(6.1 g., 22.6%) of the cycloadduct as well as a small amount (1.61 g., 5.9%) of triethylammonium phenylmethanesulfonate (m.p. 114–115°) were isolated. The characterization of the products was accomplished by mixture melting points and by comparing infrared and n.m.r. spectra of the products with those of authentic samples.

Acknowledgment.—This investigation was supported by the U. S. Army Research Office (Durham) under Contract DA-31-124-ARO-D-211 and by Public Health Service Research Grant No. CA-04536-06 from the National Cancer Institute.

1,3-Dipolar Cycloadditions. XII.[1] The Synthesis of 1,3,4-Thiadiazolidine-5-thiones

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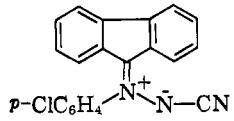
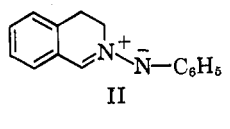
The reaction of N,N′-dialkylhydrazines with aromatic aldehydes and carbon disulfide affords a general synthesis of 3,4-dialkyl-1,3,4-thiadiazolidine-5-thiones. Instead of the first two components, hexasubstituted hexahydro-1,2,4,5-tetrazines may be used advantageously. Possible reaction mechanisms are discussed. Among the chemical and physical evidence which serves to establish the structure of the cyclic products, the n.m.r. spectra deserve attention owing to certain unusual features.

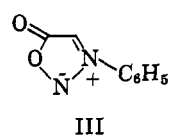
Azomethine imines have been recognized in recent years as a new class of 1,3-dipoles.[4] Those derived from diaryldiazomethanes and diazocyanides (I) are obtainable as stable, crystalline substances.[5] Upon warming with dipolarophiles, they readily undergo cycloaddition.[6] Still greater is the reactivity toward cycloaddition displayed by 3,4-dihydroisoquinoline-N-aryl imines (II). These 1,3-dipoles, however, are not stable, isolable substances, but exist in equilibrium with the head–tail dimeric form.[7] In the case of sydnones, (III), the azomethine imine system is incorporated in an aromatic nucleus and undergoes 1,3-dipolar cycloaddition with alkynes[8] and alkenes[9] followed by loss of carbon dioxide from the initially formed adduct.



I

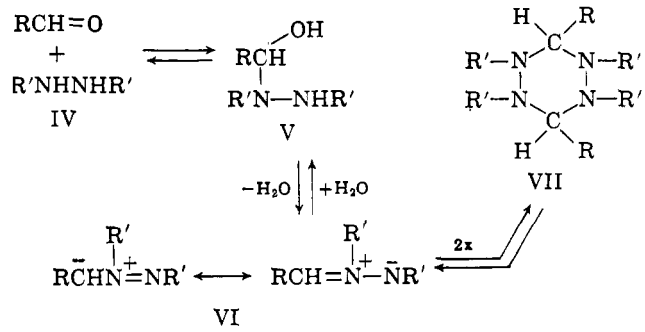


II



III

Since the azomethine imine systems discussed above yield rather specially substituted classes of compounds, we sought a more general synthesis and accordingly undertook an investigation of the reaction of N,N′-disubstituted hydrazines with carbonyl compounds. Rassow[10] had shown that N,N′-disubstituted hydrazines combine with aldehydes to form substituted hexahydro-1,2,4,5-tetrazines. These products, which have also been consider to possess the diaziridine structure, appear worthy of re-examination. The compounds which we isolated from the interaction of N,N′-dialkylhydrazines with aromatic aldehydes proved to be hexahydrotetrazines.



The formation of six-membered ring products may be viewed as proceeding *via* the carbonol–hydrazine V followed by dehydration to the azomethine imine VI. Dimerization of the latter proceeds by mutual neutralization of formal charges to yield VII. This reaction path is not unequivocal. However, it can be checked by trapping of the intermediate VI with dipolarophilic compounds. Such cycloadditions have indeed been accomplished with α,β-unsaturated esters and nitriles, as well as with acenaphthylene, isocyanates, isothiocyanates, and rhodanides.[11] In this paper we wish to report only on the reaction involving carbon disulfide as a dipolarophile.

Addition Reactions of Carbon Disulfide.—Mild warming of N,N′-dialkylhydrazines with aldehydes in carbon disulfide diluted with an inert solvent yields the corresponding 2,3,4-trisubstituted 1,3,4-thiadiazolidine-5-thiones (VIII–XIV) of Table I (method A). The nature of the aromatic aldehyde appears to have only a negligible effect upon the yield. N,N′-Dibenzylhydrazine, as well as the *p,p*′-dimethoxy derivative, and N,N′-dimethylhydrazine were used; hydrazobenzene proved unsuitable in this synthesis.

The conclusion that the intermediary azomethine imine VI adds more rapidly to the C=S double bond of carbon disulfide than it dimerizes to VII is not unambiguous. We have succeeded in achieving high yields of

(1) Paper XI: G. Binsch, R. Huisgen, and H. König, *Chem. Ber.*, **97**, 2893 (1964).

(2) From the M.S. Thesis K. K. Sun, University of Munich, 1962.

(3) NATO Postdoctoral Fellow in Munich, 1959–1960.

(4) See R. Huisgen, *Proc. Chem. Soc.*, 357 (1961); *Angew. Chem., Intern. Ed. Eng.*, **2**, 565 (1963).

(5) R. Huisgen, R. Fleischmann, and A. Eckell, *Tetrahedron Letters*, **No. 12**, 1 (1960).

(6) R. Huisgen and A. Eckell, *ibid.*, **12**, 5 (1960).

(7) R. Huisgen, R. Grashey, P. Laur, and H. Leitermann, *Angew. Chem.*, **72**, 416 (1960); R. Grashey and K. Adelsberger, *ibid.*, **74**, 292 (1962); R. Grashey, H. Leitermann, R. Schmidt, and K. Adelsberger, *ibid.*, **74**, 491 (1962).

(8) R. Huisgen, R. Grashey, H. Gotthardt, and R. Schmidt, *ibid.*, **74**, 29 (1962).

(9) R. Huisgen, H. Gotthardt, and R. Grashey, *ibid.*, **74**, 30 (1962).

(10) B. Rassow, *J. prakt. Chem.*, [2] **64**, 129 (1901); B. Rassow and M. Lummerzheim, *ibid.*, [2] **64**, 136 (1901).

(11) Unpublished results, R. Grashey and K. K. Sun.

TABLE I

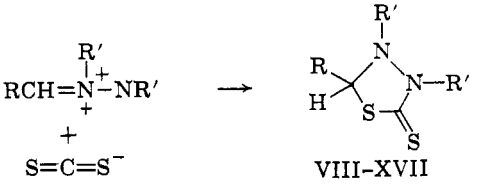
2,3,4-TRISUBSTITUTED 1,3,4-THIADIAZOLIDINE-5-THIONES[a]

Compd.	R	R′	Method	Yield, %	M.p., °C.
VIII	p-$CH_3OC_6H_4$	$C_6H_5CH_2$	A	41	136–137
IX	C_6H_5	p-$CH_3OC_6H_4CH_2$	A	60	78–79
X	p-ClC_6H_4	p-$CH_3OC_6H_4CH_2$	A	60	117–118
XI	p-$NO_2C_6H_4$	p-$CH_3OC_6H_4CH_2$	A	25	152–153
XII	p-HOC_6H_4	p-$CH_3OC_6H_4CH_2$	A	38	157–158
XIII	p-$CH_3OC_6H_4$	p-$CH_3OC_6H_4CH_2$	A	40	114–115
XIV	p-$CH_3OC_6H_4$	CH_3	A	18	89–90
XIV	p-$CH_3OC_6H_4$	CH_3	B	83	89–90
XV	p-ClC_6H_4	CH_3	B	96	86–86.5
XVI	p-$NO_2C_6H_4$	CH_3	B	84	130–131
XVII	C_6H_5	C_6H_5	B	49	160–161

[a] From N,N′-dialkylhydrazines, aldehydes, and carbon disulfide (method A) or from hexahydro-1,2,4,5-tetrazines VII and carbon disulfide (method B).

thiadiazolidines by reaction of the isolated hexahydrotetrazines VII with carbon disulfide in acetonitrile at 80–120° (method B of Table I). Example XIV convincingly demonstrates the superiority of this procedure over method A. Hexahydrotetrazine VII (R = R′ = C_6H_5) requires a temperature of 130° before it reacts with carbon disulfide. In contrast, the reaction of 1,2,4,5-tetraphenylhexahydro-1,2,4,5-tetrazine[12] with carbon disulfide has not yet been accomplished even under forcing conditions.

The assumption of a thermal dissociation of VII to a moderate equilibrium concentration of the monomeric azomethine imine VI is no more unusual than the analogous equilibrium which has been demonstrated to occur with II.[4,7] In this sense, the two methods proceed *via* the same cycloaddition of VI to carbon disulfide.



VIII–XVII

Thiadiazolidine-5-thiones[13] VIII–XVII do not form hydrochlorides and are stable towards acetic anhydride (with the exception of XII). Reaction with sodium ethoxide in boiling alcohol leads to ring cleavage. While the compounds are not attacked by sodium borohydride, hydrogen in the presence of Raney nickel or reduction with lithium aluminum hydride leads to C–S and N–N hydrogenolysis. The direction of addition of VI to carbon disulfide has been rigorously proven for the carbon disulfide adduct of azomethine imine II[14] and corresponds to "the principle of maximum gain of σ-bond energy" in the cycloaddition.[15]

The infrared spectra of the 1,3,4-thiadiazolidine-5-thiones show, as expected, no absorption in the NH or SH region. A band occurring around 9.2 μ in VIII–XVII may be associated with the C=S stretching frequency.[16] Absorption observed at 7.2 μ may possibly be associated with the NCS group.

(12) C. A. Bischoff, *Ber. deut. chem. Ges.*, **31**, 3248 (1898).

(13) For a treatise on the chemistry of 1,3,4-thiadiazolidines see W. R. Sherman, "Heterocyclic Compounds," Vol. VII, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p. 612; E. Hoggarth, "Chemistry of Carbon Compounds," Vol. IVA, E. H. Rodd, Ed., D. van Nostrand Co., Inc., New York, N. Y., 1957, p. 476.

(14) R. Grashey, unpublished results.

(15) R. Huisgen, *Angew. Chem., Intern. Ed. Eng.*, **2**, 633, 641 (1963).

(16) E. Spinner, *J. Chem. Soc.*, 1237 (1960); *J. Org. Chem.*, **23**, 2037 (1958); N. Lozach and G. Guillouzo, *Bull. soc. chim. France*, 1221 (1957).

An X-ray diffraction study carried out on 2-p-methoxyphenyl-3,4-dibenzyl-1,3,4-thiadiazolidine-5-thione (VIII) completely confirmed the proposed structure. This study, carried out by J. Karle and I. Karle, Naval Research Laboratory, Washington, D. C., will be reported in a separate communication.

Nuclear Magnetic Resonance Spectra.—The n.m.r. absorption bands, with the exception of the aromatic proton peaks, are presented in Table II. The spectrum of 2-p-methoxyphenyl-3,4-dimethyl-1,3,4-thiadiazolidine-5-thione (XIV) is in complete agreement with the proposed structure. The relative positions of the two methyl groups at N-3 and N-4 cannot be assigned unequivocally. The N-methyl groups of 3,4-dimethyl-1,3,4-thiadiazolidine-2,5-dithione (XXII) fall at τ 6.08. This low-field position relative to either τ 6.60 or 7.12 for the N–CH_3 in XIV probably is due to extra deshielding provided by the ring current associated with the conjugated π-electron system of XXII. The C-2 proton, methoxymethyl, and aromatic quartet appear in the expected regions and possess the correct integrated intensity. The spectrum of 2-p-methoxyphenyl-3,4-dibenzyl-1,3,4-thiadiazolidine-5-thione (VIII) (Figure 1) shows a pattern characteristic of all the N,N′-dibenzyl derivatives in this series, namely, nonequivalence of the protons in one benzylic set. The AB quartet has a coupling constant and chemical shift difference of 15 c.p.s. and 1.0 p.p.m., respectively. Such nonequivalence could arise either from hindered internal rotation about the C–N-4 bond due to the bulky thione sulfur or, alternatively, the asymmetric center at C-2 could cause different magnetic shielding of the benzylic protons at N-3 in the various equilibrium rotamers. The latter effect does not require hindered rotation. In order to distinguish between these two possibilities, a temperature study was carried out. The spectrum of VIII in dimethyl sulfoxide-d_6 at 30, 100, and 150° is given in Figure 2; the original AB quartet is essentially unchanged over this temperature range, thus excluding hindered internal rotation as the origin of the nonequivalence. Conformations may be drawn for VIII which place the benzylic protons at N-3 in nonequivalent magnetic environments even though rapid rotation about the CH_2–N-3 bond occurs. A further interesting point, evident from Figure 2, is that in dimethyl sulfoxide-d_6 the previously singlet methylene appears as a AB pattern. In contrast, this quartet is temperature dependent and coalesces to an A_2 pattern at 150°. This is an example of nonequivalence due to

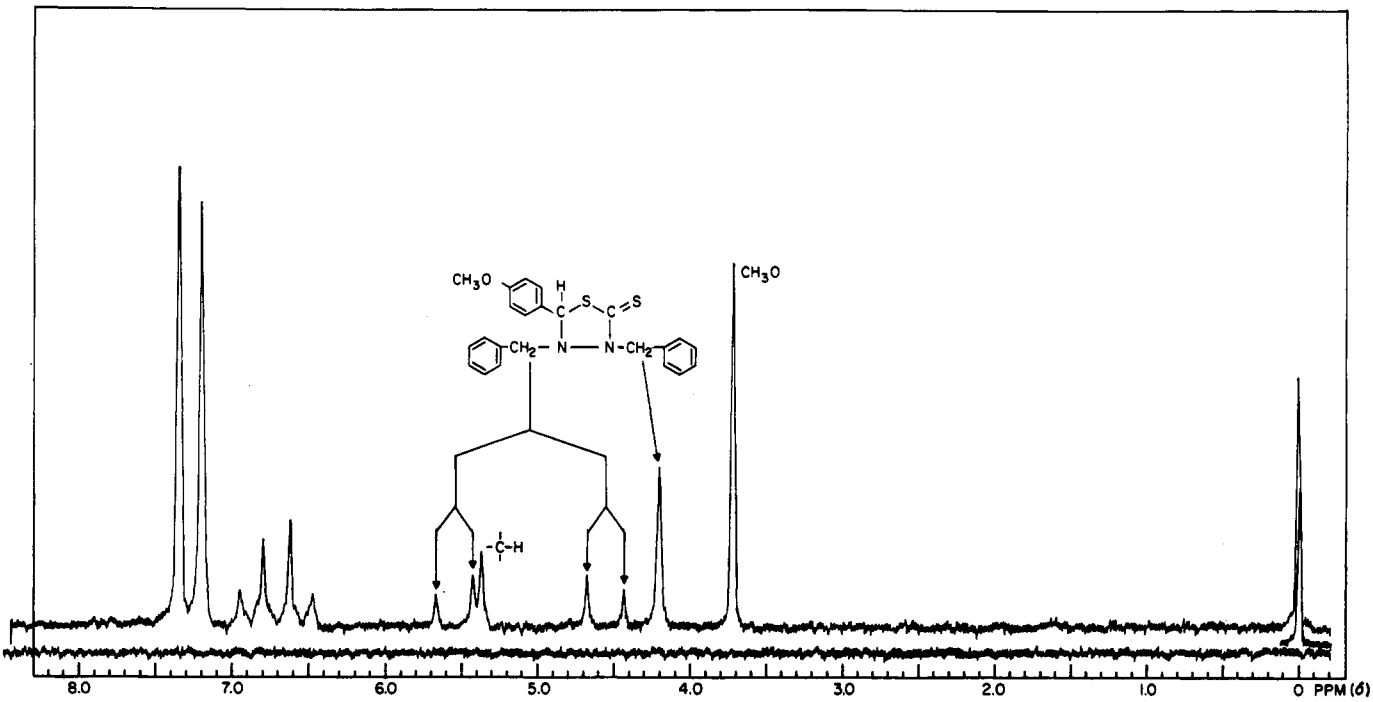


Figure 1.—N.m.r. spectrum of 2-*p*-methoxyphenyl-3,4-dibenzyl-1,3,4-thiadiazolidine-5-thione (VIII) in carbon tetrachloride.

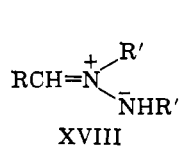
solvent–solute complexation. A reasonable site for complexation would be the polar C=S group.

Such a solvent–solute complex could account for the nonequivalence of the protons at N-4 since the two geminal protons would be in dissimilar magnetic environments. Increasing temperature would be expected to favor dissociation and consequent restoration of the A_2 pattern observed in noncomplexing solvents such as carbon tetrachloride and chloroform-*d*. These data imply that the AB quartet of VIII in carbon tetrachloride is at N-3 and the singlet methylene is at N-4. The fact that the high-field peak of the N-methyl doublet of various N-methyl amides has been identified as the N-methyl group *cis* to oxygen in the slowly interconverting rotamers also supports the assignment made for VIII.[17]

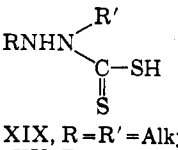
Discussion

That the aldehyde and the hydrazine IV exist in equilibrium with the azomethine imine offers a working hypothesis for the interpretation of the cycloaddition to carbon disulfide. However, this description of the mechanism is not unequivocal. Alternatively, the carbinol hydrazine V or the hydrazonium ion XVIII could interact with carbon disulfide, in which case a multistep sequence would precede ring closure to the 1,3,4-thiadiazolidine ring.

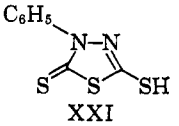
Another alternative, which merits serious consideration, involves initial reaction of the N,N′-dialkylhydrazine with carbon disulfide yielding a N-dithiocarbazic acid derivative. This product could subsequently add to the aldehyde to yield the 1,3,4-thiadiazolidine-5-thione. An analogy exists for this pathway in the cyclization reaction of phenylhydrazine-N-dithiocarbazic acid with aldehydes and ketones.[18a] With excess carbon disulfide, XX is converted to XXI.[18b] Analogously N,N′-dimethylhydrazine reacts with excess carbon disulfide to yield 3,4-dimethyl-1,3,4-thiadiazolidine-2,5-thione (XXII).[19] We have also carried out this reaction using N,N′-diethylhydrazine.



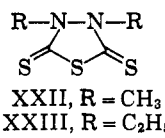
XVIII



XIX, R = R′ = Alkyl
XX, R = C_6H_5; R′ = H



XXI



XXII, R = CH_3
XXIII, R = C_2H_5

We have shown that XXII does not produce XIV upon treatment with *p*-methoxybenzaldehyde, and therefore XXII cannot be an intermediate in the formation of XIV. However, we cannot exclude the intermediacy of XIX with the same degree of certainty. It is quite improbable that such an intermediate would occur in the reactions of hexahydrotetrazines with carbon disulfide. In the three-component system (method A) it is possible that a careful kinetic comparison could allow a decision as to whether the addition of VI or XVIII to carbon disulfide or the interaction of the aldehyde with XIX comes into play.

Finally an alternative mechanism for the reaction of VII with carbon disulfide should be pointed out. In addition to the thermal dissociation to the azomethine imine VI, one must also consider the possibility of an initial electrophilic attack at the nitrogen of VII.

The 1,3-dipolar cycloaddition of diphenylnitrilimine with carbon disulfide as solvent leads only to the

(17) (a) D. G. de Kowalewski and V. J. Kowalewski, *Arkiv Kemi*, **16**, 373 (1960); (b) L. A. La Planche and M. T. Rogers, *J. Am. Chem. Soc.*, **86**, 337 (1964).

(18) (a) M. Busch, *Ber. deut. chem. Ges.*, **28**, 2635 (1895); H. Wuyts and A. Lacort, *Bull. acad. roy. med. Belg.*, **19**, 543 (1943). (b) M. Busch, *Ber. deut. chem. Ges.*, **27**, 2507 (1894).

(19) G. D. Thorn, *Can. J. Chem.*, **38**, 1439 (1960).

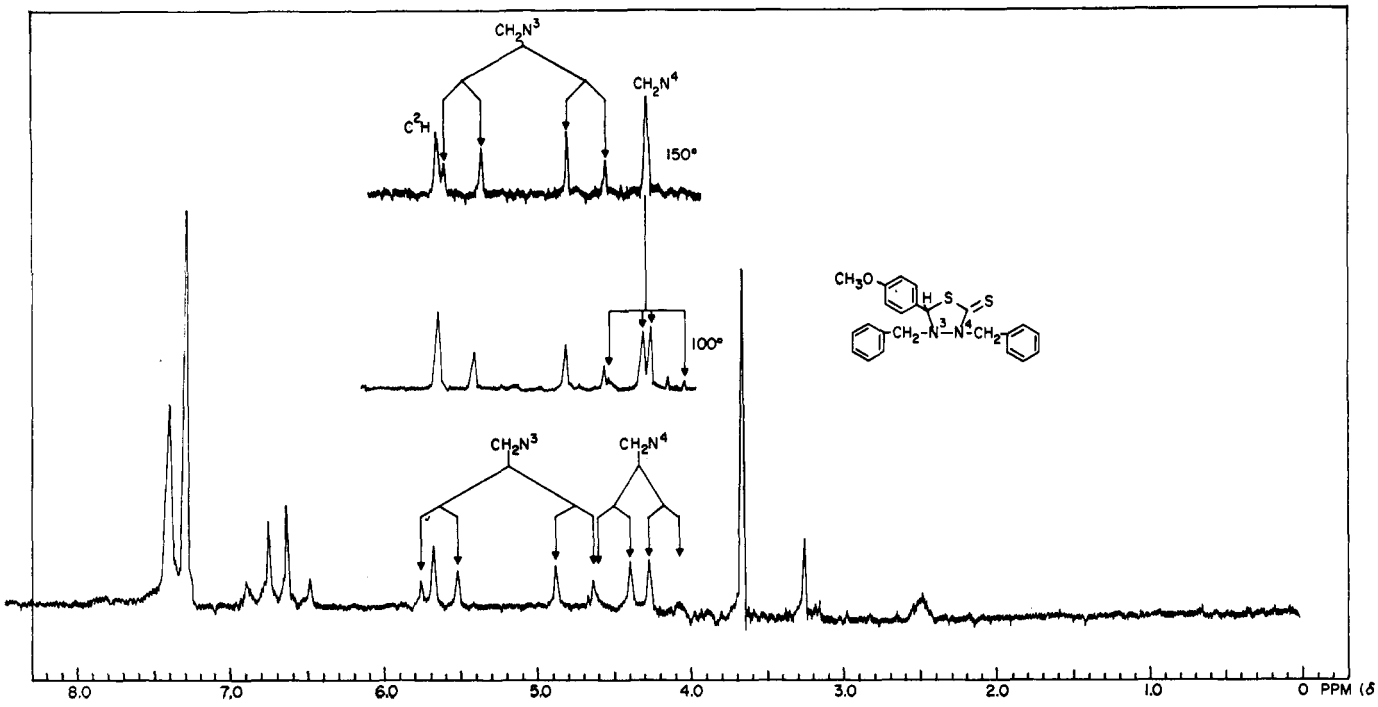


Figure 2.—Effect of temperature upon the n.m.r. spectrum of 2 *p*-methoxyphenyl-3,4-dibenzyl-1,3,4-thiadiazolidine-5-thione (VIII) in CD_3SOCD_3.

spirocyclic 2:1 adduct.[20] In contrast, all the azomethine imines thus far investigated afford only monoadducts upon reaction with carbon disulfide. Also the reaction of hexahydrotetrazine VII (R = *p*-Cl-C_6H_4; R′ = CH_3) with carbon disulfide in equimolar ratio yields no bisadduct. Likewise, experiments which aimed at adding a second mole of azomethine imine to the C=S bond of 1,3,4-thiadiazolidine-5-thione XV were unsuccessful.

Experimental

N,N′-Dimethylhydrazine was prepared by a published procedure.[21]

N,N′-Dibenzylhydrazine was prepared by sodium amalgam reduction of benzaldazine. After recrystallization from ethanol the material had m.p. 48–49° (lit.[22] 47°).

N,N′-Di-*p*-methoxybenzylhydrazine,[23] m.p. 72° (ethanol, lit.[23] 71°).

1,2,4,5-Tetramethyl-3,6-di(*p*-chlorophenyl)hexahydro-1,2,4,5-tetrazine (VII, R = *p*-ClC_6H_4; R′ = CH_3).—To a solution of 2.40 g. (40.0 mmoles) of 1,2-dimethylhydrazine in 20 ml. of acetonitrile at 70° was added a solution of 6.32 g. (45.0 mmoles) of *p*-chlorobenzaldehyde over a period of 4 hr. with stirring. After storing at room temperature overnight, the precipitated crystalline product was filtered. The colorless material weighed 5.46 g. (75%) and had m.p. 145–146°. Recrystallization from petroleum ether (b.p. 40–80°) raised the melting point to 146–148°.

Anal. Calcd. for $C_{18}H_{22}Cl_2N_4$: C, 59.18; H, 6.07; N, 15.34; mol. wt., 365.3. Found: C, 59.39; H, 6.09; N, 15.26; mol. wt., osmometric (benzene), 361.

Hydrolysis of VII (R = *p*-ClC_6H_4; R′ = CH_3).—A solution of 0.91 g. of VII in 15 ml. of 2 *N* hydrochloric acid was kept at reflux for 20 min. After extraction with ether, the extracts were dried with sodium sulfate and concentrated to dryness. The residue, 0.70 g. (100%), was identified as *p*-chlorobenzaldehyde by mixture melting point determination with an authentic sample (m.p. and m.m.p. 44–46°). The aqueous solution was concentrated *in vacuo* and the residue was crystallized from ethanol–ether yielding 0.55 g. (83%), melting point and mixture melting point with 1,2-dimethylhydrazine dihydrochloride 164° dec.

1,2,4,5-Tetramethyl-3,6-di(*p*-nitrophenyl)hexahydro-1,2,4,5-tetrazine (VII, R = *p*-$NO_2C_6H_4$; R′ = CH_3).—To a solution of 1.20 g. (20.0 mmoles) of 1,2-dimethylhydrazine in 20 ml. of acetonitrile a solution of 3.78 g. (25.0 mmoles) of *p*-nitrobenzaldehyde was added dropwise at 20° with constant stirring over a period of 3 hr. After stirring overnight, 2.17 g. (56%) of yellow crystalline material was isolated by filtration; it melted at 175–179°. Recrystallization from benzene–methanol raised the melting point to 188.5–190°.

Anal. Calcd. for $C_{18}H_{22}N_6O_4$: C, 55.95; H, 5.74; N, 21.75; mol. wt., 386.4. Found: C, 56.09; H, 5.82; N, 21.92; mol. wt., osmometric (benzene), 389.

1,2,4,5-Tetramethyl-3,6-di(*p*-methoxyphenyl)hexahydro-1,2,4,5-tetrazine (VII, R = *p*-$CH_3OC_6H_4$; R′ = CH_3).—As described above, from 1.20 g. (20.0 mmoles) of 1,2-dimethylhydrazine in 10 ml. of *n*-propyl alcohol and 3.40 g. (25.0 mmoles) of anisaldehyde in 15 ml. of the same solvent, a nearly colorless product was obtained weighing 2.79 g. (79%). The analytical sample was prepared by recrystallization from petroleum ether and had m.p. 114–115.5°.

Anal. Calcd. for $C_{20}H_{28}N_4O_2$: C, 67.38; H, 7.92; N, 15.72. mol. wt., 356.5. Found: C, 67.58; H, 7.87; N, 16.06; mol. wt., osmometric (benzene), 352.

2-(*p*-Methoxyphenyl)-3,4-dibenzyl-1,3,4-thiadiazolidine-5-thione (VIII).—A solution of 0.500 g. (3.67 mmoles) of anisaldehyde and 0.500 g. (2.36 mmoles) of N,N′-dibenzylhydrazine in 3 ml. of carbon disulfide and 3 ml. of ethanol was warmed for 12 hr. at 50°. Benzene and water were added and the benzene layer was separated and washed with sodium bisulfite and water. It was dried with magnesium sulfate and concentrated to dryness under aspirator vacuum. The oily residue, crystallized upon trituration with ether, yielded 0.390 g. with m.p. 133–134°. Recrystallization from benzene–ether raised this to 136–137°. The infrared spectrum (Nujol) showed C=S at 9.25, OCH_3 at 9.67, and aromatic CH wagging at 12.30, 12.40, 12.73, and 13.30 μ.

Anal. Calcd. for $C_{23}H_{22}N_2OS_2$: C, 67.94; H, 5.45; N, 6.89. Found: C, 68.14; H, 5.62; N, 7.01.

2-Phenyl-3,4-di(*p*-methoxybenzyl)-1,3,4-thiadiazolidine-5-thione (IX).—A solution of 1.00 g. (3.68 mmoles) of IV (R′ = *p*-$CH_3OC_6H_4CH_2$) and 1.43 g. (13.5 mmoles) of benzaldehyde in 4 ml. of carbon disulfide and 5 ml. of benzene was warmed for 12 hr. at 60°. After working up the reaction system by the method described above, 0.96 g. were obtained with m.p. 64–75°; after recrystallization from benzene–ethanol, 0.800 g. were ob-

(20) R. Huisgen, R. Grashey, M. Seidel, H. Knupfer, and R. Schmidt, *Liebigs Ann. Chem.*, **658**, 169 (1962).

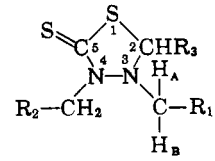
(21) H. H. Hatt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 208.

(22) Th. Curtius, *J. prakt. Chem.*, [2] **62**, 83 (1902).

(23) Th. Curtius, *ibid.*, [2] **85**, 393, 448 (1912).

TABLE II

N.M.R. SPECTRA OF 1,3,4-THIADIAZOLIDINE-5-THIONE DERIVATIVES[a]



		CH₃ or CH₂ at 3						
Compd.	Solvent	H_A	H_B	J_{AB}, c.p.s.	Δ_{AB}, p.p.m.	CH₃ or CH₂ at 4	CH at 2	OCH_3
VIII	$CDCl_3$	5.31, 5.56	4.33, 4.58	15	1.0	5.80	4.63	6.28 (R_3)
VIII	CCl_4	5.33, 5.58	4.45, 4.70	15	0.87	5.83	4.70	6.30 (R_3)
VIII	CD_3SOCD_3	5.12, 5.36	4.32, 4.48	15	1.01	H_A 5.60, 5.38 H_B 5.72, 5.92 $J \sim 12$ c.p.s. Δ 0.32 p.p.m.	4.30	6.32 (R_3)
VIII	CD_3SOCD_3, 70°	5.20, 5.44	4.30, 4.55	15	0.87	H_A 5.44, 5.63 H_B 5.73, 5.94 $J \sim 12$, c.p.s. Δ 0.28 p.p.m.	4.34	6.32 (R_3)
VIII	CD_3SOCD_3, 100°	5.20, 5.44	4.35, 4.58	15	0.85	H_A 5.48, 5.70 H_B 5.74, 5.94 $J \sim 12$ c.p.s. Δ 0.26 p.p.m.	4.34	6.32 (R_3)
VIII	CD_3SOCD_3, 150°	5.22, 5.48	4.42, 4.67	15	0.79	5.75	4.35	6.38 (R_3)
IX	CCl_4	5.42, 5.68	4.55, 4.79	15	0.88	5.90	4.69	6.22 (R_1 or R_2) 6.29 (R_1 or R_2)
X	CCl_4	5.81, 5.58	4.59, 4.35	14	1.23	5.83	4.70	6.20 (R_1 or R_2) 6.27 (R_1 or R_2)
XIII	CCl_4	5.53, 5.77	4.52, 4.75	14	1.01	5.91	4.75	6.23 (R_1, R_2, or R_3) 6.30 (R_1, R_2, or R_3) 6.32 (R_1, R_2, or R_3)
XIV	CCl_4	6.63				7.20	4.42	6.20 (R_3)
XV	CCl_4	6.60				7.12	4.48	
XVI	CCl_4	6.58				7.05	4.45	

[a] Varian A-60; chemical shifts in τ-values.

tained with m.p. 78–79°, infrared (Nujol) C=S 9.20 and O—CH_3 9.67 μ.

Anal. Calcd. for $C_{24}H_{24}N_2O_2S_2$: C, 66.02; H, 5.54; N, 6.42. Found: C, 65.90; H, 5.53; N, 6.10.

2-(*p*-Chlorophenyl)-3,4-di-(*p*-methoxybenzyl)-1,3,4-thiadiazolidine-5-thione (X).—A mixture of 1.36 g. (5.0 mmoles) of IV (R′ = *p*-$CH_3OC_6H_4$-CH_2), 2.11 g. of *p*-chlorobenzaldehyde (15.0 mmoles), and 10 ml. of carbon disulfide were kept at reflux for 10 hr. under nitrogen. After concentration first under reduced pressure, then under high vacuum, the oily residue was crystallized from methanol to yield 1.18 g. with m.p. 116–117°; an additional 0.220 g. was obtained from the mother liquors raising the yield to 60%. The analytical sample was prepared by recrystallization from methylene chloride–methanol and had m.p. 117–118° (colorless needles); infrared (Nujol) C=S 9.30, O—CH_3 9.73, and aromatic CH wagging at 12.10, 12.35, 12.50 and 13.20 μ.

Anal. Calcd. for $C_{24}H_{23}ClN_2O_2S_2$: C, 61.20; H, 4.92; N, 5.95. Found: C, 61.09; H, 4.82; N, 5.39.

2-(*p*-Nitrophenyl)-3,4-di(*p*-methoxybenzyl)-1,3,4-thiadiazolidine-5-thione (XI).—A solution of 1.36 g. (5.0 mmoles) of IV (R′ = *p*-$CH_3OC_6H_4CH_2$) and 2.27 g. of *p*-nitrobenzaldehyde (15.0 mmoles) in 10 ml. of carbon disulfide and 5 ml. of ethanol was heated at 85° (bath temperature) for a period of 24 hr. The usual work-up procedure gave 0.29 g. of a material which was only slightly soluble in methanol. This yellow material did not contain sulfur and analyzed for $C_{30}H_{28}N_4O_7$. Probably it is 3,4-di-(*p*-methoxybenzyl)-2,5-di-(*p*-nitrophenyl)-1,3,4-oxadiazolidine. The residue from the methanolic mother liquors was crystallized from ether to yield 0.61 g. of pale yellow crystals which melted at 152–153° after recrystallization from methylene chloride–methanol.

Anal. Calcd. for $C_{24}H_{23}N_3O_4S_2$: C, 59.85; H, 4.81; N, 8.73. Found: C, 59.77; H, 4.73; N, 8.30.

2-(*p*-Hydroxyphenyl)-3,4-di(*p*-methoxybenzyl)-1,3,4-thiadiazolidine-5-thione (XII).—The reaction of 0.50 g. (4.1 mmoles) of *p*-hydroxybenzaldehyde, 0.50 g. (1.84 mmoles) of IV (R′ = *p*-$CH_3OC_6H_4CH_2$), and 3 ml. of carbon disulfide in 8 ml. of benzene was carried out at 50° for a period of 12 hr. After working up, 0.32 g. was obtained which had m.p. 157–158° after recrystallization from hexane–benzene, infrared (Nujol) strong OH band at 3.0 μ.

Anal. Calcd. for $C_{24}H_{24}N_2O_3S_2$: C, 63.69; H, 5.34; N, 6.19. Found: C, 63.66; H, 5.42; N, 6.00.

Treatment of XII with acetic anhydride in pyridine at room temperature yielded the O-acetyl derivative, m.p. 108–109°, infrared (Nujol) no OH, C=O at 5.72 μ.

Anal. Calcd. for $C_{26}H_{26}N_2O_4S_2$: C, 63.13; H, 5.30; N, 5.66. Found: C, 63.10; H, 5.50; N, 5.36.

2-(*p*-Methoxyphenyl)-3,4-di(*p*-methoxybenzyl)-1,3,4-thiadiazolidine-5-thione (XIII).—The reaction of 0.50 g. (3.68 mmoles) of anisaldehyde followed the method given above for XII. Recrystallization of the crude product from benzene–ethanol yielded 0.34 g. with m.p. 114–115°.

Anal. Calcd. for $C_{25}H_{26}N_2O_3S_2$: C, 64.35; H, 5.61; N, 6.00; mol. wt., 466.6. Found: C, 64.88; H, 5.74; N, 5.88; mol. wt. (Rast), 440.

A solution of 0.10 mmoles of XII in benzene–ethanol was treated with 3.5 equiv. of sodium ethoxide and then with 0.40 mmoles of methyl iodide at 25°. After standing at room temperature for 16 hr., aqueous acetic acid was added and the product was isolated by extraction with ether; 3.2 mg. was obtained, m.p. 112–113°; mixture melting point and infrared spectrum comparison proved the identity of this material with XIII.

2-(*p*-Methoxyphenyl)-3,4-dimethyl-1,3,4-thiadiazolidine-5-thione (XIV). A.—A solution of 0.60 g. (10.0 mmoles) of N,N′-dimethylhydrazine, 1.50 g. (11.0 mmoles) of anisaldehyde, and 1.00 g. (13.2 mmoles) of carbon disulfide in 14 ml. of benzene was allowed to react for 14 hr. at 45°. The usual work-up afforded a thick oil; crystallization from ether–benzene (1:1) at −10° yielded 0.45 g., m.p. 89–90°, infrared (Nujol) C=S 9.05 and O—CH_3 9.75 μ.

Anal. Calcd. for $C_{11}H_{14}N_2OS_2$: C, 51.93; H, 5.55; N, 11.01 Found: C, 52.11; H, 5.57; N, 11.30.

B.—A solution of 0.18 g. (0.50 mmoles) of VII (R = *p*-$CH_3OC_6H_4$; R′ = CH_3) and 1.0 mmole of carbon disulfide in 2.0 ml. of acetonitrile was heated in a sealed tube at 80° for 12 hr. Crystallization of the product from carbon disulfide–methanol yielded 0.21 g. of colorless crystals, m.p. 88–90°.

Anal. Found: C, 52.04; H, 5.65; N, 11.00.

2-(*p*-Chlorophenyl)-3,4-dimethyl-1,3,4-thiadiazolidine-5-thione (XV).—From 0.73 g. (2.0 mmoles) of VII (R = *p*-ClC_6H_4; R′ = CH_3) and 4.0 mmoles of carbon disulfide in 5 ml. of acetonitrile heated in a sealed tube at 80° for 15 hr., a yield of 0.995 g. of material with m.p. 75–78° was obtained. Recrystallization from methanol yielded glistening plates, m.p. 86–86.5°.

Anal. Calcd. for $C_{10}H_{11}ClN_2S_2$: C, 46.41; H, 4.28; N, 10.83. Found: C, 46.86; H, 4.16; N, 10.83.

Treatment of XV with VII (R = *p*-ClC_6H_4; R′ = CH_3) in refluxing acetonitrile yielded no bis adduct; the components were recovered unchanged.

2-(*p*-Nitrophenyl)-3,4-dimethyl-1,3,4-thiadiazolidine-5-thione (XVI).—The analogous reaction of 1.0 mmole of VII (R = *p*-$NO_2C_6H_4$; R′ = CH_3) with 15 ml. of carbon disulfide at 120° for 100 hr. was carried out yielding 0.45 g., m.p. 129–130°. Recrystallization from methanol–carbon disulfide yielded yellow crystals of m.p. 130–131°, infrared (KBr) C=S 9.08 μ.

Anal. Calcd. for $C_{10}H_{11}N_3O_2S_2$: C, 44.60; H, 4.12; N, 15.60. Found: C, 44.73; H, 4.43; N, 15.11.

2,3,4-Triphenyl-1,3,4-thiadiazolidine-5-thione (XVII).—A solution of 0.27 g. (0.5 mmole) of VII (R = R′ = C_6H_5) in 5.0 ml. of carbon disulfide was heated at 130° for 100 hr. in a sealed tube. Upon cooling in the refrigerator, 0.170 g. of crystalline material was obtained, which was recrystallized from chloroform–methanol and had m.p. 160–161°.

Anal. Calcd. for $C_{20}H_{18}N_2S_2$: C, 68.93; H, 4.63; N, 8.04. Found: C, 68.83; H, 4.63; N, 8.29.

3,4-Dimethyl-,13,4-thiadiazolidine-2,5-dithione (XXII).—Carbon disulfide, 3.0 ml., was added slowly to 0.30 g. of 1,2-dimethylhydrazine (5.0 mmoles). Evolution of a gas was clearly observed as the reaction proceeded. After a few minutes the colorless crystalline product was collected, 0.63 g. (71%), m.p. 159–162°. The analytical sample was prepared by recrystallization from chloroform and had m.p. 163–164°, lit.[19] 168–169°.

Anal. Calcd. for $C_4H_6N_2S_3$: C, 26.94; H, 3.39; N, 15.71. Found: C, 27.04; H, 3.42; N, 15.69.

3,4-Diethyl-1,3,4-thiadiazolidine-2,5-dithione (XXIII).—This compound was prepared under conditions analogous to those used above by the interaction of 1,2-diethylhydrazine and carbon disulfide. Recrystallization from methanol yielded colorless material of m.p. 113–114°.

Anal. Calcd. for $C_6H_{10}N_2S_3$: C, 34.91; H, 4.88; N, 13.57. Found: C, 35.08; H, 4.90; N, 13.30.

The Correlation of D-*arabino*-L-*galacto*- and D-*lyxo*-D-*manno*-Nononic 1,4-Lactones

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Repetition of the cyanohydrin synthesis from D-*erythro*-L-*manno*-octose (I) has yielded the products described by Fischer and Hagenbach rather than those described by Fischer and Passmore. Direct comparisons have shown the identity of our nononic lactone and phenylhydrazide with those of Fischer and Hagenbach and also with those of Sowden and Strobach, who applied the nitromethane synthesis to the octose. The borohydride reduction of our D-*arabino*-L-*galacto*-nononic 1,4-lactone (II, whose origin was D-mannose) and of D-*lyxo*-D-*manno*-nononic lactone (V, whose origin was D-galactose) to the same nonitol (III, D-*arabino*-L-*galacto*-nonitol = D-*lyxo*-D-*manno*-nonitol) correlates the configurations assigned to these two C_9-sugar series and verifies the configurations assigned to all the related intermediate seven- and eight-carbon sugars and their derivatives. This procedure is a variation of what Hudson has termed Emil Fischer's method of obtaining conclusive proof of configuration by way of an identical active alcohol from two different aldoses. Some infrared data on aldonic lactones and phenylhydrazides are included in the Experimental section.

Many years ago Fischer and Passmore[2] described the addition of hydrogen cyanide to "*d*-mannooctose" and the isolation of a "*d*-mannononononolactone"; the lactone, upon reduction with sodium amalgam, yielded a crystalline "*d*-mannononose" that was fermented readily by fresh brewers' yeast. Subsequently, Fischer[3] wrote that Dr. R. Hagenbach had attempted a repetition of that synthesis; the result, as Hudson[4] was able to reveal through a study of Hagenbach's notebook, was the isolation of a different lactone and of an amorphous nonose that was not fermentable by yeast. The structure of Fischer and Passmore's "*d*-mannooctose" was established later as that of D-*erythro*-L-*manno*-octose (I) by Peirce[5] and confirmed by Hann, Maclay, Knauf, and Hudson.[6] While the structure of Fischer and Passmore's "*d*-mannononose" still remains a mystery, the structure of Fischer and Hagenbach's nonose was deemed to be probably that of D-*arabino*-L-*galacto*-nonose by Sowden and Strobach.[7] Those authors added nitromethane to D-*erythro*-L-*manno*-octose (I), separated the epimeric 1-deoxy-1-nitrononitols, and then by means of the Nef reaction obtained two amorphous nonoses. To one of these they assigned the D-*arabino*-L-*galacto*-nonose configuration by application of certain rules of optical rotation. The melting points and rotations (when obtainable) of this nonose and its phenylhydrazone, as well as of the corresponding nononic lactone and phenylhydrazide, were in quite good agreement with the data found in Hagenbach's notebook.[4] Furthermore, the nonose was not fermentable.

Hudson,[8] meanwhile, had added hydrogen cyanide to D-*erythro*-L-*manno*-octose (I) and isolated a crystalline nononic acid. This substance has now been found

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