to cool, the crystalline solid which formed was collected by filtration to give 0.049 g (29%) of **21**, mp 264.5–265.5°. The infrared and nmr spectra of this material were identical with those of authentic **21**.

**Transannular Cyclization of 27.**—A solution of 0.4 g of **27** and 5 ml of ether was treated with 0.2 ml of a 1:1 solution of 50% hydriodic acid in ethanol. The ether was decanted and the residue was taken up in methanol. Because a crystalline solid was not deposited from the methanolic solution, the solvent was evaporated to leave a thick residue which was dried at 50° (1.0 mm) over phosphorous pentoxide for 2 days. The infrared and nmr spectra of the dried residue (0.45 g) proved to be superimposable on those of **26**.

**Registry No.**—**11**, 16620-83-0; methiodide of **11**, 16620-59-0; **12**, 5654-83-1; **14**, 16620-61-4; methiodide of **14**, 16620-62-5; **16**, 15932-74-8; methiodide of **16**, 16620-64-7; **19**, 16620-84-1; methiodide of **20**, 16620-85-2; **21**, 16620-86-3; **23**, 16620-88-5; methiodide of **23**, 16620-87-4; **25**, 16620-89-6; **26**, 16620-90-9; **27**, 16620-91-0.

**Acknowledgment.**—The authors are grateful to Dr. Rodger Foltz for the mass spectral determinations.

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# The Preparation of 2-Hydroxyamino-α,α,α-trifluoro-*p*-toluenesulfonamide by Catalytic Hydrogenation and Its Use in the Synthesis of 2,3-Dihydro-4H-1,2,4-benzothiadiazin-4-ol 1,1-Dioxides. Studies in Infrared and Proton Magnetic Resonance Spectra

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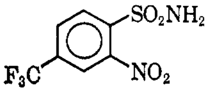
*Received December 5, 1967*

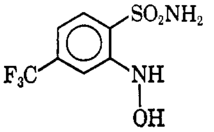
The hydrogenation of 2-nitro-α,α,α-trifluoro-*p*-toluenesulfonamide (**1**) over a palladium catalyst in ethanol proceeded rapidly (0.5 hr) at room temperature; hydrogen uptake ceased with the absorption of 2 molar equiv to give a 90% yield of pure 2-hydroxyamino-α,α,α-trifluoro-*p*-toluenesulfonamide (**2**). Reduction of **2** to the amine (**3**) required a temperature of 50–60° and about 3 hr. The acid-catalyzed cyclization of **2** with formaldehyde and acetaldehyde led to the novel 2,3-dihydro-4H-1,2,4-benzothiadiazin-4-ol 1,1-dioxides (**4a**, **b**). The ir and pmr spectra of these and related reference compounds have made possible precise spectral assignments to the several different types of NH protons in these compounds.

A recent paper[1] has described the intramolecular trapping of the intermediate hydroxyamino derivatives formed during the platinum-catalyzed reductions in ethanol of 2-nitro-2′-carboxy-, 2-nitro-2′-carbalkoxy-, and 2-nitro-2′-cyanobiphenyl; in addition, these hydrogenations formed appreciable amounts of the cyclization products arising *via* the intramolecular cyclization of the corresponding amine derivatives. The one exception was found in the reduction of 2,2′-dinitro-6,6′-dicyanobiphenyl; here, the 2,2′-dihydroxyamino-6,6′-dicyanobiphenyl which formed neither underwent intramolecular cyclization nor conversion to the diamino derivative during hydrogenation, but did cyclize during subsequent recrystallization. This report was noteworthy, since the literature contains but one earlier reference[2] to the isolation of any product other than amines (or their derivatives) from the catalytic hydrogenation of nitro compounds and that reference also involved the intramolecular trapping of the hydroxyamino and amino derivatives formed during the reduction of ethyl 2-nitrophenylacetate.

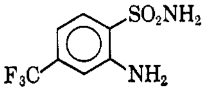
We have studied the palladium-catalyzed hydrogenation of a suspension of 2-nitro-α,α,α-trifluoro-*p*-toluenesulfonamide (**1**) in ethanol. At *ca.* 20–25°, hydrogen uptake is rapid (~0.5 hr) and ceases after the absorption of 2 molar equiv of hydrogen. Filtration of the suspended catalyst, concentration of the filtrate, and recrystallization of the residual solid gave a 90% yield of pure hydroxyamino derivative (**2**). If, however, following the absorption of the 2 molar equiv of hydrogen, the temperature was raised to 50–60° a slow uptake of hydrogen was initiated and *ca.* 3.5 hr were required to complete the reduction to the amine (**3**) even though **2** was completely in solution. Finally, when the isolated **2** was subjected to hydrogenation with fresh solvent and catalyst at 50–60° a similar slow reduction to **3** was observed.



**1**

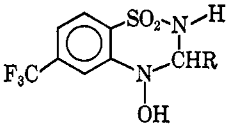


**2**

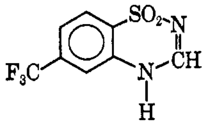


**3**

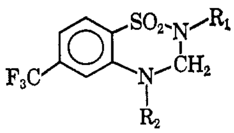
The acid-catalyzed cyclization reactions[3] of **2** with formaldehyde and acetaldehyde gave the novel 2,3-dihydro-4H-1,2,4-benzothiadiazin-4-ol 1,1-dioxides (**4a** and **b**). The reaction of **4a** with formic acid for 1 hr at 90° gave two compounds, **5**, the expected dehydration product, and **6a**, the 4-formyl ester.



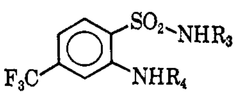
**4a**, R = H
**b**, R = $CH_3$



**5**



**6a**, $R_1 = H$; $R_2 = O_2CH$
**b**, $R_1 = R_2 = H$
**c**, $R_1 = H$; $R_2 = CHO$
**d**, $R_1 = CHO$; $R_2 = H$
**e**, $R_1 = C_2H_5$; $R_2 = H$
**f**, $R_1 = H$; $R_2 = C_2H_5$



**7a**, $R_3 = C_2H_5$; $R_4 = H$
**b**, $R_3 = H$; $R_4 = C_2H_5$

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[1] C. W. Muth, J. R. Elkins, M. L. DeMatte, and S. T. Chiang, *J. Org. Chem.*, **32**, 1106 (1967).

[2] F. J. DiCarlo, *J. Amer. Chem. Soc.*, **66**, 1420 (1944).

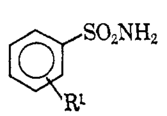
[3] H. L. Yale and J. T. Sheehan, *J. Org. Chem.*, **26**, 4315 (1961).

The acid-catalyzed cyclization of **3** with formaldehyde gave **6b**; the same procedure with **7a** gave the 2-ethyl- (**6e**), and with **7b** the 4-ethyl- (**6f**) derivatives of **6b**. The reaction of **6b** with formic acid for 1 hr at 90° gave the 4-formyl derivative (**6c**) as the major product; a careful search did not reveal the presence of any 2-formyl derivative (**6d**). When the same reactants were heated under reflux, a complex mixture of products resulted, and of these, only **6c** in small yield, was identified.

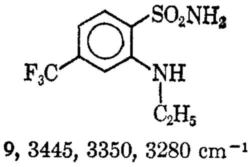
The ir and pmr spectra of the above compounds were studied in detail, and certain spectral assignments for the several different types of protons are discussed in the two sections below; the uv spectra were determined on only a few compounds when these uv data proved to be indiscriminate as to the structural details of interest in this study.

**Infrared Spectra.**—For the earlier work[3,4] in the elucidation of the structures of 1,2,4-benzothiadiazine 1,1-dioxides, low resolution spectra of the crystalline solids were adequate. In the present work, high-resolution spectra in deuteriochloroform (1 mg/ml) were necessary to minimize intermolecular hydrogen bonding.[5]

In **6b**, the 4- and 2-NH stretch absorptions were observed at 3440 and 3330 cm$^{-1}$, respectively; confirmatory evidence for these assignments was found in the model spectra of **6e** and **f**, where the corresponding maxima were seen at 3440 and 3330 cm$^{-1}$. In **6c**, the 2-NH absorption was found at 3340 cm$^{-1}$. In **4a** and **b**, two maxima were seen at 3540 and 3330 cm$^{-1}$; the former was attributable to the unbonded 4-OH[6] and the latter to the 2-NH stretch vibrations. The spectrum of **1** showed two maxima at 3455 and 3350 cm$^{-1}$; the spectrum of **2** showed four maxima at 3560,[6] 3440, 3340, and 3300 cm$^{-1}$ while **3** gave four maxima at 3470, 3440, 3370, and 3340 cm$^{-1}$. The several NH stretch assignments in **2** and **3** cannot be made unambiguously; however, it would appear that the asymmetrical and symmetrical stretch of the NH$_2$ of R–SO$_2$NH$_2$ groups are usually found at *ca.* 3450 and 3350 cm$^{-1}$, as seen in the spectra of **1**, **8a–f**, **9**, and **10**; it follows, then, that the 3440- and 3340-cm$^{-1}$ maxima in **2** and **3** are probably associated with that group in each compound; and, finally, that the band at 3300 cm$^{-1}$ in **2** is attributable to the N–H vibrational mode of the hydroxyamino group.



**8a**, R$^1$ = H, 3450, 3350 cm$^{-1}$
**b**, R$^1$ = *p*-CH$_3$, 3445, 3345 cm$^{-1}$
**c**, R$^1$ = *o*-CH$_3$, 3445, 3345 cm$^{-1}$
**d**, R$^1$ = *o*-CF$_3$, 3470, 3360 cm$^{-1}$
**e**, R$^1$ = *m*-CF$_3$, 3450, 3350 cm$^{-1}$
**f**, R$^1$ = *p*-CF$_3$, 3450, 3350 cm$^{-1}$



**9**, 3445, 3350, 3280 cm$^{-1}$

$CH_3SO_2NH_2$

**10**, 3450, 3350 cm$^{-1}$

**Proton Magnetic Resonance Spectra.**—The proton magnetic resonance spectra were determined in deuteriodimethyl sulfoxide.[7] In **6b**, the 2 proton was seen as a doublet at $\tau$ 2.10 ($J$ = 8 cps) while the 4 proton was a broad peak centered at $\tau$ 2.47. Both the 2 and 4 protons were coupled with the 3 protons, since the latter appeared as a quartet at $\tau$ 5.28 ($J_\alpha = J_\beta = 2.5$; $J_{\alpha\beta} = 8.3$)[8] which collapsed to a singlet at $\tau$ 5.28 after equilibration with deuterium oxide. In **6c**, the 2 proton was not coupled with the 3 protons and was seen together with the 5 proton as a broad, two-proton singlet centered at $\tau$ 1.33; the deshielding by the 4-formyl group of the pair of 3 protons resulted in the latter being shifted downfield 60 cps and appearing as a singlet at $\tau$ 4.68; after equilibration with deuterium oxide, the spectrum showed the broad one-proton peak of the 5 proton at $\tau$ 1.33. In **6e**, the 4 and 3 protons were seen as a broad peak at $\tau$ 2.38 and as a doublet at $\tau$ 5.03 ($J$ = 3), respectively, and in **6f**, the 2 and 3 protons were signals forming a broad peak at $\tau$ 2.12 and a doublet at $\tau$ 5.20 ($J$ = 8), respectively; deuteration of **6e** and **6f** resulted in the appearance of two singlets at $\tau$ 5.03 and 5.20, respectively. In **4a**, the 2 proton was coupled with the 3 protons and appeared as a triplet at $\tau$ 1.07 ($J$ = 8); the proton of the 4-hydroxyl group, not coupled with the 3 protons, appeared as a singlet at $\tau$ −0.33; the 3 protons formed a doublet at $\tau$ 5.25 ($J$ = 8) which collapsed to a singlet at $\tau$ 5.23 after equilibration with deuterium oxide. In **4b**, the protons at 2 and 4 were seen as broad peaks at $\tau$ 2.34 and −2.28, respectively, while the single 3 proton appeared as a multiplet at $\tau$ 5.08 ($J$ = 20); treatment with deuterium oxide gave a multiplet at $\tau$ 5.07 ($J$ = 20).

In **3**, the two pairs of equivalent protons of the sulfonamido and the amino groups were seen as singlets at $\tau$ 2.52 and 3.75, respectively; both pairs were exchangeable.

## Experimental Section[9]

**2-Nitro-$\alpha,\alpha,\alpha$-trifluoro-*p*-toluenesulfonamide** (**1**).—A suspension of 367 g (0.82 mol) of bis(2-nitro-$\alpha,\alpha,\alpha$-trifluoro-*p*-tolyl) disulfide in 1800 ml of 90% acetic acid was diffused with gaseous chlorine at 35–40° for 6 hr. The clear solution which formed was concentrated *in vacuo* from a hot water bath, the residue was treated with 500 ml of toluene, and the toluene solution, containing the sulfonyl chloride, was added dropwise at room temperature to 500 ml of aqueous ammonia (*d* 0.9). The solution was heated on the steam bath for 1 hr to give crude **1**; this was extracted with 400 ml of 20% aqueous sodium hydroxide and filtered, and the filtrate treated with excess 20% aqueous hydrochloric acid. The solid was filtered, washed with cold water, and recrystallized from water to give 362 g (84% yield) of **1**: mp 169–170°; $\lambda_{\max}^{\text{EtOH}}$ m$\mu$ ($\epsilon$) 276 (sh) (16,000), 266 (16,500).

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[4] H. L. Yale, K. Losee, and J. Bernstein, *J. Amer. Chem. Soc.*, **82**, 2042 (1960).

[5] The author is indebted to Miss Barbara Keeler of this institute for these spectra. The effects of concentration on hydrogen bonding could not be carried out owing to the low solubility of these compounds in deuteriochloroform.

[6] Unbonded hydroxyl groups are not very sensitive to changes in molecular structure, so that this group in **2**, **4a**, and **4**. would be expected to have similar absorption maxima. *Cf.* R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1966, p 61.

[7] The author is indebted to Dr. A. I. Cohen of this institute for these spectra.

[8] This notation is that of ref 6, p 81.

[9] All melting points were determined in capillary tubes in an electrically heated oil bath and are uncorrected. Elemental analyses were carried out by Mr. J. F. Alicino and his associates of this institute.

*Anal.* Calcd for $C_7H_5F_3N_2O_4S$: C, 31.11; H, 1.86; N, 10.37. Found: C, 31.14; H, 1.93; N, 10.33.

**2-(Hydroxyamino)-α,α,α-trifluoro-*p*-toluenesulfonamide (2).**—Two identical experiments, each involving 30.0 g (0.11 mol) of **1**, 5.0 g of 5% Pd–C, and 300 ml of absolute ethanol were shaken at 20–25° under 50 psi of hydrogen; approximately 0.5 hr was required for the uptake of 0.22 mol. Work-up of the combined runs gave 51.0 g (90% yield) of colorless **2**: mp 184–185° dec after recrystallization from water; $\lambda_{\max}^{\mathrm{EtOH}}$ m$\mu$ ($\epsilon$) 313 (3100), 247 (8200), 213 (23,300).

*Anal.* Calcd for $C_7H_7F_3N_2O_3S$: C, 32.83; H, 2.76; N, 10.93. Found: C, 32.74; H, 2.73; N, 10.93.

The compound was soluble in dilute aqueous sodium hydroxide forming an orange-yellow solution; acidification gave a colorless solution from which unchanged **2** precipitated; a test of **2** with aqueous ferric chloride was negative.

**2-Amino-α,α,α-trifluoro-*p*-toluenesulfonamide (3). A. By Hydrogenation of 1.**—Two identical reaction mixtures as in the above experiment were hydrogenated at 50–60° under 50 psi of hydrogen; approximately 3.5 hr were required for the absorption of 0.33 mol. The two runs were combined and worked up to give 54.0 g (96% yield) of colorless **3**: mp 148–149° after recrystallization from water; $\lambda_{\max}^{\mathrm{EtOH}}$ m$\mu$ ($\epsilon$) 320 (4200), 247 (10,100), 213 (24,100).

*Anal.* Calcd for $C_7H_7F_3N_2O_2S$: N, 11.66; S, 13.35. Found: N, 11.80; S, 13.35.

The compound was soluble in dilute aqueous sodium hydroxide forming a colorless solution; acidification precipitated unchanged **3**.

B. **By Hydrogenation of 2.**—A solution of 25.6 g (0.1 mol) of **2**, 5.0 g of 5% Pd–C, and 300 ml of absolute ethanol was heated to 50–60° and shaken under 50 psi of hydrogen. Again, *ca.* 3 hr were required for the theoretical uptake of hydrogen to occur. Work-up as above gave 21.3 g (88% yield) of **3**, mp 148–149° after recrystallization from water.

**2,3-Dihyro-2-ethyl-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine 1,1-Dioxide** (**6e**).—A solution of 2.51 g (0.0094 mol) of 2-amino-N-ethyl-α,α,α-trifluoro-*p*-toluenesulfonamide,[3] 0.82 g (0.01 mol) of 37% aqueous formaldehyde, 1.0 ml of 10% aqueous hydrochloric acid, and 50 ml of 95% ethanol was heated under reflux for 24 hr and concentrated to dryness *in vacuo*. The residue was recrystallized from hexane to give 2.20 g (84% yield) of **6e**, mp 72–74°.

*Anal.* Calcd for $C_{10}H_{11}F_3N_2O_2S$: C, 42.84; H, 3.96; N, 10.00. Found: C, 42.85; H, 3.85; N, 10.27.

**2,3-Dihydro-4-ethyl-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine 1,1-Dioxide** (**6f**).—A solution of 2.68 g (0.01 mol) of 2-(ethylamino)-α,α,α-trifluoro-*p*-toluenesulfonamide,[3] 0.82 g (0.01 mol) of 37% aqueous formaldehyde, 1.0 ml of 10% aqueous hydrochloric acid, and 50 ml of 95% ethanol was heated under reflux for 3 hr and concentrated to dryness *in vacuo*. The residue was recrystallized from Skellysolve E to give 2.42 g (85% yield) of **6f**, mp 99–101°.

*Anal.* Calcd for $C_{10}H_{11}F_3N_2O_2S$: C, 42.84; H, 3.96; N, 10.00. Found: C, 42.72; H, 3.83; N, 10.14.

**2,3-Dihydro-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazin-4-ol 1,1-Dioxide** (**4a**).—Employing the procedure used to prepare **6f** but with **2** gave a 95% yield of **4a**: mp 164–166° after recrystallization from 10% 2-propanol–90% water; $\lambda_{\max}^{\mathrm{EtOH}}$ m$\mu$ ($\epsilon$) 320 (2600), 255 (9200), 213 (18,200).

*Anal.* Calcd for $C_8H_7F_3N_2O_3S$: C, 35.82; H, 2.63; N, 10.44; S, 11.95. Found: C, 36.05; H, 2.66; N, 10.41; S, 12.17.

**2,3-Dihydro-3-methyl-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine-4-ol 1,1-Dioxide** (**4b**).—A solution of 2.54 g (0.01 mol) of **2**, 0.44 g (0.01 mol) of acetaldehyde, 1.0 ml of 10% aqueous hydrochloric acid, and 50 ml of 95% ethanol was heated under reflux for 24 hr and concentrated to dryness *in vacuo*. The brown syrupy residue was covered with 10% aqueous hydrochloric acid and kept at room temperature until it solidified. The brown solid was recrystallized once from benzene and once from toluene to give 0.60 g (21% yield) of **4b**, mp 160–162 dec.

*Anal.* Calcd for $C_9H_9F_3N_2O_3S$: N, 9.91; S, 11.36. Found: N, 9.84; S, 11.47.

**2,3-Dihydro-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine 1,1-Dioxide** (**6b**).—The procedure employed with **6f** but starting with **3** gave a 95% yield of **6b**: mp 163–165° after recrystallization from water; $\lambda_{\max}^{\mathrm{EtOH}}$ m$\mu$ ($\epsilon$) 327 (35,000), 253 (12,500), 213 (22,300).

*Anal.* Calcd for $C_8H_7F_3N_2O_2S$: C, 38.10; H, 2.80; N, 11.11. Found: C, 38.30; H, 2.89; N, 11.34.

The compound was soluble in dilute aqueous sodium hydroxide forming a colorless solution; acidification precipitated unchanged **6b**.

**2,3-Dihydro-3-methyl-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine 1,1-Dioxide.**—This compound was synthesized in view of the low yield obtained with **4b** above. A 0.01 *M* run, employing the same conditions but substituting **3** for **2** gave a 74% yield of product, mp 195–197°.

*Anal.* Calcd for $C_9H_9F_3N_2O_2S$: C, 40.60; H, 3.41; N, 10.50. Found: C, 40.40; H, 3.40; N, 10.23.

**Dehydration of 4a to 5.**—A suspension of 0.5 g (0.0019 mol) of **4a** and 5 ml of 98–100% formic acid was heated under anhydrous conditions on the steam bath for 1 hr and concentrated to dryness *in vacuo*. The residue was desiccated for 24 hr over potassium hydroxide pellets to give a sticky solid; this was extracted with 10 ml of anhydrous ether to give 0.20 g of a colorless solid, mp 175–187°. The latter was extracted with 5 ml of boiling anhydrous toluene and the hot suspension filtered. The colorless crystals which separated from the cooled filtrate were filtered to give 0.070 g of **6a**, mp 169–171°.

*Anal.* Calcd for $C_9H_7F_3N_2O_4S$: C, 36.48; H, 2.38; N, 9.43; CHO, 10.83. Found: C, 36.43; H, 2.23; N, 9.37; CHO, 10.91.

The toluene-insoluble material was recrystallized from water to give 0.050 g of **5**, mp 263–265°; a mixture melting point with authentic **5**[3] was 263–265°, and the ir spectra of the two samples were identical.

*Anal.* Calcd for $C_8H_5F_3N_2O_2S$: C, 38.40; H, 2.02; N, 11.20. Found: C, 38.45; H, 2.27; N, 11.05.

The 10-ml anhydrous ether extract (see above) was evaporated to dryness to give a yellow oil. The oil could be induced to solidify partially following extraction with hexane; this semisolid material was only partially soluble in boiling benzene. The hot benzene solution was decanted from an oil and allowed to cool; an oil separated but scratching converted this to a solid, mp 90–170°; its ir spectrum showed both NH and CO absorption. It was apparent that the formic acid reaction had led to a complex mixture of products.

In $CDCl_3$, the ir spectrum of **6a** showed the anticipated maxima at 3330 cm$^{-1}$ for the 2-NH proton. In $d_6$-DMSO, the pmr spectrum of **6a** gave the expected broad two-proton peak of the 2 and 5 hydrogens at $\tau$ 1.33; the three protons were again deshielded by the carbonyl oxygen and appeared as a broad singlet at $\tau$ 4.67. The formyl proton was a singlet at $\tau$ 0.87. Following equilibration with deuterium oxide, the signal at $\tau$ 1.33 was seen as a broad one-proton peak; the remainder of the spectrum was unchanged.

**Reaction of 6b with Formic Acid. A. 2,3-Dihydro-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine-4-carboxaldehyde 1,1-Dioxide** (**6c**).—A mixture of 2.0 g (0.0079 mol) of **6b** and 20 ml of 98–100% formic acid was heated for 1 hr on the steam bath under anhydrous conditions and then concentrated to dryness *in vacuo*. The crystalline residue, mp 173–177°, weighed 2.05 g. Recrystallization from 20 ml of 2-propanol gave 1.57 g (71% yield) of colorless **6c**, mp 184.5–186.0°.

*Anal.* Calcd for $C_9H_7F_3N_2O_3S$: C, 38.56; H, 2.52; N, 10.00. Found: C, 38.67; H, 2.37; N, 10.28.

The 2-propanol mother liquors from the recrystallization of **6c** were evaporated to dryness. The residual oil was induced to crystallize by the addition of 5 ml of bezene. Filtration gave 0.48 g of solid, mp 120–130°. The ir spectrum showed a single CO and two NH bands. Recrystallization from 10 ml of benzene–hexane (1:1) gave 0.20 g of solid, mp 126–132°, with unchanged ir spectrum. Elemental analyses (Found: C, 38.64; H, 2.86; N, 11.06) were indicative of a mixture of products.

B.—When the reactants of procedure A were heated under reflux for 18 hr and concentrated to dryness *in vacuo*, the residual oil showed two strong NH and one carbonyl band in the ir. The oil was induced to crystallize by the addition of 50 ml of anhydrous ether to give 0.96 g of solid, mp 194–196°; this solid had the same ir spectrum as the oil. Attempts to obtain a single homogenous product from this solid were unsuccessful.

The 50 ml of anhydrous ether (see above) was evaporated to dryness. The residue, 1.4 g of oil, was dissolved in 15 ml of boiling benzene, the solution filtered, and the filtrate cooled to give 0.15 g of crude **6c**; recrystallization from 2-propanol gave 0.13 g of pure **6c**, mp 184.5–186.0°; the ir spectrum of this material and the **6c** described above were identical.

**Registry No.**—**1**, 577-61-7; **2**, 16156-17-5; **3**, 657-70-5; **4a**, 16156-19-7; **4b**, 16156-20-0; **5**, 655-67-4; **6a**, 16156-22-2; **6b**, 720-49-0; **6c**, 16156-24-4; **6e**, 16156-25-5; **6f**, 16156-26-6; **8a**, 98-10-2; **8b**, 70-55-3; **8c**, 88-19-7; **8d**, 1869-24-5; **8e**, 672-58-2; **8f**, 830-43-3; **9**, 724-94-7; **10**, 3144-09-0; 2,3-dihydro-3-methyl-6-(trifluoromethyl)-4H-1,2,4-benzothiadiazine 1,1 dioxide, 16156-28-8.

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# Alkylation of Alkylidenebisdimethylamines

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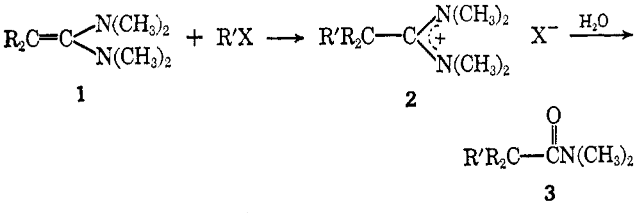
*Received January 23, 1968*

Alkylation of alkylidenebisdialkylamines (enediamines) with alkyl halides gave both C and N alkylation. Carbon alkylation afforded the amidinium salts, **2**, which were readily hydrolyzed to the amides, **3**. This carbon–carbon bond-forming reaction thus provides a convenient new route to substituted amides. The initial products of N alkylation are unstable and react with the starting enediamine, in the case of 2-methylpropenylidenebisdimethylamine, to yield condensation product, **6**, and an N,N-dimethylalkylamine. Elimination of hydrogen halide from butyl halides by the strongly basic enediamines also was observed.

Alkylation of enamines has become an important synthetic tool for the preparation of substituted ketones and aldehydes.[1,2] Analogously, the alkylation of alkylidenebisdialkylamines (enediamines), which have recently become conveniently accessible,[3] offers a new route to carboxylic acids and amides. Although the alkylation of enediamines with methyl and ethyl iodides has been observed previously,[4] the scope of this reaction and its utility for organic synthesis have not been elaborated.

## Results

Alkylation of vinylidenebisdimethylamine (**1a**) and 2-methylpropenylidenebisdimethylamine (**1b**) with methyl iodide, benzyl bromide or chloride, and allyl bromide in acetonitrile solution gave the amidinium salts **2c–h** in good yield. The salts were characterized by elemental analysis and nmr spectroscopy and in the case of **2c** and **2e** by comparison with authentic samples prepared by independent syntheses. The reaction of vinylidenebisdimethylamine with butyl bromide and of 2-methylpropenylidenebisdimethylamine with butyl bromide and iodide, as well as benzyl chloride, afforded mixtures of salts from which the amidinium salts could not be isolated.

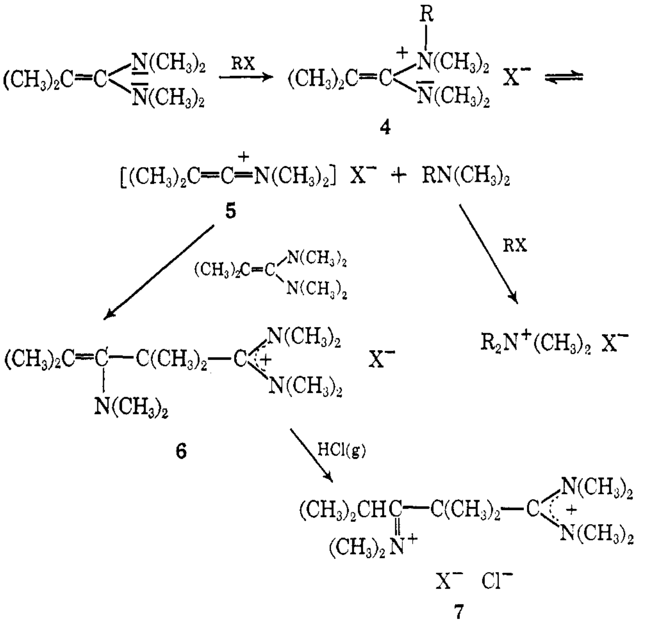


a, $R = H$
b, $R = CH_3$
c, $R = H; R' = CH_3$
d, $R = R' = CH_3$
e, $R = H; R' = C_6H_5CH_2$
f, $R = CH_3; R' = C_6H_5CH_2$
g, $R = H; R' = CH_2{=}CHCH_2$
h, $R = CH_3; R' = CH_2{=}CHCH_2$
i, $R = H; R' = n\text{-}C_4H_9$
j, $R = CH_3; R' = n\text{-}C_4H_9$

The amidinium salts, or the crude salt mixtures in those cases where no amidinium salt could be isolated, were hydrolyzed with dilute sodium hydroxide to afford moderate to good yields of the N,N-dimethylamides, **3e–j**. The yields of amides, shown in Table I, were calculated on the basis of the starting alkylidenebisdimethylamine and therefore represent over-all yields.

The reaction of benzyl chloride with 2-methylpropenylidenebisdimethylamine also afforded 6% of N,N-dimethylbenzylamine in addition to the expected amide (**3f**). Examination by nmr spectroscopy of the aqueous solution remaining after extraction of the amide indicated considerable quantities of ammonium or amidinium salts. These were precipitated as the fluorophosphates and fractionally crystallized to obtain 18% of dibenzyldimethylammonium fluorophosphate and 13% of the condensation product **6**, X = $PF_6$ (Scheme I). Compound **6** was characterized by elemental analysis and nmr spectroscopy and by conversion with dry hydrogen chloride to a second salt whose nmr spectrum was consistent with structure **7**. Compound **6** in the form of its iodide also was isolated

SCHEME I



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