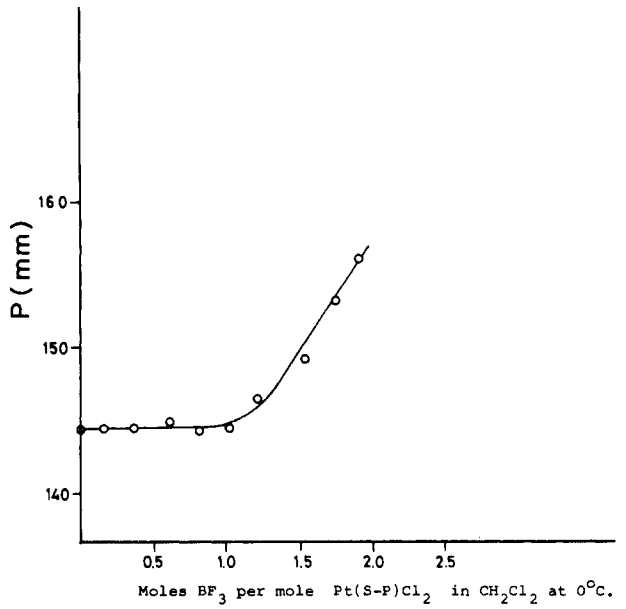

Figure 1. Tensimetric titration of $Pt(S\text{-}P)Cl_2$ with BF_3 at 0 °C.

white solid dissolved during the first few minutes of stirring forming a clear yellow solution. Stirring was continued at room temperature for 2 h. The solution was then filtered, and solvent was removed under reduced pressure. The pale-yellow residue was collected, washed with cold methanol (3 × 5 mL) and diethyl ether (20 × 10 mL), and then dried under vacuum at 50 °C.

Preparation of $[Pt(S\text{-}P)I_2]\cdot BF_3$. To a stirred suspension of $[Pt(S\text{-}P)I_2]$ (0.35 g, 0.5 mmol) in dry chloroform (30 mL) was added $(C_2H_5)_2O\cdot BF_3$ (5 mmol BF_3). The mixture was further stirred at room temperature for 2 h. The suspended yellow solid did not dissolve completely upon the addition of $(C_2H_5)_2O\cdot BF_3$ and a color change from bright yellow to orange-yellow was observed. The reaction mixture was filtered, the solid residue was discarded, and the filtrate was concentrated, under reduced pressure, to a volume of 10 mL. Addition of diethyl ether (30 mL) precipitated a pale-yellow solid which was then filtered, washed with diethyl ether, and dried under vacuum at 50 °C.

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Registry No. $[Pt(S\text{-}P)Cl_2]$, 92763-60-5; $[Pt(S\text{-}As)Cl_2]$, 108150-97-6; $[Pt(S\text{-}P)I_2]$, 108150-98-7; $[Pt(S\text{-}P)Cl_2]\cdot BF_3$, 108150-99-8; $[Pt(S\text{-}As)Cl_2]\cdot BF_3$, 108151-00-4; $[Pt(S\text{-}P)I_2]\cdot BF_3$, 108151-01-5; K_2PtCl_4, 10025-99-7; $(C_2H_5)2O\cdot BF_3$, 109-63-7.

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1,3-Dipolar Cycloaddition of Nitrile Oxides with *cis*- and *trans*-Ethylene-Substituted Δ^2-Isoxazoline Derivatives

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1,3-Dipolar cycloaddition reactions of 2,4,6-trimethylbenzonitrile oxide with dimethyl maleate, dimethyl fumarate, and diethyl fumarate were used for the synthesis of polyfunctional 2-isoxazoline ring systems.

Nitrile oxides have been considered as one of the most important precursors for the synthesis of isoxazole and 2-isoxazoline ring systems upon their reaction with substituted acetylenes (*1-3*) and ethylenes (*4-7*), respectively. Continuing our previous work on the synthesis of polyfunctional heterocycles containing isoxazole and 2-isoxazoline ring systems (*8*), we report in the present paper further details on the reaction of 2,4,6-trimethylbenzonitrile oxide (I) with disubstituted ethylenes as shown in Scheme I.

Experimental Section

2,4,6-Trimethylbenzonitrile oxide was prepared as previously reported (*9*). Melting points were measured with a Buchi 510 capillary melting point apparatus. The nuclear magnetic resonance spectra were recorded on a Bruker AM 300 (300 MHz) using tetramethylsilane as an internal reference and shifts (δ) are reported in ppm. Elemental analyses were performed by the analytical Laboratory of the Universität Bielefeld, West Germany.

Preparation of cis-Dimethyl-3-(2,4,6-trimethylphenyl)-4,5-dihydro-4,5-isoxazoledicarboxylate (II). To a solution of 4.83 g (30 mmol) of freshly prepared 2,4,6-trimethylbenzonitrile oxide in 40 mL of tetrahydrofuran was added 4.61 g (32 mmol) of dimethyl maleate. The resulting mixture was heated under reflux for 6 h. Tetrahydrofuran was removed on a rotary evaporator at diminished pressure. Distillation of the yellow thick liquid yielded 7.5 g (82%) of the product, bp 150-155 °C/0.01 mmHg. The product was solidified near room temperature: mp 124-125.5 °C; NMR ($CDCl_3$) δ 6.86 (2 H, s), 5.56 (1 H, d, J = 6.4 Hz), 4.69 (1 H, d, J = 6.4 Hz), 3.84 (3 H, s), 3.59 (3 H, s), 2.26 (3 H, s), 2.17 (6 H, s).

trans-Dimethyl-3-(2,4,6-trimethylphenyl)-4,5-dihydro-4,5-isoxazoledicarboxylate (III). To a solution of 8.05 g (50 mmol) of freshly prepared 2,4,6-trimethylbenzonitrile oxide in 80 mL of tetrahydrofuran was added 7.63 g (53 mmol) of dimethyl fumarate. The resulting mixture was heated under reflux for 5 h. After removal of tetrahydrofuran on a rotary evaporator at diminished pressure, the residue was recrystallized from

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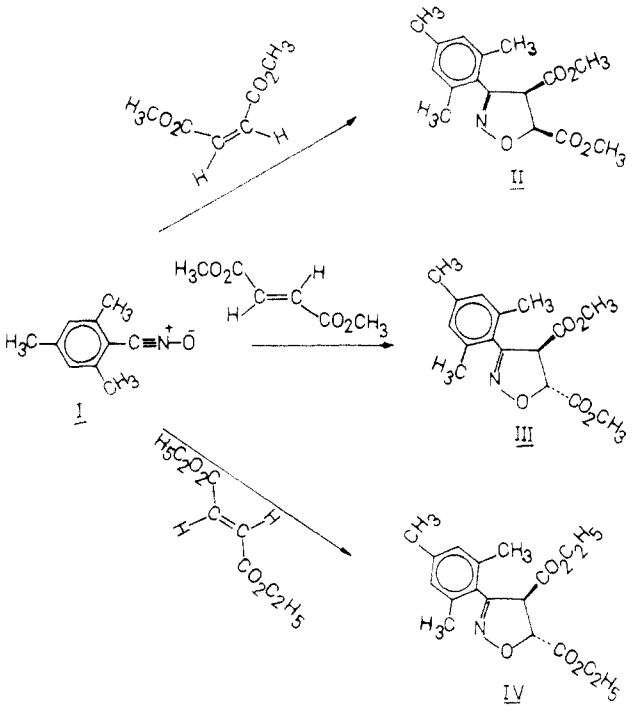
Scheme I



petroleum ether to yield 11.9 g (78%) of the product: mp 125–126.5 °C; NMR ($CDCl_3$) δ 6.88 (2 H, s), 5.57 (1 H, d, J = 6.5 Hz), 4.71 (1 H, d, J = 6.5 Hz), 3.85 (3 H, s), 3.60 (3 H, s), 2.28 (3 H, s), 2.19 (6 H, s).

***trans*-Diethyl-3-(2,4,6-trimethylphenyl)-4,5-dihydro-4,5-isoxazoledicarboxylate (IV).** To a solution of 6.44 g (40 mmol) of freshly prepared 2,4,6-trimethylbenzonitrile oxide in 50 mL of tetrahydrofuran was added 7.2 g (42 mmol) of diethyl fumarate. The resulting mixture was heated under reflux for 8 h. Tetrahydrofuran was removed on a rotary evaporator at diminished pressure. Distillation of the oily residue yielded 11.1 g (83%) of the product, bp 145–149 °C/0.005 mmHg; NMR ($CDCl_3$) δ 6.85 (2 H, s), 5.52 (1 H, d, J = 7 Hz), 4.67 (1 H, d, J = 7 Hz), 4.28 (2 H, q, J = 7.2 Hz), 4.01 (2 H, q, J = 7.2 Hz), 2.25 (3 H, s), 2.18 (6 H, s), 1.32 (3 H, t, J = 7.2 Hz), 0.97 (3 H, t, J = 7.2 Hz).

Elemental analyses (C, H, N) for compounds II–IV in agreement with theoretical values were obtained and submitted for review.

***Elemental Analyses*.** The results are shown as follows.

***Compound II*.** Anal. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.73; H, 6.39; N, 4.65.

***Compound III*.** Anal. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: C, 62.66; H, 6.41; N, 4.56.

***Compound IV*.** Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.55; H, 7.17; N, 4.29.

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Registry No. I, 2904-57-6; II, 108295-19-8; III, 100854-03-3; IV, 108295-20-1; dimethyl maleate, 624-48-6; dimethyl fumarate, 624-49-7; diethyl fumarate, 623-91-6.

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Synthesis and Antibacterial Activity of 2-[[ω-(Dialkylamino)alkyl]thio]-3-aryl(or alkyl)-6,8-disubstituted-4(3*H*)-quinazolinones

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Synthesis of 47 new 2-[[ω-(dialkylamino)alkyl]thio]-3-aryl(or alkyl)-6,8-disubstituted-4(3*H*)-quinazolinones, 2–6, from the corresponding 2-thio-4(3*H*)-quinazolinones, 1, has been described. Fifteen of them were screened for their antibacterial activity by the Rideal Walker drop serial dilution method against two common bacteria, *Staphylococcus aureus* and *Escherichia coli*.

A number of quinazolin-4-one derivatives (*1–4*) have been found to exhibit high activity against a variety of microbes parasitizing animals and plants. Tregubenko et al. (*5*) have synthesized several 2-(N,N-disubstituted aminoethylthio)-3-aryl-4(3*H*)-quinazolinones and -thiones and evaluated them as radioprotective agents. Furthermore, 2-((N-substituted aminoethyl)thio)-3-aryl-6-iodo-4(3*H*)-quinazolinones have been reported (*6*) to be either CNS stimulants or depressants on mice.

In view of our continuing interest (*1*) in the syntheses and biological activities of 4(3*H*)-quinazolinones, we report here the synthesis of a series of 2-[[ω-(dialkylamino)alkyl]thio]-3-aryl(or alkyl)-6,8-disubstituted-4(3*H*)-quinazolinones (**2–6**).

The title compounds **2–6** were prepared (Scheme I) by heating an appropriately substituted anthranilic acid with an isothiocyanate to give 2-thio-3-aryl(or alkyl)-6,8-disubstituted-4-(3*H*)-quinazolinone (**1**) and subsequent treatment with suitable dialkylaminoalkyl bromide hydrobromide salts. The reaction proceeds to completion within a few minutes probably due to

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