which formed was filtered, washed with dilute hydrochloric acid and dried *in vacuo* at 56°, m.p. 104–108° (dec.).

Anal. Calcd. for $C_{32}H_{47}N_2O_6AuCl_4$: C, 42.95; H, 5.29; N, 3.13; Au, 22.03. Found: C, 42.99, 42.91; H, 5.44, 5.19; N, 3.53, 3.41; Au, 21.70, 21.88.

No crystalline derivatives were obtained from fractions (1) and (2) of the chromatographic separation.

Chromatographic Separation of the Unsaturated Bases (VII and VIII).—A solution of 1.75 g. of the mixed bases in 25 cc. of dry benzene was passed through an 8" column of alumina. A partial elution was carried out with first 10 cc. of dry benzene, then 20 cc. of a 3% solution of ethanol in benzene. The column was extruded, dried and sectioned. The following fractions were obtained: (1) all of the color was located in the upper 0.25" of the column, and this was discarded; (2) 0.18 g. of colorless glass from the next 2" of the column; (3) 0.61 g. of colorless glass from the lower 5.75" of the column; (4) 0.86 g. of colorless glass from the original solvent and eluent solvents.

Ozonolysis of fraction (3) and working up as described before gave 0.11 g. (40%) of 2-ethyl-4,5-dimethoxybenzaldehyde semicarbazone and 0.03 g. (13%) of 2-ethyl-4,5-dimethoxybenzoic acid. The other, nitrogen containing cleavage product of the ozonolysis could not be obtained in crystalline form or as a crystalline derivative.

LAWRENCE, KANSAS RECEIVED OCTOBER 17, 1950

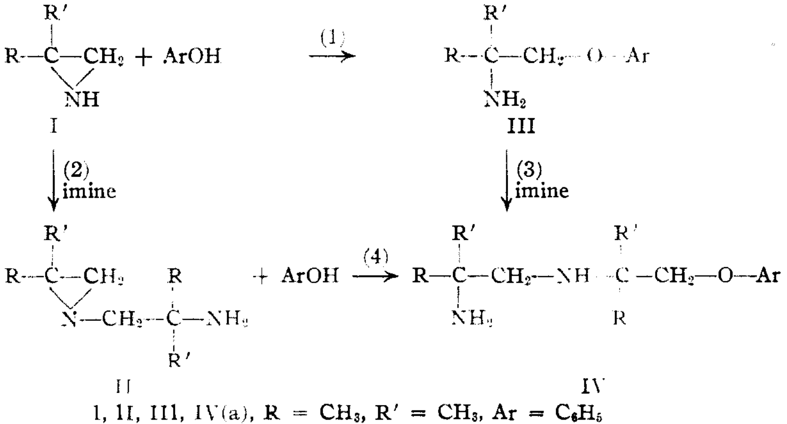
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, UNIVERSITY OF WISCONSIN, AND THE METCALF CHEMICAL LABORATORY, BROWN UNIVERSITY]

Reactions of Ethylenimines. III. With Phenols

BY LEALLYN B. CLAPP

Phenols act as reactants and as acid catalysts in opening the ethylenimine ring,  $RR'-\overset{NH}{CH-CH_2}$, at the unsubstituted carbon atom to give mixtures of compounds of the types $RR'CNH_2-CH_2-O-Ar$ and $RR'-CNH_2-CH_2-NH-CRR'-CH_2-O-Ar$. The reaction is accompanied by dimerization to a piperazine and polymerization. With a large excess of the phenol, the β-amino ether is the predominant product.

The three-membered ring in an ethylenimine opens readily in the presence of nucleophilic agents with an acid catalyst. Carbon substituted (or disubstituted on the same carbon) ethylenimines open at the secondary (or tertiary) carbon in reactions involving hydrolysis[1] or alcoholysis,[2] but open predominantly at the primary carbon with amines in the presence of ammonium chloride[3] and exclusively at this carbon with thiophenol.[4] In reactions of ethylenimines with ammonia[3,5] and amines[3,5,6] which give mainly α,β-diamines, dimerization of the imine to a piperazine and polymerization are significant competing reactions.



I, II, III, IV(a), $R = CH_3$, $R' = CH_3$, $Ar = C_6H_5$
(b), $R = C_2H_5$, $R' = H$, $Ar = C_6H_5$

When a phenol is the nucleophilic agent as well as the acid catalyst for the ring cleavage, products in which the imine to phenol ratio is 1:1 (III) and 2:1 (IV), respectively, are formed on an approximately equal basis (using threefold of phenol), along with some piperazines and polymers of the imine.

The product of the reaction of one molecule of 2-ethylethylenimine with one of phenol proved to be β-aminobutyl phenyl ether (IIIb), a result of ring opening at the primary carbon and the products with 2,2-dimethylethylenimine and other phenols are assumed to have an analogous structure (IIIa). The compound from two molecules of 2-ethylethylenimine with one of phenol was β-(β-aminobutyl)-aminobutyl phenyl ether (IVb).

Based on the imine present in the reaction mixture (threefold in phenol) the total yields of the two isolated products containing phenols diminish with acid strength from about 60% for phenol itself to 17% for 2,6-dimethylphenol. However, the yields do not follow acid strength alone in reactions with acids which are not homologs of phenol; nucleophilic character appears also to be an important factor in the over-all picture. For example, thiophenol in reacting with 2,2-dimethylethylenimine gives a 92% yield[4] of the β-amino sulfide whereas *o*-, *m*- and *p*-nitrophenol and *p*-bromophenol, acids of comparable strength, act only as catalysts for the polymerization of this imine and give no yields of adducts at all. The still stronger carboxylic acids, such as benzoic, again give good yields of the corresponding β-amino esters.[7]

Having an ortho position occupied in a phenol does not decrease the yields of amino ethers, but, as expected, if both ortho positions are occupied, the yields are much lower. The yields of products from 2,5-dimethylphenol and *p*-methoxyphenol, respectively, with 2,2-dimethylethylenimine are nearly equal and about half those from *o*- and *p*-cresol.

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[1] T. L. Cairns, THIS JOURNAL, **63**, 871 (1941).

[2] D. S. Tarbell and P. Noble, Jr., *ibid.*, **72**, 2657 (1950).

[3] L. B. Clapp, *ibid.*, **70**, 184 (1948).

[4] G. Meguerian and L. B. Clapp, *ibid.*, **73**, 2121 (1951).

[5] A. L. Wilson, U. S. Patents 2,318,729–2,318,730 (1943).

[6] G. J. Braz and V. A. Skorodumov, *Compt. rend. acad. sci. U. R. S. S.*, **55**, 315 (1947).

[7] Unpublished results, Brown University.

Whether the diamino ethers are formed from imine reacting with β-amino ether (equations 1, 3) or from a dimer of the imine with phenol (equations 2, 4) cannot be concluded from the present work but some evidence was obtained. Whereas β-(β-aminobutyl)-aminobutyl phenyl ether (IVb) and β-(β-aminoisobutyl)-aminoisobutyl phenyl ether (IVa) are formed in about equal amounts from the corresponding imine and phenol, compound IVb was obtained in 27% yield from β-aminobutyl phenyl ether (IIIb) and 2-ethylethylenimine but IVa could not be made from the corresponding ether IIIa and imine Ia. In this second case it is clear that steric hindrance will be much more significant than it would be in the cleavage of the ring in the imine dimer by phenol (equation 4). Jones[8] has suggested that the first step in the polymerization of an imine is dimerization to an N-substituted ethylenimine. A phenol may be just a strong enough acid to catalyze the polymerization and at the same time a reactive enough nucleophilic agent to cut the polymerization short at the dimeric stage (as well as at the monomeric and perhaps higher stages) by competing as a reactant in the ring opening.

Differences in the polarity of the solvents, chloroform,[9] methanol and ethanol make little change in the yields of β-amino ethers. A non-polar solvent, however, such as carbon tetrachloride or petroleum ether and a temperature above 60° both favor polymerization. The yield of β-amino ether

TABLE I

REACTION OF RR'C——CH$_2$ WITH PHENOLS
\ /
NH

R	R'	Phenol	Solvent	Temp., °C.	Amino[a] ether, % III	Di-amino[a] ether, % IV	Tri-amino[a] ether, %	Poly-mer,[b] %
CH$_3$	CH$_3$	[c]	CHCl$_3$	25	22	27	8	20[d]
CH$_3$	CH$_3$	[c]	CHCl$_3$	61	34	29	13	17
CH$_3$	CH$_3$	[e]	CHCl$_3$	61	51	21		18
CH$_3$	CH$_3$	[c]	CCl$_4$	76	13	4		76
CH$_3$	CH$_3$	[c]	Ligroin	60–68	16	4		75
CH$_3$	CH$_3$	[f]	CHCl$_3$	61	14	18		28
CH$_3$	CH$_3$	[f]	CH$_3$OH	65	13	18		39
CH$_3$	CH$_3$	[f]	C$_2$H$_5$OH	78	8	12		40
H	H	[c]	CHCl$_3$	61	28[g]			
H	H	[c]	None	100	33			[h]

[a] Physical properties, *etc.*, given in Table II. [b] Based on the formula $\left(\mathrm{RR'CH—CH_2}\right)_n$ with NH bridging. [c] Reactions run with 0.14 mole of imine and 0.42 mole of phenol as described in the experimental part for 2-ethylethylenimine and phenol. [d] The difference in the sum of the percentage yields and 100 represents losses in in-between fractions and unreacted imine. [e] With 0.14 mole of imine and 1.4 moles of phenol. [f] With 0.14 mole of imine and 0.42 mole of 2,5-dimethylphenol. [g] B.p. 228–230°; benzamide, m.p. 95.8–96.4°; R. Schreiber, *Ber.*, **24**, 189 (1891), records the b.p. 228–229° (755 mm.) and the benzamide, m.p. 93°, from acetic acid. [h] 52% piperazine isolated.

TABLE II

AMINO ETHERS (RR'CNH$_2$—CH$_2$OAr), DIAMINO ETHERS (RR'CNH$_2$—CH$_2$—NH—CRR'—CH$_2$OAr), AND THEIR DERIVATIVES

Ar	Amino ether, %	Diamino ether, %	B.p.,[a] °C.	Mm.	d^{25}_4	n^{25}_D	MR_D Calcd.	MR_D Found	Nitrogen Calcd.	Nitrogen Found	Benzamide M.p., °C.	Benzamide Carbon, % Calcd.	Benzamide Carbon, % Found	Benzamide Hydrogen, % Calcd.	Benzamide Hydrogen, % Found	Benzamide Nitrogen, % Calcd.	Benzamide Nitrogen, % Found
							R = C$_2$H$_5$ R' = H										
C$_6$H$_5$	30[b]		74–77	0.9	0.9837	1.5130	49.84	50.48	8.48	8.39	91.6–92.0					5.20	5.31
		30	122–123	.8	.9711	1.5055	71.92	72.25	11.85	11.72	201–202	75.85	75.80	7.26	7.39	6.30	6.29
p-CH$_3$-C$_6$H$_4$	23		88–89	.9	.9747	1.5102	54.46	55.02	7.81	7.52	108–109	76.29	76.14	7.47	7.40	4.94	4.87
		20	134–137	.9	.9624	1.5044	76.54	77.08	11.19	11.02	180–182	75.95	75.74	7.47	7.56	6.11	6.15
							R = CH$_3$ R' = CH$_3$										
C$_6$H$_5$	34		75–77	1.3	.9748	1.5058	49.84	50.35	8.48	8.55	105.4–106.0	75.81	76.28	7.11	7.33	5.20	4.91
		29	111–113	1.1	.9597	1.4982	71.92	72.21	11.85	11.49	95–97					6.30	6.16
		13[c]	130–138	0.8													
p-CH$_3$-C$_6$H$_4$	35		84	1.3	.9598	1.5033	54.46	55.23	7.81	8.02	98.5–99.5	76.29	76.19	7.47	7.23		
		23	116–117	0.8	.9495	1.4971	76.54	77.17	11.19	10.98	124.5–126					6.11	6.50
o-CH$_3$-C$_6$H$_4$	37		84–85	1.4	.9620	1.5044	54.46	55.21	7.81	8.06	136–137	76.29	76.31	7.47	7.30		
		21	109–110	0.8	.9543	1.4996	76.54	77.12	11.19	10.95	139.4–140.6	75.95	75.36	7.47	7.54	6.11	6.17
2,5(CH$_3$)$_2$C$_6$H$_3$	14		99–100	1.8	.9505	1.5015	59.08	59.96	7.25	7.28	106–108	76.73	76.57	7.80	7.56	4.71	4.88
		18	127–130	1.1	.9428	1.4963	81.15	81.97	10.60	10.82	132–134.5					5.93	5.90
2,6(CH$_3$)$_2$C$_6$H$_3$	7		77–79	0.9	.9544	1.4998	59.08	59.54	7.25	7.39	81.8–82.6					4.71	4.79
		10[d]	125–127	1.0	.9479	1.4955	81.15	81.41	10.60	10.38							
p-CH$_3$OC$_6$H$_4$	16		104	1.0[e]					7.17	7.15	87.0–88.4					4.68	4.99
		18	131–134	0.8	.9940	1.5033	78.18	79.27	10.51	10.65	136.6–137.8					5.90	5.80

[a] B.p. of the analytical sample, uncorrected. [b] M.p. of the phenylthiourea 113–113.5°. *Anal.* Calcd. for C$_{17}$H$_{20}$N$_2$OS: C, 67.96; H, 6.71; N, 9.33. Found: C, 68.49; H, 6.66; N, 9.28. [c] May be a triamino ether from three molecules of imine and one of phenol; Calcd. for C$_{18}$H$_{33}$N$_3$O: N, 13.66. Found: N, 13.22. 12.79. [d] M.p. of the phenylthiourea 135–137°. *Anal.* Calcd. for C$_{23}$H$_{33}$N$_3$OS: N, 10.52. Found: N, 10.64. [e] M.p. 39–42°.

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(8) G. D. Jones, A. Langsjoen, M. M. C. Neumann and J. Zomlefer, *J. Org. Chem.*, **9**, 125 (1944); G. D. Jones, *ibid.*, **9**, 484 (1944).

(9) Noticeable heat is evolved when any of the three imines used in this research was dissolved in chloroform, which may indicate hydrogen bonding involving C-H-N bonds. Evidence for N-H-N hydrogen bonding of imines in carbon tetrachloride solution has been reported (H. W. Thompson and G. P. Harris, *J. Chem. Soc.*, 301 (1944)).

from a reaction mixture tenfold in phenol is enhanced considerably at the expense of diamino ether formation. These results are summarized in Table I.

Experimental[10]

The amino ethers and diamino ethers for which physical constants and derivatives are listed in Table II were prepared in a manner analogous to that described in method A for β-aminobutyl phenyl ether and β-(β-aminobutyl)-aminobutyl phenyl ether, respectively. The derivatives were prepared by standard procedures.

β-Aminobutyl Phenyl Ether. Method A.—To a solution of 40 g. (0.42 mole) of reagent grade phenol in 200 ml. of refluxing chloroform, 10 g. (0.14 mole) of 2-ethylethylenimine in 50 ml. of chloroform was added dropwise over a half-hour period while the solution was stirred mechanically. Refluxing was continued for three hours. The chloroform was distilled at atmospheric pressure and the remainder was subjected to fractional distillation from a modified Claisen flask. After removing the unreacted phenol, the following fractions were collected: b.p. 80–105° (5 mm.), 105–118° (5 mm.) and 118–145° (5 mm.). From the second fraction, another distillation gave 8.0 g., b.p. 108–113° (5mm.), of a colorless liquid with an amine odor which contained traces of phenol. A constant index of refraction could not be obtained by repeated distillation. The sample was dissolved in excess 5% hydrochloric acid and extracted with 100 ml. of ether in three portions. The acid solution was then made slightly alkaline with 5% sodium hydroxide and the free amino ether extracted with ether. Distillation at reduced pressure in a nitrogen atmosphere gave a sample of analytical purity which was used for the density and index of refraction measurements; yield 7.0 g., 30%, b.p. 74–77° (0.9 mm.).

Method B.—A Gabriel synthesis of β-aminobutyl phenyl ether following the procedure of Cope, *et al.*,[11] as used by Meguerian[4] on the sulfur analog established the structure of the product of b.p. 74–77° (0.9 mm.) just described. Over-all yield in the four reactions was 4%. The phenylthiourea of the product from the Gabriel synthesis resulted in a m.p. 112–114° and the mixed m.p. with the phenylthiourea from IIIb, m.p. 113–113.5°, gave no depression.

β-(β-Aminobutyl)-aminobutyl Phenyl Ether. Method A.—The third fraction, b.p. 118–145° (5 mm.), from the reaction (preceding paragraph) of 2-ethylethylenimine and phenol was redistilled, b.p. 142-151° (3 mm.), yield 5.6 g., from which 5.0 g., 30%, of pure β-(β-aminobutyl)-aminobutyl phenyl ether was obtained using the same method of purification as described for β-aminobutyl phenyl ether.

Method B.—One and one-tenth grams of 2-ethylethylenimine was sealed in a glass tube with 7.6 g. of β-aminobutyl phenyl ether and 0.2 g. of ammonium chloride.[3] After 44 hours in an oil-bath at 100°, a fraction, b.p. 117-120° (0.8 mm.), $n^{25}D$ 1.5053, was obtained; yield 1.0 g., 27.4%. A polymer was formed to the extent of 45.4% and 25% of unreacted imine was recovered. The benzamide of this compound, recrystallized from chloroform and petroleum ether (b.p. 60–68°) gave a m.p. 198–200°. The mixed m.p. with the benzamide from the product in method A gave no depression.

A Diethylpiperazine.[12]—The forerun of the distillation of the β-aminobutyl phenyl ether, b.p. 80–105° (5 mm.). crystallized on cooling and was found to contain 0.4 g. of a molecular compound of phenol and a piperazine, presumably 2,5-diethylpiperazine. The compound was recrystallized from petroleum ether (b.p. 60–68°), m.p. 72–73.5°. Since the analysis did not distinguish the molecular compound, $C_{26}H_{30}N_2O_2$, from the amino ether, $C_{10}H_{15}NO$, the phenylthiourea and oxalate derivatives were prepared directly from the molecular compound. The phenylthiourea was recrystallized from a large volume of absolute methanol and sublimed above 200° (0.06 mm.); m.p., closed tube, 244-246° dec.

Anal. Calcd. for $C_{22}H_{28}N_4S_2$: C, 64.04; H, 6.84. Found: C, 64.00; H, 6.82.

The oxalate was recrystallized from water and sublimed above 200° (0.06 mm.); m.p. 300–301° (dec.) in closed tube. The piperazine previously reported[3] gave the same oxalate, m.p. 298-301° dec.

Anal. Calcd. for $C_{10}H_{20}N_2O_4$: C, 51.71; H, 8.68. Found: C, 51.87; H, 8.65.

Acknowledgment.—Most of the work described was done at the University of Wisconsin during a leave of absence. I appreciate the kindness of the Organic Chemistry Department in extending the facilities of their laboratories to me for this work. Most of the analyses were performed there by Messrs. B. G. Buell and E. A. Shiner.

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(10) All m.p.'s are corrected; b.p.'s are uncorrected.

(11) A. C. Cope, H. R. Nace, W. R. Hatchard, W. H. Jones, M. A. Stahlmann and R. B. Turner, THIS JOURNAL, **71**, 554 (1949).

(12) No evidence for the formation of a piperazine in reactions involving 2,2-dimethylethylenimine was obtained.

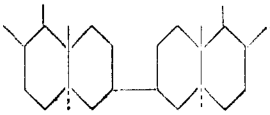
PROVIDENCE 12, R. I. RECEIVED DECEMBER 13, 1950

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, FACKENTHAL LABORATORIES OF FRANKLIN AND MARSHALL COLLEGE]

Bisteroids. I. Bicholestanyl. The Structure of Bicholesteryl and 3,3'-Bis-3,5-cholestadiene[1]

BY EDWARD N. SQUIRE

Three methods for the preparation of bicholestanyl (X) are described and the preparation of cholestanylmagnesium chloride is reported for the first time. Evidence is presented which confirms the appointed structures of bicholesteryl and 3,3'-bis-3,5-cholestadiene. Comparisons of the specific and molecular rotations of several steroids and their bisteroid derivatives are demonstrated and the ultraviolet absorption spectra of 3,3'-bis-3,5-cholestadiene in ether and alcohol solvents are illustrated.



IA

The preparation of steroid hydrocarbons with the general structure shown in IA and with a variety of groups at C_{17} was undertaken with the aim of studying their physical and physiological properties.[2] To this end bicholestanyl (X) was prepared as a means of determining the most effective synthetic route to the desired compound. Five avenues of approach were apparent. (1) The formation of cholestenone pinacol followed by dehydration[3] and hydrogenation. The dehydration has been described by Windaus, who employed

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(1) Presented at the Philadelphia Meeting of the American Chemical Society, April, 1950.

(2) E. N. Squire and E. W. Squire, unpublished results, have found in feeding experiments with 3-4 months old male hamsters that 55% of the orally administered bicholesteryl (IV) is not excreted. Feeding experiments using the saturated hydrocarbon, bicholestanyl (X), were therefore of interest.

(3) A. Windaus, *Ber.*, **39**, 521 (1906).