									
2-Methylthio-4-allylamino-	81	82–84	$C_8H_{11}N_3S$	53.01	6.12	23.18		53.21	6.20	22.96	
		83–84[b]									
2-Benzylthio-4-allylamino-	63	64–66	$C_{14}H_{15}N_3S$	65.34	5.88	16.33		65.52	5.74	16.42	
		65–67[b]									
2-Methyl-4-allylamino-	27	109 (1.6)	$C_8H_{11}N_3$	64.40	7.43	28.16		64.20	7.58	28.19	
2-Amino-4-allylamino-	29	116–117	$C_7H_{10}N_4$	55.98	6.71	37.31		55.75	6.66	37.09	
		117–119[b]									

[a] Crude material. [b] Analytical sample.

arrangement took place to give approximately equal quantities of **4**, **5**, and two other unidentified compounds, followed by extensive polymerization and tar formation.

The allyl pyrimidinyl sulfides presented in Table II were synthesized and studied under conditions which lead to rearrangement of the corresponding allyl pyrimidinyl ethers.[14] The general result was rapid and extensive decomposition. The simplest mixture resulted from 2-phenyl-4-allylthiopyrimidine. Of five major components separated by v.p.c., the first three were eliminated as Claisen rearrangement products because of their low retention times. The fourth (25%), with ultraviolet and infrared spectra nearly identical with starting material (both had a single ultraviolet maximum at 256 mμ in ethanol), had a slightly greater retention time during v.p.c. and has been tentatively identified as the propenyl pyrimidinyl sulfide.[17] The fifth component (18%) did not have spectral properties consistent with published data[18] that would permit an assignment of structure as a Claisen rearrangement product, although bicyclic structures could not be ruled out.

Although N-allylaniline does not undergo Claisen rearrangement, it is interesting to note that Marcinkiewicz recently rearranged N-allylnaphthylamine and predicted the rearrangement of 2-allylaminopyridine.[19] To complete the investigation in pyrimidines, the 2-substituted 4-allylaminopyrimidines presented in Table II were prepared and heated in N,N-diethyl-*m*-toluidine at 255°. Although these compounds were considerably more stable than the allyl ethers or sulfides, there was no evidence of the formation of Claisen rearrangement products during the slow decomposition of starting material. An authentic sample of 2-benzylthio-4-amino-5-allylpyrimidine, a possible product from the rearrangement of 2-benzylthio-4-allylaminopyrimidine was found to decompose at a rate faster than the starting material disappeared under the same conditions.

(14) After the work described here had been initiated, the major products of the rearrangement of allyl phenyl sulfide were shown to be propenyl phenyl sulfide, thiachroman, and 2-methyl-2,3-dihydrobenzothiophene, depending on reaction conditions.[15] *o*-Allylthiophenol was not a major product despite an earlier report.[16]

(15) C. Y. Meyers, C. Rinaldi, and L. Bonoli, *J. Org. Chem.*, **28**, 2440 (1963), and leading references therein.

(16) C. D. Hurd and H. Greengard, *J. Am. Chem. Soc.*, **72**, 3356 (1930).

(17) These components condensed in the exit port even with the detector block at 325°. Some material was trapped by removing the outer fittings and inserting small glass tubing almost into the detector. This process did not permit the collection of sufficient sample for adequate characterization.

(18) E. Spinner, *J. Chem. Soc.*, 1237 (1960).

(19) S. Marcinkiewicz, J. Green, and P. Mamalis, *Tetrahedron*, **14**, 208 (1961).

Experimental Section[20]

Product Distribution Analyses.—These were determined on either an F & M Model 500 or an F & M Model 720 gas chromatograph. Columns were 2 ft. in length and consisted of 20% silicon gum rubber (SE-30) on hexamethyldisilazane-treated Chromosorb W.[21] Temperature programming to 300° at the rate of 7.5°/min. was generally used with a helium flow of 60 cc./min. Starting temperatures varied from 75 to 180°.

For each series in Table I, synthetic mixtures of starting material and *ortho*-rearrangement products[22] were prepared to determine the area response of products in relation to starting material over the range of concentrations at which the analyses were determined.

Unless otherwise noted, the allyl pyrimidinyl ether was mixed with three times the weight of solvent. Rearrangements were carried out in sealed Pyrex glass tubes in a stirred and thermostated oil bath. Mixtures resulting from rearrangement were dissolved in twice the weight of pyridine. A sample of unrearranged solution was treated in the same manner and all calculations for the product distributions were made in relation to the starting ether through the use of the calibration for the relative area responses.

Statements in the text regarding the presence or absence of compounds resulting from rearrangement are based on standard chromatographic techniques involving the use of retention times, peak enhancements, and trapping of samples for infrared and ultraviolet spectra determinations.

2-Phenyl-4-hydroxypyrimidine.[23]—Ethyl sodium formylacetate[24] (258 g., 1.94 moles) was added to a solution of 239 g. (1.24

(20) Melting points are corrected and boiling points are uncorrected. Analyses were by Galibraith Laboratories, Knoxville, Tenn., and Alfred Bernhardt, Mülheim, Germany. Where possible, samples have been submitted for inclusion in the Sadtler collection of infrared spectra. Magnesium sulfate was used as the drying agent in all cases where drying was conducted in the presence of a solvent.

(21) Chromosorb W (60–80 mesh) was washed thoroughly with 10% sodium hydroxide solution, 4 *N* hydrochloric acid, and finally with water. After drying at 110° for 16 hr., the support was treated with hexamethyldisilazane: J. Boheman, S. H. Langer, R. H. Perett, and J. H. Purnell, *J. Chem. Soc.*, 2444 (1960).

(22) Authentic samples of 2-phenyl-3-allyl-4-pyrimidone, 2-methyl-3-allyl-4-pyrimidone, and 2-trifluoromethyl-4-ethoxypyrimidone were obtained through the courtesy of Mr. James P. Jonak. The preparation of these compounds from the corresponding 2-substituted 4-hydroxypyrimidines will be described in a forthcoming publication.

(23) E. Cherbuliez and K. N. Stavritch, *Helv. Chim. Acta*, **5**, 267 (1922). This compound was prepared by the decarboxylation of 2-phenyl-4-hydroxy-5-pyrimidinecarboxylic acid. The preparation given here is much more direct.

(24) S. Gabriel, *Ber.*, **37**, 3640 (1904).

moles) of benzamidine hydrochloride dihydrate in 1 l. of water. After standing 24 hr. with occasional stirring, the orange mixture was brought to pH 4 with 6 *N* hydrochloric acid. The precipitate was collected, washed with water, and dried to give 156 g. (73%) of tan powder, m.p. 206–208°. A total of 110 g. (51%) of product was obtained as several crops of crystals after recrystallization from 2–3 l. of ethanol: first crop, m.p. 209–210°.

2-Phenyl-4-chloropyrimidine.[25]—2-Phenyl-4-hydroxypyrimidine (61 g.) was refluxed 2 hr. with 300 ml. of phosphorus oxychloride. Most of the phosphorus oxychloride was removed *in vacuo*, and the liquid remaining was poured over crushed ice. The solid that separated was dissolved in ether, washed well with water, and dried. The ether was spin evaporated *in vacuo*, and the residue was recrystallized from 150 ml. of petroleum ether (b.p. 66–75°) to give 50 g. (67%) of product, m.p. 71–75°. Additional material was obtained from the filtrate.

2-Phenyl-4-allyloxypyrimidine.—Sodium (2.30 g., 0.10 g.-atom) was dissolved in 50 ml. of allyl alcohol and added to a solution of 19.06 g. (0.10 mole) of 2-phenyl-4-chloropyrimidine in 50 ml. of allyl alcohol. After 1 hr. excess allyl alcohol was spin evaporated *in vacuo*. Water and ether were added to the residue, and the ether layer was washed well with water. After drying the ether was removed by flash distillation, and the product was distilled *in vacuo:* b.p. 105° (0.1 mm.). The distillate weighed 19.90 g. (94%).

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.61; H, 5.66; N, 13.41.

2-Phenyl-4-hydroxy-5-allylpyrimidine.—Benzamidine hydrochloride dihydrate was dried *in vacuo* over phosphorus pentoxide 24 hr. to m.p. 168–171°. Anhydrous benzamidine hydrochloride (7.83 g., 0.050 mole) and ethyl α-allylformylacetate[26] (7.80 g., 0.050 mole) were added to a solution of 2.30 g. (0.10 g.-atom) of sodium in absolute ethanol. After stirring at room temperature for 24 hr., the ethanol was spin evaporated *in vacuo* and 200 ml. of water was added. The mixture was brought to pH 7 with acetic acid and crystallization occurred slowly from a gum. The product was collected, washed with water, and dried. The crude material weighed 4.98 g. (47%), m.p. 188–191°. After recrystallization from 150 ml. of ethanol, 2.60 g. (25%) of white needles was obtained: m.p. 195–196°; $\lambda_{max}^{50\%\ EtOH}$ 242 mμ (ε 13,200), 291 mμ (ε 10,600); $\lambda_{max}^{0.1\ N\ NaOH}$ 231 mμ (ε 22,000), 283 mμ (ε 11,100).

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20. Found: C, 73.78; H, 5.87; N, 13.37.

2-Phenyl-4-hydroxy-5-allylpyrimidine by Rearrangement.—A solution of 2-phenyl-4-allyloxypyrimidine (4.0 g.) and N,N-diethyl-*m*-toluidine (12.0 g.) was heated under reflux at an oil bath temperature of 250° for 16 hr. Most of the solvent was removed *in vacuo* and on cooling crystals separated. These were collected and washed with a small quantity of ether. After the crude product (1.19 g., 30%, m.p. 179–186°) was recrystallized from ethanol (Norit), 0.40 g. of product was obtained: m.p. 193–194°. Additional product could be obtained from the filtrate.

2-Substituted 4-Allylthiopyrimidines.[27]—The procedure given here is typical for the preparation of the liquid 2-substituted 4-allylthiopyrimidines in Table II.

A. 2-Benzylthio-4-allylthiopyrimidine.—2-Benzylthio-4-chloropyrimidine (10.00 g., 0.0423 mole) was dissolved in 150 ml. of ethanol and mixed with a solution of 8.96 g. (0.0846 mole) of sodium carbonate in 80 ml. of water. As the mixture was stirred, 3.14 g. (0.0423 mole) of allyl mercaptan was added in one portion. Stirring was continued and the mixture was refluxed gently for 1 hr. After solvents were spin evaporated *in vacuo*, water and ether were added to the residue. The ether layer was washed with water and dried. The ether was flash distilled and the product was distilled *in vacuo*.

B. 2-Amino-4-allylthiopyrimidine.—The above procedure was followed and the solvent was spin evaporated *in vacuo*. The solid residue was collected by filtration, washed with water, and dried to give 85% of crude product melting at 117–125°. The analytical sample was obtained by successive crystallizations from ethyl acetate (twice), benzene, ethanol, and finally ethyl acetate.

2-Substituted 4-Allylaminopyrimidines.[27]—The procedure given here is typical for the preparation of the solid 2-substituted 4-allylaminopyrimidines in Table II.

A. 2-Benzylthio-4-allylaminopyrimidine.—2-Benzylthio-4-chloropyrimidine (15.0 g., 0.0633 mole) was dissolved in 150 ml. of ethanol. Allylamine (7.62 g., 0.134 mole) was added and the solution was refluxed 2 hr. After most of the ethanol was spin evaporated *in vacuo*, water and ether were added to the oily residue. The ether solution was washed with water, dried, and evaporated. The oily solid which remained was crystallized from benzene–petroleum ether. The analytical sample was obtained by an additional crystallization.

B. 2-Methyl-4-allylaminopyrimidine.—The general procedure presented above was followed except that evaporation of the ether extracts gave an oil which was distilled *in vacuo*.

2-Benzylthio-4-chloro-5-allylpyrimidine.[28]—A mixture of 3.40 g. of dry 2-benzylthio-4-hydroxy-5-allylpyrimidine[2] and 20 ml. of phosphorus oxychloride was heated at reflux for 3 hr. Excess phosphorus oxychloride was removed *in vacuo*, and the dark brown viscous oil that remained was poured into ice–water. The mixture was extracted with ether, and the ether layer was washed well with water and dried. Removal of the ether by flash distillation left an oil which was distilled *in vacuo:* b.p. 196° (1.3 mm). The distillate weighed 2.32 g. (65%).

Anal. Calcd. for $C_{14}H_{13}ClN_2S$: C, 60.75; H, 4.73; N, 10.12. Found: C, 60.53; H, 5.06; N, 10.33.

2-Benzylthio-4-amino-5-allylpyrimidine.[28]—2-Benzylthio-4-chloro-5-allylpyrimidine (1.09 g.) was added to 40 ml. of ethanol which had been previously saturated with ammonia at 0°. The mixture was sealed in a tube and heated at 150° for 20 hr. The tube was opened and the ethanol was evaporated to leave an oily residue. Water was added to the oil, and after trituration the oil solidified. The pulverized solid was collected and washed with water. After drying, crystallization from petroleum ether gave long, slender white crystals. The analytical sample, 0.22 g. (22%), was obtained by an additional crystallization from the same solvent: m.p. 66–67°.

Anal. Calcd. for $C_{14}H_{15}N_3S$: C, 65.33; H, 5.87; N, 16.33. Found: C, 64.73; H, 5.93; N, 15.92.

Allylation of 2-Methylthio-4-hydroxypyrimidine.—2-Methylthio-4-hydroxypyrimidine (14.22 g., 0.10 mole) and 86% potassium hydroxide (6.52 g., 0.10 mole) were placed in 250 ml. of absolute ethanol. The mixture was heated, and when solution occurred, 12.1 g. (0.10 mole) of allyl bromide was added. After refluxing 1.5 hr., the ethanol was spin evaporated *in vacuo*. Chloroform was added to the oily residue. The organic layer was washed with water, 10% sodium hydroxide solution, and more water and then dried. Evaporation of the chloroform left 17.1 g. (94%) of mixed allylation products as a tan oil.

Part of the mixture (8.5 g.) was chromatographed on 200 g. of neutral alumina.[29] The sample was applied to the column as a benzene solution. Anhydrous ether eluted 1.24 g. (15%) of 2-methylthio-4-allyloxypyrimidine. Ethyl acetate eluted 2.22 g. (26%) of 2-methylthio-3-allyl-4-pyrimidone, which after evaporation of the solvent crystallized on several days standing: m.p. 35–51°. The analytical sample was obtained by several recrystallizations from about 15 ml. of petroleum ether: m.p. 52–55°, λ_{max}^{EtOH} 291 mμ (ε 8700).

Anal. Calcd. for $C_8H_{10}N_2OS$: C, 52.72; H, 5.53; N, 15.37. Found: C, 52.41; H, 5.52; N, 15.03.

Acetone eluted 0.71 g. (8%) of 2-methylthio-1-allyl-4-pyrimidone, which crystallized on evaporation of the solvent: m.p. 73–88°. This was recrystallized several times from about 20 ml. of 1:1 benzene–petroleum ether to obtain an analytical sample, m.p. 95–97°, λ_{max}^{EtOH} 234 mμ (ε 29,000).

Anal. Calcd. for $C_8H_{10}N_2OS$: C, 52.72; H, 5.53; N, 15.37. Found: C, 52.79; H, 5.49; N, 14.99.

Allylation Products of 2-Benzylthio-4-hydroxypyrimidine.—These allylation products were previously reported[3] as being oils, but they crystallized during subsequent preparation once seed crystals became available.

(25) S. Ruhemann and A. S. Hemmy, *Ber.*, **30**, 2022 (1897). No yield was stated. We feel the preparation given here is a better procedure.

(26) W. J. Croxall and J. O. Van Hook, *J. Am. Chem. Soc.*, **72**, 803 (1950).

(27) Leading references for the preparation of intermediates are given in ref. 2.

(28) This compound was prepared by John H. Bayless, Senior Thesis, University of Buffalo, 1962.

(29) Woehlm alumina was purchased from Alupharm Chemicals, New Orleans, La.

2-Benzylthio-3-allyl-4-pyrimidone, m.p. 42–43°, is very soluble in benzene, relatively insoluble in petroleum ether, and can be crystallized conveniently from the mixed solvents.

2-Benzylthio-1-allyl-4-pyrimidone, m.p. 64–66°, can be crystallized from benzene in which it is moderately soluble.

2,4-Diallyloxypyrimidine (1).—2,4-Dichloropyrimidine (100 g., 0.672 mole) was dissolved in 500 ml. of allyl alcohol. To this was added a solution of 30.9 g. (1.34 g.-atoms) of sodium dissolved in 600 ml. of allyl alcohol. After standing 1 hr., the mixture was spin evaporated *in vacuo*. The oily residue was mixed with ether and the ether solution was washed several times with water. After drying over magnesium sulfate, the ether was removed by flash distillation and the product was distilled *in vacuo*, b.p. 85° (0.5 mm.). The distillate weighed 116.6 g. (90% yield).

Anal. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.81; H, 6.34; N, 14.66.

1-Methyl-4-allyloxy-2-pyrimidone (2).—2,4-Diallyloxypyrimidine (20 g.) was mixed with 60 ml. of freshly distilled methyl iodide and the reaction mixture was placed in the dark at room temperature. After 24 hr. most of the methyl iodide was evaporated, during which time several crops of crystals were collected and washed with small quantities of ether. The dried crude product weighed 14.9 g. (90%), m.p. 109–113°. After recrystallization from a small amount of benzene, 12.4 g. (74%) of white crystals was obtained: m.p. 110–112°, λ_{max}^{EtOH} 276 mμ (ε 6100).

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.06; N, 16.86. Found: C, 58.12; H, 5.97; N, 16.54.

1-Methyl-3-allyl-2,4-pyrimidinedione (1-Methyl-3-allyluracil) (3).—1-Methyl-4-allyloxy-2-pyrimidone (1.00 g., 0.00602 mole) was heated 1.75 hr. at 240°. After cooling to room temperature, methylene chloride was added to the dark viscous residue. Insoluble material (0.06 g.) was removed by filtration and the filtrate was chromatographed on 75 g. of neutral alumina.[29] 1-Methyl-3-allyl-2,4-pyrimidinedione (0.70 g., 70%) was eluted from the column with ethyl acetate. An analytical sample was obtained by chromatographing the product a second time using the above procedure: λ_{max}^{EtOH} 266 mμ (ε 8700).

Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.06; N, 16.86. Found: C, 57.64; H, 6.27; N, 16.87.

1-Allyl-4-allyloxy-2-pyrimidone (4).—2,4-Diallyloxypyrimidine (5.0 g., 0.0260 mole) and allyl iodide (5.0 g., 0.0297 mole) were mixed and placed in the dark for 72 hr. Excess allyl iodide was removed under reduced pressure at room temperature. The red residue was mixed with a small volume of benzene and chromatographed on 125 g. of neutral alumina.[29] 1-Allyl-4-allyloxy-2-pyrimidone (4.8 g., 96%) was eluted with chloroform. The analytical sample was obtained by chromatographing the product a second time using the above procedure: λ_{max}^{EtOH} 274 mμ (ε 6000).

Anal. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.17; H, 6.52; N, 14.24.

1,3-Diallyl-2,4-pyrimidinedione (1,3-Diallyluracil) (5)—1-Allyl-4-allyloxy-2-pyrimidone (1.00 g.) was heated 1.75 hr. at 240°. After cooling to room temperature, methylene chloride–chloroform (1:1) was added to the dark viscous residue. The sample was chromatographed on 75 g. of neutral alumina.[29] 1,3-Diallyl-2,4-pyrimidinedione (0.62 g., 62%) was eluted from the column with chloroform. The analytical sample was obtained by chromatographing the product a second time using the above procedure: λ_{max}^{EtOH} 266 mμ (ε 9300).

Anal. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.39; H, 6.45; N, 14.35.

The Vapor Phase Rearrangement of Thioncarbonates and Thioncarbamates

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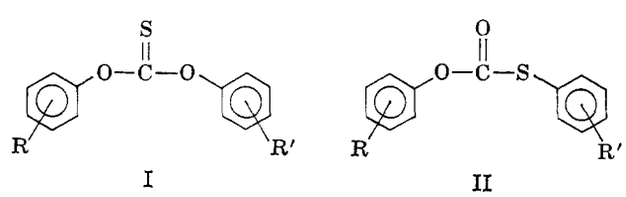
The Schönberg rearrangement of aryl thioncarbonates has been carried out in a vapor phase pyrolysis with considerable improvement in yield. These results have been reconciled with the cyclic four-membered transition state proposed by Powers and Tarbell and extended to the vapor phase rearrangement of thioncarbamates as an efficient and simple method of preparing certain difficultly available substituted aryl thiols. A procedure involving the steps of these vapor phase rearrangements is conceived as the most generally effective route for deoxygenation of certain substituted phenols which are otherwise not readily subject to reduction or hydrogenolysis (with Raney nickel).

The rearrangement of diaryl thioncarbonates, first described by Schönberg and Vargha[2] has later been shown, largely through the efforts of Tarbell and coworkers,[3,4] to be of synthetic importance in the preparation of substituted thiophenols. The rearrangement is apparently applicable to both symmetrical and unsymmetrical diaryl thioncarbonates. The original reaction conditions call for heating the substrate (neat) at temperatures of 275–300°, and yields are reported to be 50–80%. However, as emphasized by Powers and Tarbell,[4] considerable formation of decomposition products can occur at levels of even 50% conversion of I to II in cases where protracted periods of heating are required.



I II

R or R′ = NO_2, Cl, OMe, or Me

Kinetic data taken by Powers and Tarbell[4] support a first-order rate law governing the rearrangement. Furthermore, where R or R′ are electron-withdrawing substituents, rate accelerations are experienced, and, in unsymmetrically substituted thioncarbonates, the rearrangement was shown[4] to occur primarily in the direction of the ring bearing the most electron-withdrawing substituent. On this basis, the driving force of the rearrangement originates from the nucleophilic character of the sulfur in displacements on carbon and the leaving-group tendency of the oxygen that correlates with its high electronegativity. These facts are quite in keeping with a four-membered cyclic transition state.[4]

(1) Part of the work discussed in this article has been abstracted from the Ph.D. Thesis submitted by E. R. Evans in partial fulfillment of the requirements of the University of Delaware, June 1965.

(2) A. Schönberg and L. Vargha, *Ber.*, **63**, 178 (1930).

(3) H. P. Al-Kazimi, D. S. Tarbell, and D. Plant, *J. Am. Chem. Soc.*, **77**, 2479 (1955).

(4) D. H. Powers and D. S. Tarbell, *ibid.*, **78**, 70 (1956).