oxaziridine. Unfortunately, our attempt to detect thionitrosomethane directly also failed.[6]

Experimental Section

2-Methyl-3,6-dihydro-1,2-thiazine (7). A mixture of 260 mg (1.93 mmol) of *trans*-2-methyl-3-phenyloxaziridine (4), 221 mg (1.93 mmol) of cyclohexene episulfide and 1 mL (12 mmol) of butadiene in 2 mL of chloroform gave a 69% yield of 2-methyl-3,6-dihydro-1,2-thiazine (7) after 2.5 h of reaction at room temperature: bp 50–51 °C (12 mm); IR 1435 (s), 1410 (m), 1195 (m), 1085 (s), 1010 (m), and 820 (m) cm^{-1}; NMR ($CDCl_3$) δ 6.07 (d, 1 H, =CH), 5.68 (d, 1 H, =CH), 3.47 (m, 2 H, CH_2), 3.20 (m, 2 H, CH_2), 2.85 (s, 3H, CH_3). Anal. Calcd for C_5H_9NS: C, 52.13; H, 7.88; N, 12.16. Found: C, 51.70; H, 7.97; N, 11.89. *cis*-Oxaziridine 4 gave 53% of thiazine 7 under the same reaction conditions.

In a similar procedure without butadiene, the mixture gave 57% of cyclohexene, 71% of benzaldehyde, 25% of azomethane, and 9% of sulfur diimide 5 accompanying 30% of the recovered *trans*-4 after 1 h of reaction at room temperature. The yields described here were determined by VPC or NMR by using undecane or dibenzyl ether as an internal reference. The isolation of thiazine 7 was accomplished by a large-scale experiment with approximately 40% yield. Methylthiazine 7 decomposed slowly during the repeated chromatography purification procedure. In a similar procedure, we obtained 2-ethyl- or 2-isopropyl-3,6-dihydro-1,2-thiazine as a liquid [bp 54–55 °C (9 mm) for the ethyl compoound Et and bp 56–57 °C (6 mm) for the isopropyl compound]. Reaction times, temperatures, and yields of each derivative were 12 h at room temperature and 26% for the ethyl compound and 12 h at 80 °C and 33% for the isopropyl thiazine, respectively.

Dimethylsulfur Diimide (5). The use of 2-methyl-3-(*p*-nitrophenyl)oxaziridine and ethylene sulfide was convenient for the preparation of dimethylsulfur diimide due to its low boiling point. A mixture of 3.6 g (0.02 mol) of *cis*- or *trans*-methyl(*p*-nitrophenyl)oxaziridine and 0.8 g (0.013 mol) of ethylene sulfide was distilled by using a dry ice cooling trap under reduced pressure, and the fraction was redistilled to obtain 5 (bp 90–92 °C) in a yield which varied considerably with the initial mixing conditions. The physical properties coincided well with those of an authentic sample.[4]

Registry No. *trans*-4, 40264-03-7; *cis*-4, 39245-63-1; 5, 13849-02-0; 7, 72952-29-5; 2-ethyl-3,6-dihydro-1,2-thiazine, 72952-30-8; 2-isopropyl-3,6-dihydro-1,2-thiazine, 72952-31-9; cyclohexene episulfide, 286-28-2; cyclohexene, 110-83-8; benzaldehyde, 100-52-7; azomethane, 503-28-6; *trans*-2-isopropyl-3-phenyloxaziridine, 57527-58-9; *trans*-2-ethyl-3-phenyloxaziridine, 57527-57-8; *cis*-methyl(*p*-nitrophenyl)oxaziridine, 28944-73-2; *trans*-methyl(*p*-nitrophenyl)-oxaziridine, 28958-67-0; ethylene sulfide, 420-12-2.

(6) The solution of an equimoler mixture of cyclohexene sulfide and *trans*-4 in $CDCl_3$ at −20 °C did not show any other signal except one of starting materials, diimide 5, and azomethane in NMR. The formation of thiazine 7 was not observed when butadiene was added after the completion of the reaction between episulfide and oxaziridine in chloroform.

Reaction of Pyrroles with Diethyl Azodicarboxylate

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Diethyl azodicarboxylate (DADC) has been widely used as a dienophile, especially to synthesize pyridazine derivatives.[1] Among the diene systems examined, furfural diacetate was the only heterocyclic aromatic compound which reacted with DADC to give a Diels–Alder adduct.[2] The known reactivity of pyrroles as a diene system with dimethyl acetylenedicarboxylate (DMAD)[3] prompted us to determine if a similar type of addition reaction takes place with DADC.

In the present paper we report the reactions of pyrrole and some of its derivatives with DADC in protic and in aprotic solvents.

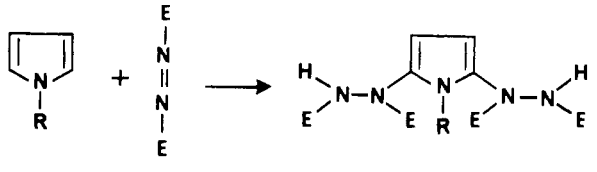
Table I. Yields and Reaction Conditions for Michael-Type Additions of DADC to Pyrroles

pyrrole	R	reflux, h (yield, %) ether	reflux, h (yield, %) ethanol	mp, °C
1a	H	24 (56)	12 (0)[a]	58–60
1b	CH_3	24 (66)	12 (86)	172–173
1c	n-C_4H_9	24 (33)	12 (59)	149
1d	C_6H_5	72 (0)[b]	12 (32)	80–80.5
1e	p-$CH_3OC_6H_4$	48 (9)	12 (52)	162
1f	p-$O_2NC_6H_4$	72 (0)[b]	12 (4)	158–159
1g	2,6-$(CH_3)_2C_6H_3$	72 (0)[b]	12 (17)	128–130

[a] Yellow gummy material was obtained which could not be characterized. [b] No adduct formed even after refluxing in benzene for 72 h.

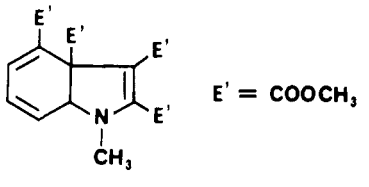
Results and Discussion

Most pyrroles examined in our laboratory gave 1:2 adducts (2) with DADC under the conditions specified in Table I. In contrast to the structure of the product (3) from the reaction with DMAD, adduct 2 was derived from Michael-type addition of DADC at both α positions of the pyrroles. The presence of a band at approximately 3300



1 2

E = $COOC_2H_5$



3

E' = $COOCH_3$

cm^{-1} in the IR spectra of the adducts strongly suggests the presence of a secondary amine. Two distinctive bands at approximately 1745 and 1700 cm^{-1} are consistent with two different carbonyl functions. Structure 2 shows that the ring and the side chains are not conjugated. This is supported by the low λ_{max} values which are between 220 and 235 nm for most of the adducts.

As shown in Table I, the yield of the 1:2 adduct varies depending upon the solvents employed and upon the substituents on the nitrogen of pyrrole. In general, the yields were greater in the protic solvent ethanol than in the aprotic solvents ether or benzene. It has been reported that Michael-type addition takes place when pyrroles react with DMAD.[4] Similarly, the initial addition of DADC to

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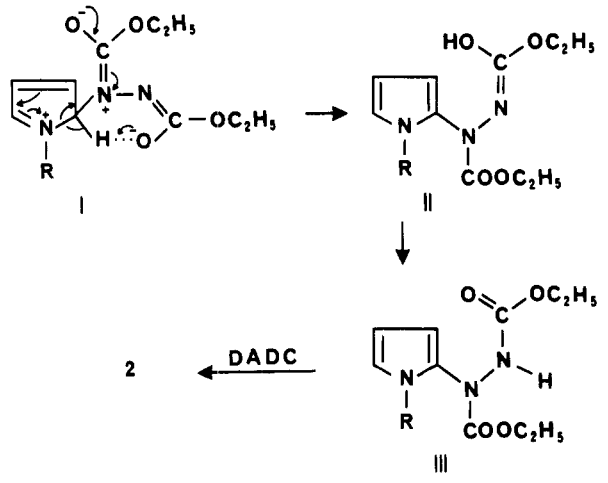
pyrroles probably forms a zwitterionic intermediate I.



Then, an α hydrogen may be transferred intramolecularly through a six-membered transition state when the reaction is carried out in the aprotic solvent. However, the facile solvation or intermolecular protonation by the protic solvent may be an explanation for the observation of increased yield.

With the exception of *p*-methoxyphenylpyrrole (**1e**), the 1-arylpyrroles did not give the adduct in aprotic solvents even after prolonged heating. The reaction did take place in the protic solvent; however, the yields were relatively low compared to those of the 1-alkyl derivatives. The relative yields of **2d–g** seem to be in line with the steric and electronic effects of the aryl groups.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Beckman IR-18 spectrophotometer. Ultraviolet and visible spectra were recorded on a Schimadzu double-beam spectrophotometer. NMR spectra were recorded on a Varian T-60 spectrometer in $CDCl_3$ containing Me_4Si as an internal reference. Mass spectra were obtained by using a Finnigan Model 3300 mass spectrometer. Elemental analyses were performed by the Institute of Physical and Chemical Research, Wako-shi, Saitama-ken, Japan.

Starting Materials. Commercial pyrroles (**1a** and **1b**) and DADC were distilled before use. Pyrroles (**1c–1g**) were prepared by literature methods.[5,6]

Typical Method of Preparation of the Adducts in Ether: 2,5-Bis(*N*,*N*'-diethoxycarbonylhydrazinyl)pyrrole (2a). A solution of pyrrole (1.34 g, 20.0 mmol) and DADC (6.96 g, 40.0 mmol) in anhydrous ether (30 mL) was refluxed for 24 h. The solvent was removed by evaporation, and the residual solid was recrystallized from ethanol (95%) to give **2a** as white powder (4.50 g, 56%): IR (KBr) 3300 (NH), 2990, 1730 (C=O), 1620, 1473, 1400, 1325, 1248, 1052 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (t, 12 H, J = 7 Hz, CH_3), 4.10 (q, 8 H, J = 7 Hz, OCH_2), 6.25 (s, 2 H, 2- and 3-H), 6.80–7.80 (br, 3 H, NH); UV (MeOH) 230 nm (ϵ 8130); mass spectrum, *m/e* (%) 415 (8, M^+), 414 (12), 255 (45), 240 (19), 179 (25), 149 (40), 94 (100).

Anal. Calcd for $C_{16}H_{25}N_5O_8$: C, 46.26; H, 6.07; N, 16.86. Found: C, 46.00; H, 5.99; N, 16.54.

Typical Method of Preparation of the Adducts in Ethanol: 2,5-Bis(*N*,*N*'-diethoxycarbonylhydrazinyl)-1-methylpyrrole (2b). A solution of 1-methylpyrrole (0.80 g, 10.0 mmol) and DADC (3.48 g, 20.0 mmol) in absolute ethanol (30 mL) was refluxed for 12 h. After the solution was cooled to room temperature, ether (10 mL) was added and the solution was kept in a refrigerator for 24 h to give precipitates. The precipitates were collected by filtration and recrystallized from ethanol–ether (1:2 v/v) to give **2b** as white prisms (2.80 g, 86%): IR (KBr) 3300 (NH), 2992, 1750 and 1715 (C=O), 1570, 1500, 1472, 1370, 1312, 1253, 1180, 1050, 750 cm^{-1}; NMR ($CDCl_3$) δ 1.42 (dt, 12 H, J = 7.0 Hz, CH_3), 3.48 (s, 3 H, NCH_3), 4.20 (dq, 8 H, J = 7.0 Hz, OCH_2), 6.20 (s, 2 H, 3- and 4-H), 7.00 (br, 2 H, NH); UV (EtOH) 225 nm (ϵ 13200); mass spectrum, *m/e* (%) 429 (66, M^+), 356 (24), 341 (71), 269 (100), 223 (62), 163 (43), 149 (28), 136 (33), 93 (52).

Anal. Calcd for $C_{17}H_{27}N_5O_8$: C, 47.55; H, 6.34; N, 16.31. Found: C, 47.52; H, 6.35; N, 16.29.

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Registry No. 1a, 109-97-7; **1b**, 96-54-8; **1c**, 589-33-3; **1d**, 635-90-5; **1e**, 5145-71-1; **1f**, 4533-42-0; **1g**, 15898-23-4; **2a**, 73018-03-8; **2b**, 73018-04-9; **2c**, 73037-74-8; **2d**, 73018-05-0; **2e**, 73018-06-1; **2f**, 73018-07-2; **2g**, 73018-08-3; DADC, 4114-28-7.

Supplementary Material Available: Full IR, NMR, UV, and mass spectra and elemental analysis data for compounds **2c–2g** (2 pages). Ordering information is given on any current masthead page.

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Synthesis and Identification of Isomeric Methylpyrazine Derivatives

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The condensation of an α,β-dicarbonyl compound with a 1,2-diamine is a useful method for preparation of pyrazine derivatives.[1] The procedure[2] for the condensation of biacetyl with aminomalonamide gave the best yields (93%) of 2-hydroxy-3-carboxamido-5,6-dimethylpyrazine.

Jones claimed[2] to have obtained 2-hydroxy-3-carboxamido-5-methylpyrazine from the condensation of methylglyoxal with aminomalonamide, but later work[3] has shown that the 6-methyl isomer is formed exclusively in this reaction. The condensation of methylglyoxal bisulfite with aminomalonamide has been reported to give the 6-methylpyrazine derivative.[4] In this case, the 6-substituted isomer was the only isolable product.

We have now found that condensation of 2-amino-2-deoxy-D-glucose oxime (**1**) with methylglyoxal gives 2-(D-*arabino*-tetrahydroxybutyl)-6-methylpyrazine 4-*N*-oxide (**3**) and that condensation of 1-amino-1-deoxy-D-fructose oxime (**9**) with methylglyoxal gives 2-(D-*arabino*-tetrahydroxybutyl)-5-methylpyrazine 1-*N*-oxide (**11**) as the principal products (Scheme I). Minor amounts of an isomer were detected in each of the reaction mixtures by NMR but were not isolated.

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