TABLE I
RELATIVE INTENSITIES OF DISCUSSED FRAGMENTS[a]

Compounds	N_2^+	CNH_2^+	$C_3H_3^+$	M–HCN	M–C_2H_4	M–C_2H_3O
2-Methylcarbazole			5			
Imidazole		48		80		
2-Ethylbenzimidazole		11	12	5		
Indole		11	10	38		
3-Acetylindole		9	6			100
Pyrrole		84	84	64		
1-Methylpyrrole		17	37		28	
1-Phenylpyrrole		9	26		52	
3-Acetyl-2,4-dimethylpyrrole		17	15			100
2-Methylpyrazine		23	34	56		
2,5-Dimethylpyrazine		18	46	10		
2,6-Dimethylpyrazine		25	67	6		
Pyrazole	49[b]	49[b]	29	60		
3-Methylpyrazole	44[b]	44[b]	11	10		
3,5-Dimethylpyrazole	23		33		6	
Indazole	14[b]	14[b]	12	33		
2-Aminopyrimidine		45	13			
4,6-Dimethylpyrimidine		29	54	29		
3-Amino-1,2,4-triazole	100[b]	100[b]		28		
4-Amino-1,2,4-triazole	100[b]	100[b]		5		

[a] Intensities are given in per cent of base peak and are listed only if they are greater than 5%. [b] Combination of both N_2^+ and CNH_2^+.

improbability of intermolecular collisions, N_2^+ may be considered a significant contributor only when nitrogen atoms are adjacent in the molecule. Therefore, with the exception of such molecules, CNH_2^+ appears to be the main contributor to a *m/e* of 28. Of the compounds investigated, pyrrole had the largest *m/e* of 28 attributed to CNH_2^+. This might be anticipated, as this fragment may be formed in two ways from pyrrole and does not require rearrangement for formation. Owing to the many possible rearrangements that could occur, it does not seem feasible to make structural predictions based on the appearance of a *m/e* of 28. However, the absence of such a *m/e* of 28 could be of value. For example, based on this investigation, the absence of a *m/e* of 28 would eliminate the possibility of adjacent nitrogen atoms in a given nitrogen heterocyclic compound. Additionally, the possibility of an unsubstituted ring nitrogen atom between two carbon atoms with two hydrogen atoms attached to the C–N structure would be eliminated.

Another positive ion which appeared in significant amount was $C_3H_3^+$, which is most probably the cyclopropenium cation.[4] A peak at a *m/e* of 39 appeared in the spectra of all molecules examined in which there were three or more carbon atoms in a chain with at least three hydrogen atoms among them. A comparison of the values for the *m/e* of 39 for the various compounds studied and their structures demonstrates clearly the correlation between the number of ways a fragment may form and its probability of formation. For example, it is interesting to note that the per cent of the base peak for the $C_3H_3^+$ fragment of 2,6-dimethylpyrazine was almost twice that of the 2-methylpyrazine. Such comparisons cannot, of course, be made between unrelated compounds. The high stability of the carbazole ring structure is reflected in a lower degree of fragmentation than is observed in the pyrazines. Again, the widespread appearance of the *m/e* 39 peak makes its absence in a given spectrum especially important. Based on this investigation, the nonappearance of a significant *m/e* of 39 indicates the absence of a three-carbon chain with at least three hydrogen atoms attached.

Formation of the neutral molecule HCN was indicated several times during this investigation as a driving force for the formation of a positive ion[6]; however, the formation pattern fails to be consistent enough for correlation. This apparent inconsistency also is present in the pattern of formation of the neutral C_2H_4 molecule.

A consideration of the effects produced by the presence of an acetyl group on a nitrogen heterocyclic ring, as evidenced by both data obtained in this study and other reported spectra,[6] reveals that a correlation may be established. It may apparently be concluded that no acetyl group is present on a given nitrogen heterocyclic ring if a significant parent ion minus 43-*m/e* peak is not present in the spectrum.

8,9,10,11-Tetrahydro-12*H*-benzo[5,6]quinoxalino-[2,3-*e*][1,4]diazepin-12-ones. Examples of a New Heterocyclic Ring System

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Received March 6, 1964

The present note describes the preparation of several 8,9,10,11-tetrahydro-12*H*-benzo[5,6]quinoxalino-[2,3-*e*][1,4]diazepin-12-ones (Va–e), examples of a hitherto unreported heterocyclic ring system. The products are shown in Table III.

The first member of the new series, 8,9,10,11-tetrahydro-12*H*-benzo[5,6]quinoxalino[2,3-*e*][1,4]-diazepin-12-one (Va), was prepared by the sequence shown. Treatment of ethyl cyanoacetate with 2-amino-

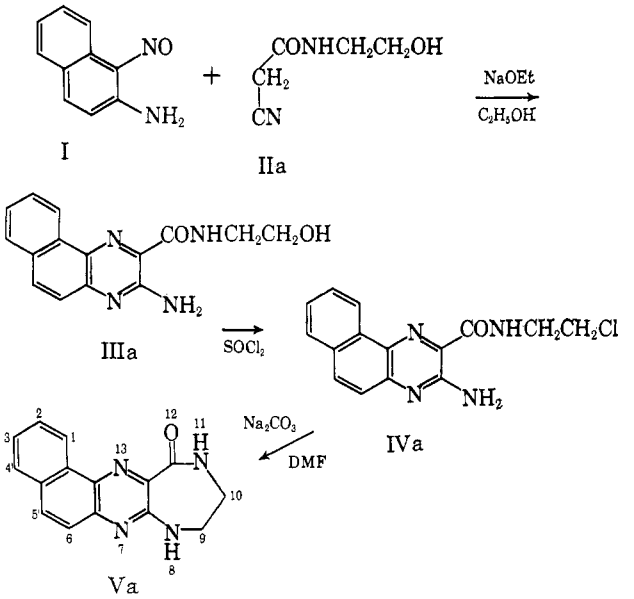
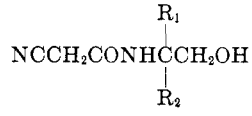


TABLE I

2-CYANO-*N*-(2-HYDROXYALKYL)ACETAMIDES

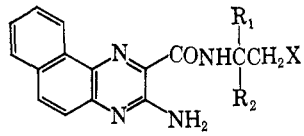


No.	R_1	R_2	M.p., °C.	Recrystg. solvent[a]	Yield, %	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
IIa[b]	H	H	61–62	A	65	$C_5H_8N_2O_2$	46.87	6.29	21.87	46.81	6.20	21.97
b	C_2H_5	H	87–88	A, B	92	$C_7H_{12}N_2O_2$	53.83	7.74	17.94	54.08	7.76	17.83
c	CH_3	CH_3	68–70	A, B	90	$C_7H_{12}N_2O_2$	53.83	7.74	17.94	53.64	7.81	17.62
d	CH_3	CH_2OH	130.5–131.5	A, C	74	$C_7H_{12}N_2O_3$	48.83	7.03	16.27	49.02	7.30	16.42

[a] A = ethyl acetate, B = petroleum ether (b.p. 30–60°), C = ethanol. [b] O. K. Behrens, J. Corse, D. E. Huff, R. G. Jones, Q. F. Soper, and C. W. Whitehead, *J. Biol. Chem.*, **175**, 771 (1948).

TABLE II

3-AMINO-*N*-(2-SUBSTITUTED ALKYL)BENZO[*f*]QUINOXALINE-2-CARBOXAMIDES

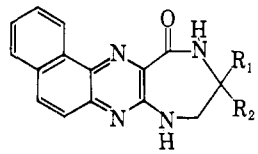


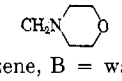
No.	R_1	R_2	X	M.p., °C.	Recrystg. solvent[a]	Yield, %	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
IIIa	H	H	OH	181–182	C	66	$C_{15}H_{14}N_4O_2$	63.82	5.00	19.85	64.24	5.21	19.91
b	C_2H_5	H	OH	210–212	C	72	$C_{17}H_{18}N_4O_2$	65.79	5.85	18.05	65.84	5.80	18.07
c	CH_3	CH_3	OH	200–203	C	53	$C_{17}H_{18}N_4O_2$	65.79	5.85	18.05	65.75	5.82	18.16
d	CH_3	CH_2OH	OH	218–219.5	D, E	54	$C_{17}H_{18}N_4O_3$	62.56	5.56	17.17	62.55	5.27	16.90
IVa	H	H	Cl	231.5–232.5	A	75	$C_{15}H_{13}ClN_4O$	59.90	4.36	18.63	60.04	4.24	18.43
b	C_2H_5	H	Cl	211–212	B	96	$C_{17}H_{17}ClN_4O$	62.10	5.21	17.04	62.15	5.16	16.92
c[b]	CH_3	CH_3	Cl	100–105		70							
d	CH_3	CH_2Cl	Cl	183–184	A	71	$C_{17}H_{16}Cl_2N_4O$	56.20	4.44	15.42	56.36	4.49	15.60

[a] A = benzene, B = xylene, C = ethanol, D = water, E = *N*,*N*-dimethylformamide. [b] Attempts to obtain an analytically pure sample were unsuccessful. The compound was used without further purification.

TABLE III

8,9,10,11-TETRAHYDRO-12*H*-BENZO[5,6]QUINOXALINO[2,3-*e*][1,4]DIAZEPIN-12-ONES



No.	R_1	R_2	M.p., °C.	Recrystg. solvent[a]	Yield, %	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
Va	H	H	258–260	D	75	$C_{15}H_{12}N_4O$	68.17	4.58	21.20	68.43	4.62	21.23
b	C_2H_5	H	168–170	B, D	91	$C_{17}H_{16}N_4O$	69.84	5.52	19.17	69.94	5.41	18.92
c	CH_3	CH_3	200–205	B, C	67	$C_{17}H_{16}N_4O$	69.84	5.52	19.17	69.84	5.50	19.18
d	CH_3	CH_2Cl	215–216	A	56	$C_{17}H_{15}ClN_4O$	62.48	4.63	17.15	61.96	4.59	16.60
e	CH_3		192–194	A	44	$C_{21}H_{23}N_5O_2$	66.82	6.14	18.56	66.64	6.06	18.81

[a] A = benzene, B = water, C = methanol, D = *N*,*N*-dimethylformamide.

ethanol yielded 2-cyano-*N*-(2-hydroxyethyl)acetamide (IIa). The reaction of 1-nitroso-2-naphthylamine (I) with IIa gave 3-amino-*N*-(2-hydroxyethyl)benzo[*f*]-quinoxaline-2-carboxamide (IIIa).[1] 3-Amino-*N*-(2-chloroethyl)benzo[*f*]quinoxaline-2-carboxamide (IVa) was obtained by the reaction of IIIa with thionyl chloride. Cyclodehydrochlorination of IVa with sodium carbonate in boiling *N*,*N*-dimethylformamide proceeded smoothly to afford Va in excellent yield. The other examples of this new ring system (Vb–d) were prepared in similar fashion *via* the reaction sequence previously described. The intermediates IIb–d, IIIb–d, and IVb–d are given in Tables I and II.

The reaction of 10-chloromethyl-8,9,10,11-tetrahydro-10-methyl-12*H*-benzo[5,6]quinoxalino[2,3-*e*][1,4]-diazepin-12-one (Vd) with morpholine afforded 8,9,10,-11-tetrahydro-10-methyl-10-morpholinomethyl-12*H*-benzo[5,6]quinoxalino[2,3-*e*][1,4]diazepin-12-one (Ve).

8,9,10,11-Tetrahydro-12*H*-benzo[5,6]quinoxalino[2,3-*e*][1,4]diazepin-12-thione was prepared by the reaction of Va with phosphorus pentasulfide in boiling pyridine solution.

Experimental[2]

The procedures for the preparation of compounds IId, IIId, IVd, and Vd are general and were used in the preparation of the other members of the series (given in Tables I–III).

(1) D. G. I. Felton, T. S. Osdene, and G. M. Timmis, *J. Chem. Soc.*, 2895 (1954).

(2) Melting points were taken in capillary tubes (Thomas–Hoover capillary melting point apparatus) on a corrected basis.

2-Cyano-*N*-[1,1-bis(hydroxymethyl)ethyl]acetamide (IId).—A solution of 10.5 g. of 2-amino-2-methyl-1,3-propanediol and 11.3 g. of ethyl cyanoacetate in 50 ml. of absolute ethanol was heated under reflux for 1 hr. The solvent was removed *in vacuo* on a rotary evaporator. The solid residue amounted to 21 g., m.p. 127–130°. Recrystallization from ethyl acetate–ethanol afforded 12.7 g. of product, m.p. 130.5–131.5°.

3-Amino-*N*-[1,1-bis(hydroxymethyl)ethyl]benzo[*f*]quinoxaline-2-carboxamide (IIId).—To a solution of 0.9 g. of sodium metal in 200 ml. of absolute ethanol was added 6.9 g. of 1-nitroso-2-naphthylamine and 7.4 g. of 2-cyano-*N*-[1,1-bis(hydroxymethyl)-ethyl]acetamide. The reaction mixture was heated under reflux for 35 min. The solvent was removed *in vacuo* on a rotary evaporator. The solid residue was triturated with glacial acetic acid and then was washed with water. Continuous extraction of the solid with benzene afforded a total of 7 g. of product, m.p. 211–213°. Recrystallization from aqueous *N*,*N*-dimethylformamide afforded 4 g. of product, m.p. 218–219.5°.

3-Amino-*N*-[1,1-bis(chloromethyl)ethyl]benzo[*f*]quinoxaline-2-carboxamide (IVd).—A solution of 10 g. of 3-amino-*N*-[1,1-bis-(hydroxymethyl)ethyl]benzo[*f*]quinoxaline-2-carboxamide in 100 ml. of thionyl chloride was heated under reflux for 2 hr. The solvent was removed *in vacuo* on a rotary evaporator. The residue was made basic with 10% sodium carbonate solution, filtered, and washed thoroughly with water. The crude product amounted to 7.9 g., m.p. 176–181°. Several recrystallizations from benzene raised the melting point to 183–184°.

10-Chloromethyl-8,9,10,11-tetrahydro-10-methyl-12*H*-benzo-[5,6]quinoxalino[2,3-*e*][1,4]diazepin-12-one (Vd).—To a solution of 3 g. of IVd in 20 ml. of *N*,*N*-dimethylformamide was added 1.5 g. of powdered, anhydrous sodium carbonate. The reaction mixture was allowed to boil under reflux for 1 hr. and was then filtered. Water was added to the filtrate until precipitation of the product was complete. After filtration, the product had m.p. 212–214° and weighed 3.9 g. Recrystallization from benzene afforded 1.5 g. of product, m.p. 215–216°.

8,9,10,11-Tetrahydro-10-methyl-10-morpholinomethyl-12*H*-benzo[5,6]quinoxalino[2,3-*e*][1,4]-diazepin-12-one (Ve).—A solution of 3 g. of Vd in 30 ml. of morpholine was heated under reflux for 24 hr. The reaction mixture was cooled in ice and 10 ml. of water was added. A yellow precipitate was deposited which after removal by filtration amounted to 3 g., m.p. 192–193°. Several recrystallizations from benzene afforded 1 g. of product, m.p. 192–194°

8,9,10,11-Tetrahydro-12*H*-benzo[5,6]quinoxalino[2,3-*e*][1,4]-diazepin-12-thione—To a solution of 2 g. of Va in 30 ml. of dry pyridine was added 2 g. of phosphorus pentasulfide. The reaction mixture was boiled under reflux for 80 min., cooled to room temperature, and poured into 70 ml. of hot water. The precipitate which deposited amounted to 2.5 g. After recrystallization from aqueous pyridine, the melting point was 254–256°.

Anal. Calcd. for $C_{15}H_{12}N_4S$: C, 64.26; H, 4.32; N, 19.99; S, 11.44. Found: C, 64.66; H, 4.17; N, 19.96; S, 11.55.

Acknowledgment.—The authors are indebted to Mr. Ronald D. Stewart for technical assistance and Dr. Gordon Ellis and staff for microanalytical results.

The Synthesis of a 1,3-Benzothiazine by a Novel Rearrangement of an N-Substituted Saccharin Derivative

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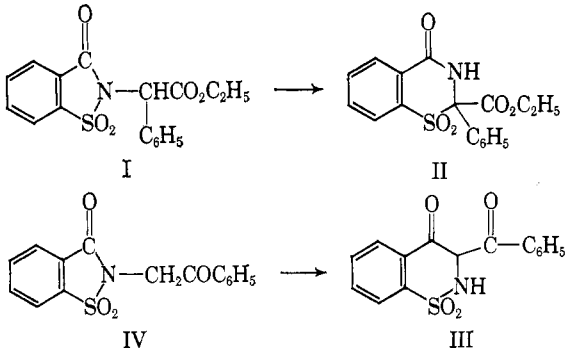
Received February 18, 1964

We wish to report the base-catalyzed ring expansion of an N-substituted saccharin derivative to give a 1,3-benzothiazine. Treatment of N-(α-phenylcarbethoxymethyl)saccharin (I) with sodium ethoxide in ethanol resulted in the formation of ethyl 3,4-dihydro-4-oxo-2-phenyl-2*H*-1,3-benzothiazine-2-carboxylate 1,1-dioxide (II) in 44% yield. This is in contrast to the work of Abe, *et al.*,[1] who obtained the 1,2-benzothiazine, III, when IV was made to undergo the same reaction



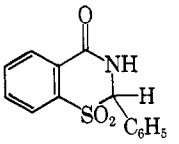
I II

IV III

conditions.[2] The latter reaction, which involves cleavage of a carboxamide linkage, has its counterpart in the phthalimide series.[3] These divergent reaction paths may be related to the relative stabilities of the carbanions formed by abstraction of an α-hydrogen from either I or IV. The formation of III from IV could arise by initial ethanolysis of the amide followed by a Dieckmann ring closure. On the other hand, the formation of the more stable carbanion from I may be favored over ethanolysis and this could react by direct attack on the electrophilic SO_2 group to give II.[4]

Reaction of II with sodium hydride in dimethylformamide followed by the addition of methyl iodide afforded the N-methyl derivative V. When this was subjected to aqueous ethanolic sodium hydroxide at room temperature, rapid saponification and decarboxylation took place to give 3-methyl-2-phenyl-2*H*-1,3-benzothiazin-4(3*H*)-one 1,1-dioxide (VI).

Alkaline treatment of the parent compound (II) resulted in destruction of the 1,3-benzothiazine system as was shown by the rapid liberation of benzaldehyde as well as by the isolation of *o*-carboxybenzenesulfinic acid.[5] Evidently, initial saponification and decarboxylation took place to give VII. Since the N-methyl derivative (VI) was stable to base, the cleavage of the ring may have been initiated by alkaline removal of the amide proton. The instability of VII to alkali was



VII

confirmed by the immediate odor of benzaldehyde which was detected when a crystalline sample was stirred with aqueous alkali. Compound VII was isolated

(1) K. Abe, S. Yamamoto, and K. Matsui, *J. Pharm. Soc. Japan*, **86**, 1058 (1956); *Chem. Abstr.*, **51**, 3499 (1957).

(2) We have confirmed this work.

(3) S. Gabriel and J. Colman, *Ber.*, **33**, 980, 2630 (1900); **35**, 2421 (1902).

(4) Both of these mechanisms have been offered to explain the related rearrangement of α-phthalimidoacetic esters and α-phthalimido ketones to give 4-hydroxyisocarbostyrils; W. J. Gensler, "Heterocyclic Compounds," Vol. 4, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1952, p. 378; C. R. Hauser and S. W. Kantor, *J. Am. Chem. Soc.*, **73**, 1437 (1951).

(5) H. Böhme and W. Schmidt [*Arch. Pharm.*, **286**, 330 (1953)] report the formation of *o*-carboxybenzenesulfinic acid by acid hydrolysis of 3,4-dihydro-2-methyl-4-oxo-2*H*-1,3-benzothiazine 1,1-dioxide.