afforded 0.389 g (92%) of benzaldehyde having and IR and ^1H NMR spectrum identical with those of an authentic sample.

Registry No. Mercury trifluoroacetate, 2923-15-1; polystyrene, 9003-53-6; 2-*n*-pentyl-1,3-dithiolane, 74585-39-0; 2-*n*-pentyl-1,3-dithiane, 21777-32-2; 2-phenyl-1,3-dithiolane, 5616-55-7; 2-phenyl-1,3-dithiane, 5425-44-5; 2-methyl-2-*n*-pentyl-1,3-dithiane, 81255-44-9; 2-propyl-2-hexyl-1,3-dithiane, 74327-18-7; 2-methyl-2-phenyl-1,3-dithiane, 6331-22-2; 1,4-dithiaspiro[4.5]decane, 177-16-2; 1,5-dithiaspiro[5.5]undecane, 180-96-1; cholestan-3-one cyclic 1,3-propanodiyl mercaptole, 51018-45-2; 2-methyl-2-benzoyl-1,3-dithiane, 4883-01-6; hexanal, 66-25-1; benzaldehyde, 100-52-7; 2-heptanone, 110-43-0; 2-nonanone, 821-55-6; acetophenone, 98-86-2; cyclohexanone, 108-94-1; cholestan-3-one, 15600-08-5; 1-octene, 111-66-0.

Efficient Synthesis of 3,4,5-Trimethoxybenzaldehyde via Reissert Aldehyde Synthesis

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3,4,5-Trimethoxybenzaldehyde (**1c**, TMBA) is an important intermediate in the synthesis of both drugs and alkaloids. Until recently, the only satisfactory method for large-scale preparation has been the Rosenmund reduction of 3,4,5-trimethoxybenzoyl chloride.[1] While this method has been improved,[2] it still suffers from being inconvenient to run in the laboratory. Catalyst poisoning can also be a problem.

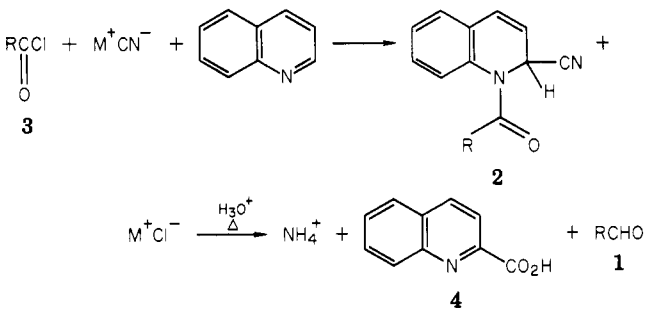
The Reissert aldehyde synthesis (Scheme I)[3] is ideally suited to run in the laboratory as it requires no special apparatus or catalyst and utilizes inexpensive reagents such as sodium cyanide (or hydrogen cyanide), quinoline (or isoquinoline), and sulfuric acid in addition to the appropriate acid chloride. Many investigators have used this method for the preparation of many aldehydes,[4] but in the case of TMBA, only low yields have been reported for the synthesis of the Reissert intermediate, as well as its subsequent hydrolysis.[5-7]

Our own investigations into an efficient and convenient, as well as inexpensive, method of TMBA preparation prompted us to report our success with this method.

Results and Discussion

The preparation of 3,4,5-trimethoxybenzoyl chloride (**3c**) was straightforward from the corresponding acid and thionyl chloride. The preparation of the Reissert intermediate, **2**, was accomplished in 95% yield using the following biphasic conditions: nearly 1 equiv of aqueous sodium cyanide[8] was rapidly stirred with quinoline while a dichloromethane solution of the acid chloride was added dropwise. Failure of this method occurs when excess sodium cyanide is added and may possibly be the reason for poor yields reported by past workers. The hydrolysis of **2** was effected in nearly quantitative yield with refluxing 30% sulfuric acid.

Scheme I. Reissert Aldehyde Synthesis[a,b]



[a] a, R = alkyl; b, R = aryl; c = 3,4,5-trimethoxybenzoyl. [b] M = H, Na, K.

This efficient synthesis of TMBA requires only small quantities of solvents and involves only simple workup procedures. The quinaldic acid, **4**, can even be decarboxylated for the recycle of quinoline,[9,10] constituting a synthesis consuming only cyanide. This route to TMBA should be a convenient alternative to the Rosenmund reduction.

Experimental Section

Preparation of 1,2-Dihydro-1-(3,4,5-trimethoxybenzoyl)-2-quinolinecarbonitrile. NaCN was obtained from Fisher Scientific and used without further purification. Quinoline was obtained from Eastman, redistilled, and stored over KOH. 3,4,5-Trimethoxybenzoyl chloride was vacuum distilled prior to use [180 °C (15 mmHg)].

A three-neck, 250-mL, round-bottom flask, equipped with mechanical stirrer, baffle, addition funnel, and nitrogen inlet (vented through a safety bubbler), was charged with 160 mmol (8.3 g) of NaCN and 25 mL of H_2O, and the suspension was stirred to dissolve the salt. Then 170 mmol (22.0 g) of quinoline in 50 mL of CH_2Cl_2 was added. As the mixture was briskly stirred, 167 mmol (38.6 g) of 3,4,5-trimethoxybenzoyl chloride in 75 mL of CH_2Cl_2 was added via the addition funnel over 2.5 h. Initially the mixture became orange and then turned yellow. TLC showed that only trace amounts of the acid chloride remained (Et_2O–hexane). After stirring for an additional 2 h, the mixture was poured into a separatory funnel, and the CH_2Cl_2 layer was withdrawn. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL) and discarded. The combined CH_2Cl_2 layers were extracted first with saturated Na_2CO_3 solution (2 × 100 mL), then with 10% HCl (2 × 100 mL), and finally with H_2O (2 × 100 mL). The CH_2Cl_2 solution was dried over K_2CO_3 and placed in a 500-mL distillation flask with 250 mL of EtOH. The solvent was distilled through a Vigreux column to a temperature of 80 °C. Crystallization began, and after cooling to 0 °C, the crystals were collected, washed with 50 mL of EtOH, and vacuum dried at 80 °C to give 35.0 g of white crystals, mp 184–187 °C; ^1H NMR ($CDCl_3$, 60 MHz) δ 3.65 (s, 6 H), 3.85 (s, 3 H), 6.05 (dd, J = 4.5 Hz, 2 H), 6.5 (s, 2 H), 6.55–7.25 (m, 5 H). Anal. Calcd. for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.81; H, 5.18; N, 8.06. A second crop of crystals, 17.8 g, was obtained from the mother liquors, mp 159–161 °C.[11] The combined weight, 52.8 g, represents a 95% yield of **2**.

Preparation of 3,4,5-Trimethoxybenzaldehyde by Hydrolysis of 2. SG Extra charcoal was obtained from R. W. Greefe and Co. A three-neck, 500-mL, round-bottom flask, equipped

(1) K. W. Rosenmund, *Ber. Dtsch. Chem. Ges.*, **51**, 585 (1918). For a review of this method, see E. Mossetig and R. Mozingo, *Org. React.*, **4**, 362 (1948).

(2) J. A. Peters and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, **100**, 21 (1981), and references therein.

(3) A. Reissert, *Ber. Dtsch. Chem. Ges.*, **38**, 1603, 1610, 3415, 3427 (1905).

(4) For a review of this method, see E. Mosettig, *Org. React.*, **8**, 218 (1954); W. E. McEwen and R. L. Cobb, *Chem. Rev.* **55**, 51 (1955); F. D. Popp, *Adv. Heterocycl. Chem.*, **9**, 1 (1968).

(5) N. Sugasawa and I. Tsuda, *J. Pharm. Sci.*, **56**, 557 (1936); *Chem. Abstr.*, **32**, 5836 (1936).

(6) H. Buchanan et al., *J. Chem. Soc.*, 325 (1944).

(7) There is a recent patent concerning the use of the Reissert method to produce TMBA. However, the yields are not given for any steps in the process [see *Chem. Abstr.*, **90**, 104001a (1979); J. M. Cuixart Grande (Tresquim, S.A.) Spanish Patent 465 841 (1978)].

(8) When excess sodium cyanide is used, considerable polymer is formed. The yield of desired product drops considerably.

(9) D. L. Hamick et al., *J. Chem. Soc.*, 1724 (1938); 1809 (1939); 173, 659 (1949).

(10) M. Zelinski, *J. Chem. Phys.*, **47**, 3686 (1967).

(11) This material is spectroscopically identical upon comparison of a 60-MHz NMR spectrum and appears to be either a polymorph or geometrical isomer of the higher melting form.

0022-3263/82/1947-2213$01.25/0

with a thermometer, mechanical stirrer, condenser, baffle, and N_2 inlet (vented through a safety bubbler) was charged with 30 mmol (10.5 g) of **2**, followed by the addition of 400 mL of 30% H_2SO_4. The suspension was heated to 107 °C (reflux) with rapid stirring until the mixture became a homogeneous orange solution (~1 h). Then 1.0 g of SG Extra charcoal was added, and the mixture was heated at reflux for 15 min, filtered over Celite, and then cooled to room temperature, whereupon the organic product was extracted into CH_2Cl_2 (3 × 100 mL). This CH_2Cl_2 solution was extracted first with 10% Na_2CO_3 solution (2 × 25 mL) and then with H_2O (2 × 25 mL) and dried over K_2CO_3. The dried solution was placed in a 500-mL distillation flask with 100 mL of hexane. Atmospheric distillation of ~350 mL of solvent, followed by cooling to 0 °C, produced crude solid TMBA. The crude solid was dissolved in boiling hexane. Insolubles, 0.5 g, were filtered and identified as the starting material **2** (accounting for ~5% of **2**). The filtered hexane solution was cooled, producing 5.6 g (95% yield) of white TMBA, mp 75-77 °C, which was spectroscopically identical with an authentic sample of commercially available material from the Monsanto Co. Inc.

Registry No. 1, 86-81-7; 2, 81340-18-3; 3, 4521-61-3; quinoline, 91-22-5.

New Method for the Synthesis of Chloro-Substituted Dibenzo[*b*,*f*][1,4,5]thiadiazepines and Their 5,6-Dihydro Derivatives

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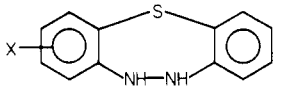
The parent compound (1, X = H) of the 5,6-dihydrodibenzo[*b*,*f*][1,4,5]thiadiazepine system has been of interest due to its potential aromatic character[1] and its acid-catalyzed reactions (benzidine rearrangement).[2] It has also been used as a key intermediate in the synthesis of the sulfur-bridged analogue of the antiinflamatory compound phenylbutazone.[3]



1

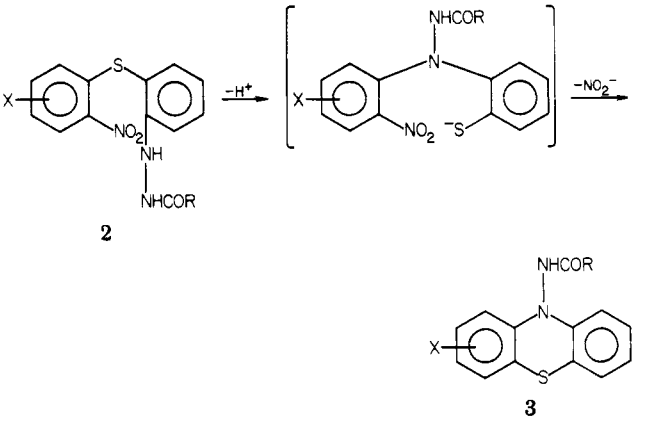
The first attempted syntheses[1,4] of this compound, based on the reductive cyclization of bis(*o*-nitrophenyl) sulfide, afforded it in very poor yield, and it was not until 1971 that Szmant[5,6] achieved this synthesis in an acceptable yield, following a four-step procedure.

In this paper, we report a new and apparently useful method for the preparation of substituted compounds 1 (X = electronegative group) and the corresponding dehydro compounds **7**.

The method is based on the previously reported synthesis[7] of 10-(acylamino)phenothiazine derivatives **3** by cyclization of compounds **2** via base-catalyzed Smiles rearrangement (Scheme I).

It was considered that this cyclization procedure could be applied to compounds **4**, which apparently meet the required conditions for the Smiles rearrangement and further cyclization to produce compounds **5** (Scheme II).

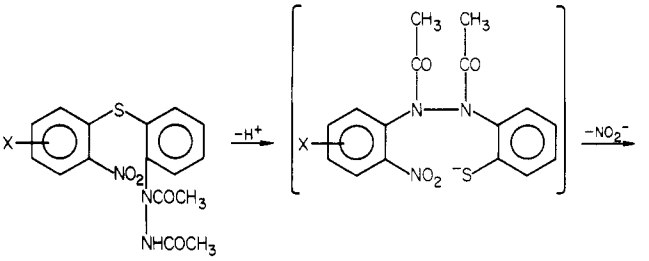
Scheme I



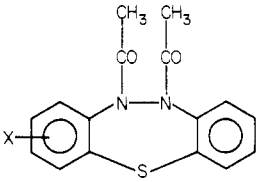
2

3

Scheme II



4a, X = 4-Cl
b, X = 5-Cl
c, X = 6-Cl
d, X = H



5a, X = 2-Cl
b, X = 3-Cl
c, X = 4-Cl

Table I. Properties and Yields of 2-Nitrophenyl 2-(α,β-Diacetylhydrazino)phenyl Sulfides[a]

compd	X	% yield	mp,[b] °C
4a	4-Cl	91	204-206
4b	5-Cl	89	150-152
4c	6-Cl	85	181-183
4d	H	78	110-112

[a] Satisfactory analyses (±0.3 for C, H, and N) were reported for all compounds in this table. [b] Recrystallized from benzene. All these compounds showed the following common IR and NMR spectroscopic data: IR (Nujol): 3270-3260 (NH), 1720-1715, 1660-1655 (C=O), 1520-1510; 1345-1340 cm^{-1} (NO_2); NMR (Me_2SO-d_6) δ 1.9-2.0 (s, 3 H, CH_3), 2.1 (s, 3 H, CH_3), 6.8-7.9 (m, 6 or 7 H, aromatic protons), 8.2-8.4 (m, 1 H, H-3, aromatic proton), 8.5-8.9 (s, 1 H, NH).

For reasons of simplicity, only the cases in which X in compound **4** is 4-Cl, 5-Cl, 6-Cl, and H (Table I) have been studied, i.e., substitution by a weak electronegative atom ortho, meta, and para to the sulfur atom and in the unsubstituted compound.

The reaction did not take place for compound **4d**, although no starting material was recovered. However, compounds **4a-c** did react to give compounds **5a** in 81%

(1) N. L. Allinger and G. A. Youngdale, *J. Am. Chem. Soc.*, **84**, 1020 (1962).
(2) L. D. Hartung and H. J. Shine, *J. Org. Chem.*, **34**, 1013 (1969).
(3) H. S. Lowrie, *J. Med. Pharm. Chem.*, **5**, 1362 (1962).
(4) M. F. Grundon and B. T. Johnson, *J. Chem. Soc. B*, **253** (1966).
(5) H. Harry Szmant and Y. L. Chow, *J. Org. Chem.*, **36**, 2887 (1971).
(6) K. Michel and M. Matter, *Helv. Chim. Acta*, **44**, 2204 (1961).
(7) C. Corral, J. Lissavetzky, and G. Quintanilla, *J. Heterocycl. Chem.* **15**, 1137 (1978).

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