

Elucidation of the pathways in the reactions of the cyclohexane-1,2-dicarboxylic anhydrides with methylhydrazine and 1,1-dimethylhydrazine seems to possess general applicability. The scope and limitation of the hydrazine-anhydride reactions are being investigated in our laboratory.

### Experimental Section

Melting points, uncorrected, were determined on a Thomas-Hoover apparatus using open capillaries. Infrared spectra were recorded on a Beckman IR-8, using KBr disks for the solid compounds and smears on sodium chloride for the semisolid and liquid compounds. Only the bands for C=O and NH stretching frequencies in wavenumber  $\nu_{\max}$  ( $\text{cm}^{-1}$ ) were reported.  $^1\text{H}$  NMR spectra were determined on a JEOL C-60 HL and R-12 using trifluoroacetic acid (TFA) as a solvent and sodium 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionate (TTP) as a reference.  $^{13}\text{C}$  NMR spectra were determined on a Bruker WH-90 using  $\text{D}_2\text{O}$  as a solvent and  $\text{Me}_4\text{Si}$  as reference. The mass spectra were measured on a Du Pont 21-491 instrument. The thin layer chromatography was done on microscope slides coated with silica gel HF 254 + 366 (Brinkmann Instruments, Inc.). All evaporations were carried out in vacuo in a rotatory evaporator. The elemental analyses were done by Schwarzkopf Microanalytical Laboratories, Woodside, N.Y. The single crystal x-ray analysis was done on a Syntex  $\text{P}_{21}$  diffractometer.

The following two experimental procedures exemplify the general method of synthesis of the compounds derived from *cis*- and *trans*-cyclohexane-1,2-dicarboxylic anhydrides.

**Reaction of Methylhydrazine (1) with *cis*-Cyclohexane-1,2-dicarboxylic Anhydride (3).** A mixture of 5.0 g (0.038 mol) of 3 and 1.75 g (0.038 mol) of 1 was left at room temperature for 24 h at which time the reaction was complete, determined by using TLC. The semisolid residue was washed several times with cold  $\text{CCl}_4$  and dried to give 5.50 g (80%) of a mixture of 6 and 8 with a ratio of 70:30 (estimated from the NMR spectrum of the mixture). The imide 6 dissolved out of the mixture by using hot  $\text{CCl}_4$ . The sample of 6 for analysis was crystallized from a mixture of heptane and MeOH. The  $\text{CCl}_4$ -insoluble residue, 8, was crystallized from a mixture of benzene and MeOH.

**Reaction of 1,1-Dimethylhydrazine (2) with *trans*-Cyclohexane-1,2-dicarboxylic Anhydride (4).** A mixture of 5.0 g (0.038 mol) of 4 and 5.40 g (0.09 mol) of 2 was heated under reflux for 12 h at which time the reaction was complete, determined by using TLC. The excess 2 was evaporated. The product was dried to give 7.50 g of a mixture of 13, 19, and 20 in the approximate ratio of 30:10:50, determined from the NMR spectrum. This mixture was heated in three successive 75-ml portions of  $\text{CCl}_4$ . The residue was filtered and dried to give 3.25 g (40%) of 20. The combined filtrates were evaporated to dryness. This solid was heated in three successive 75-ml portions of heptane. The heptane-insoluble residue was dried to give 0.6 g (8%) of 19. Evaporation of the combined filtrates, followed by washing and drying of the residue, afforded 2.25 g (30%) of 13.

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**Registry No.**—1, 60-34-4; 2, 57-14-7; 3, 13149-00-3; 4, 14166-21-3; 6, 18886-75-4; 7, 60498-47-7; 8, 60498-48-8; 9, 60498-49-9; 10, 60498-50-2; 12, 60498-52-4; 13, 18886-73-2; 14, 60498-53-5; 17a, 60498-54-6; 17b, 60498-55-7; 19, 60387-17-9; 20, 60498-56-8.

### References and Notes

- (1) For the previous paper in this series, see J. Nematollahi, S. Kasina, and D. Maness, *J. Heterocycl. Chem.*, **11**, 351 (1974).
- (2) Support of this investigation by the University of Texas Research Institute is gratefully acknowledged.
- (3) There are a number of currently employed chemotherapeutic compounds with hydrazine moieties and imide structures. Tuberculostatic isonicotinic acid hydrazide, anticonvulsant substituted succinimides, and antihypertensive 1-hydrazinophthalazine may be cited as examples. Additionally, we are planning to employ some of our bicyclic compounds for azasteroids synthesis.
- (4) S. Simonsen, R. Loghry, J. Nematollahi, and S. Kasina, *J. Heterocycl. Chem.*, **13**, 936 (1976).
- (5) S. Simonsen and J. Nematollahi, unpublished results.
- (6) We have observed that a homogeneous mixture of 1,1-dimethylhydrazinium salt of a carboxylic acid and 1,1-dimethylhydrazine gives dimethylammonium salt (see also ref 1). The absence of such species in the reaction of 4 with 2 is due to the precipitation of the hydrazinium salt, 17b, from the reaction mixture.

## A Unique Rearrangement of 3,4-Dihydro-5H-1,3,4-benzotriazepin-5-ones to 3-Methylamino-4(3H)-quinazolinones<sup>1</sup>

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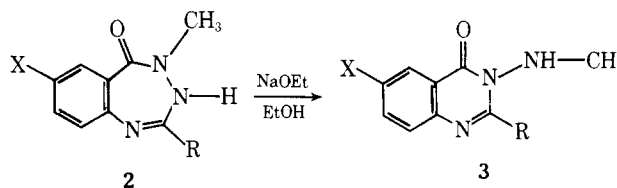
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Ring contractions of benzo-fused seven-membered heterocyclics are well known in the literature and the field has recently been reviewed.<sup>2</sup> The majority of these rearrangements involve 1,4-benzodiazepines being converted to quinazolinones and quinoxalines but there are additional examples involving 1,5-benzodiazepines, various benzoxazepines, and benzothiazepines. However, with the exception of a photocatalyzed contraction of 3,1,4-benzoxadiazepines and an acid-induced rearrangement of 1,2,5-benzotriazepines, there have been very few studies on three heteroatom seven-membered systems.<sup>3,4</sup>

Recently we reported the synthesis of 3,4-dihydro-5H-1,3,4-benzotriazepin-5-ones (**2a-g**) by the reaction of anthranilhydrazides<sup>5</sup> (1) and ortho esters.<sup>6</sup> We have found these benzotriazepines to be extremely labile to alkoxide-induced ring contraction to 3-methylamino-4(3H)-quinazolinones (**3a-g**) (Scheme I).

Scheme I



The latter products were identified by unique features of their  $^1\text{H}$  NMR spectra, for example, an *N*-methyl doublet at  $\delta$  2.47–2.85 and a mutually coupled NH quartet at  $\delta$  6.17–6.38. Both of these resonances were considerably more shielded than the corresponding groups in the initial benzotriazepine, e.g., in **2a** the *N*-methyl appeared as a singlet at  $\delta$  3.22 and the NH as a doublet (coupled to  $\text{C}_2$  H) at  $\delta$  8.65.

Upfield shifts for both the *N*-methyl and the NH resonances would be in accord with their rearrangement into loci no longer  $\alpha$  to the deshielding influences of the nodal planes of the C=O and the  $\text{N}_1\text{-C}_2$  double bond in **2a-g**. Furthermore, the presence of a newly formed  $\text{-NHCH}_3$  moiety in the product is evidenced by the observed splittings.

Additional support for the assignment of the rearrangement products as 3-methylamino-4(3H)-quinazolinones was provided by alternative syntheses (Scheme II). Methyl 2-eth-

Scheme II

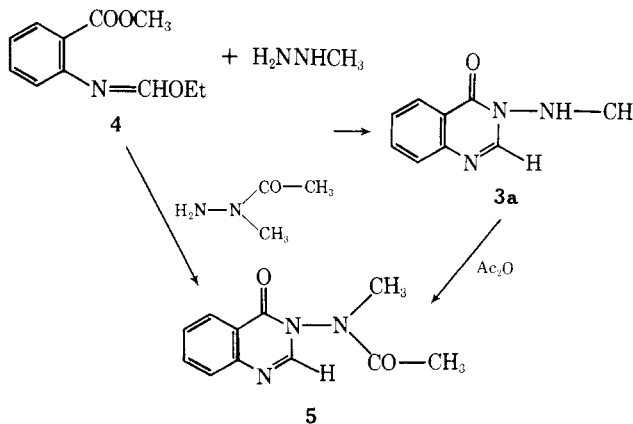


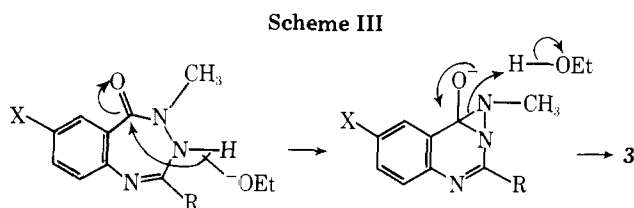
Table I. 3-Methylamino-4(3H)-quinazolinones<sup>a</sup>

Registry no.	Compd	X	R	Yield, %	Mp, °C	Formula
60512-86-9	3a	H	H	50	108–109	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O
59169-44-7	3b	H	CH <sub>3</sub>	95	111.5–112.0	C <sub>10</sub> H <sub>11</sub> N <sub>3</sub> O
60512-87-0	3c	Cl	H	72	151–152	C <sub>9</sub> H <sub>8</sub> ClN <sub>3</sub> O
60512-88-1	3d	NO <sub>2</sub>	H	59	193–195	C <sub>9</sub> H <sub>8</sub> N <sub>4</sub> O <sub>3</sub>
60512-89-2	3e	Cl	CH <sub>3</sub>	93	132–133	C <sub>10</sub> H <sub>10</sub> ClN <sub>3</sub> O
60512-90-5	3f	Cl	C <sub>6</sub> H <sub>5</sub>	86	100.5–101.0	C <sub>15</sub> H <sub>12</sub> ClN <sub>3</sub> O
60512-91-6	3g	Cl	C <sub>2</sub> H <sub>5</sub>	94	154–155	C <sub>11</sub> H <sub>12</sub> ClN <sub>3</sub> O

<sup>a</sup> Analytical data were within ±0.3% for C, H, N. Ed.

oxymethyleneiminobenzoate<sup>6</sup> (4) upon condensation with methylhydrazine yielded 3a, identical in all respects with the material obtained from the rearrangement of 2a. In addition, treatment of 4 with 1-acetyl-1-methylhydrazine gave 5, which was also obtained by acetylation of 3a.

One plausible mechanism for this ring contraction is depicted in Scheme III. Base extraction of the N<sub>3</sub>H proton would



lead to a resonance stabilized anion whose transannular attack on the carbonyl could give a diaziridine intermediate. Ring opening of the latter would produce the 3-methylaminoquinazolinones.

### Experimental Section

Infrared spectra of solids were obtained in KBr disks and of liquids as thin films between NaCl plates on a Beckman IR-33 spectrophotometer. The <sup>1</sup>H NMR spectra were obtained on a Hitachi Perkin-Elmer R20A nuclear magnetic resonance spectrometer. Combustion analyses were provided by Dr. George I. Robertson, Florham Park, N.J.

**A General Procedure for Rearrangement of 3,4-Dihydro-5H-1,3,4-benzotriazepin-5-ones (2a–g) to 3-Methylamino-4(3H)-quinazolinones (3a–g).** A solution of 50 mmol of the requisite benzotriazepine (2a–g) in 50 ml of anhydrous ethanol was treated with a freshly prepared solution of 5.0 mmol of NaOEt in 25 ml of absolute ethanol (obtained by dissolution of 0.12 g of sodium in the 25 ml of alcohol). The deep red solution which resulted was heated with stirring at reflux for 20 h, chilled, and filtered in vacuo. The resulting 3-methylamino-4(3H)-quinazolinones were recrystallized from ethanol to analytical purity. The nitro isomer (3d) was recrystallized from 3:1 acetic acid–ethanol. Yields and properties are reported in Table I.

**3-Methylamino-4(3H)-quinazolinone (3a) from Methyl 2-Ethoxymethyleneiminobenzoate (4).** Methyl 2-ethoxymethyleneiminobenzoate<sup>6</sup> (4, 10.36 g, 50.0 mmol) was treated with 3.00 g (6.0 mmol) of methylhydrazine. Two minutes after the addition, evolution of considerable heat was noted and the product 3a began to precipitate. The reaction mixture was chilled in an ice bath and the solid collected on a filter and washed with ether. Analytically pure, white crystals of the quinazolinone (8.00 g, 92%) were collected: mp 109–110.5 °C; ir (KBr) 3230 (N–H), 1675 (C=O), and 1650 cm<sup>-1</sup> (C=N); NMR (CDCl<sub>3</sub>) δ 2.89 (s, 3, CH<sub>3</sub>), 5.97 (s, 1, NH), 7.20–8.30 (m, 5, ArH and C<sub>2</sub>H). The compound was spectrally identical (<sup>1</sup>H NMR and ir), of identical melting point, and of undepressed mixture melting point with the material obtained by rearrangement of 2a.

**3-(N-Acetyl-N-methylamino)-4(3H)-quinazolinone (5) from Methyl 2-Ethoxymethyleneiminobenzoate (4).** A solution was prepared from 50.0 mmol of 4 and 1-acetyl-1-methylhydrazine.<sup>7</sup> Immediately it developed a deep red color and precipitated the product quinazolinone (5). The mixture was chilled in ice, and the solid was filtered, washed with ether, and recrystallized twice from ethanol to yield 6.40 g (59%) of 5: mp 119–120 °C; ir (KBr) 1690 (C=O), 1675 (C=O), and 1650 cm<sup>-1</sup> (C=N); NMR (CDCl<sub>3</sub>) δ 1.97

and 2.36 (s, 3, COCH<sub>3</sub>), 3.40 and 3.59 (s, 3, NCH<sub>3</sub>),<sup>8</sup> and 7.30–8.50 (m, 5, ArH and C<sub>2</sub>H).

Anal. Calcd for C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>: C, 60.82; H, 5.10; N, 19.34. Found: C, 61.01; H, 5.08; N, 19.17.

**Acetylation of 3-Methylamino-4(3H)-quinazolinone. Preparation of 5.** A mixture of 0.10 mol of acetic anhydride and 0.048 mol of 3a was stirred and heated at reflux for 2 h and cooled to room temperature, and the excess acetic anhydride was removed on a rotary evaporator. The viscous, amber oil which resulted was induced to crystallize by trituration with a small quantity of ether. The crude product was recrystallized from ethanol to give 8.05 g (78%) of analytically pure 5, mp 120–121 °C, identical in all respects with the material obtained by condensation of 4 and 1-acetyl-1-methylhydrazine.

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**Registry No.**—2a, 59169-76-5; 2b, 59169-80-1; 2c, 59169-77-6; 2d, 59169-79-8; 2e, 59169-81-2; 2f, 59169-88-9; 2g, 59169-84-5; 4, 59204-51-2; 5, 60512-92-7; methylhydrazine, 60-34-4; 1-acetyl-1-methylhydrazine, 3530-13-0.

### References and Notes

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- As another example of the slow rotation of bulky groups around the N<sub>3</sub> quinazolinone nitrogen [see J. B. Taylor, D. R. Harrison, and F. Fried, *J. Heterocycl. Chem.*, **9**, 1227 (1972)], the N-methyl and the acetyl methyl resonances were evidenced as two temperature-dependent double peaks in the ratio of 2:1 at room temperature.

### Acidity Functions of Hydrochloric Acid, Perchloric Acid, and Sulfuric Acid and pK<sub>a</sub> Values of Some Primary Aromatic Amines in 50% Volume/Volume Aqueous Ethanol<sup>1</sup>

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The general applicability of the Hammett acidity function has been strongly questioned.<sup>2</sup> In spite of this, this parameter still remains the principal measure of the ability of a medium to transfer a proton to a base. In fact many treatments of deviations from Hammett acidity function behavior are expressed in terms of the acidity function.<sup>3</sup> The original deter-