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[Lab. of Medicinal Chemistry]

Carboxyflavins, Novel Inhibitors of Taq DNA Polymerase.Yoshiyuki MIZUSHINA, Takamasa UENO, Yuso GOTO, Yoshiaki ISOBE,
Magoichi SAKO,* Takehito FUJITA, Kosaku HIROTA, Hideya HAYASHI
and Kengo SAKAGUCHI

Carboxyflavins were found to be potent selective inhibitors of Taq DNA polymerase in a polymerase chain-reaction. The inhibitions were dose-dependent, and complete inhibitions were observed at the concentration of 3.0 μM . Carboxyflavins were much less, or not sensitive to the DNA polymerases such as calf thymus DNA polymerase α , rat DNA polymerase β , human immunodeficiency virus type 1 reverse transcriptase, the Klenow Fragment of *E. coli* DNA polymerase I, and T4 DNA polymerase. To our knowledge, there is no other report of an agent that selectively inhibits only a thermophilic polymerase. Interestingly, the carboxyflavins were able to prevent DNA synthesis in the murine lymphoid leukemia cell line L-1210 *in vitro*; almost complete inhibitory levels were achieved in the range of less than 10 μM .

[*J. Org. Chem.*, **63**, 6947-6951 (1998)]

[Lab. of Medicinal Chemistry]

**Facile Synthesis and NO-Generating Property of 4H-[1,2,5]Oxadiazolo-
[3,4-d]pyrimidine-5,7-dione 1-Oxides.**Magoichi SAKO,* Souichi ODA, Seiji OHARA, Kosaku HIROTA and
Yoshifumi MAKI

4H-[1,2,5]Oxadiazolo[3,4-d]pyrimidine-5,7-dione 1-oxides are conveniently prepared in high yields by the oxidative intramolecular cyclization of 6-amino-5-nitro-1H-pyrimidine-2,4-diones employing iodosylbenzene diacetate as an oxidant in the presence of lithium hydride. The generation of nitric oxide (NO) and NO-related species from the N-oxides occurs in the presence of thiols such as N-acetylcysteamine, cysteine, and glutathione under physiological conditions. The evidence for the NO-generation derives from mechanistic interpretations for the reaction of the N-oxides with thiols and other chemical observations. It should be noted that no formation of the NO and NO-related species was observed in reactions of the deoxygenated compound of the N-oxide and 6-amino-1,3-dimethyl-5-nitroso (or nitro)-1H-pyrimidine-2,4-dione with N-acetylcysteamine under similar conditions.

[*Tetrahedron Lett.*, **39**, 4063-4066 (1998)]

[Lab. of Pharm. Synthetic Chemistry]

**The First Synthesis of Monoazaporphyrins Bearing a Nitrogen Atom
at the Peripheral Position**

Shigeo KAI, Mikio SUZUKI and Yukio MASAKI*

2-Aza-3,7,8,12,13,17,18-heptaalkylporphyrins and their zinc complexes were synthesized by the use of improved '3+1' condensation of 2,5-bis [(5'-carboxy-3',4'-dialkylpyrrol-5'-yl)methyl]-3,4-diethylpyrroles and 2,5-bis [(N,N,N-trimethylammonio)-methyl]-4-methylimidazole ditriflate under non-acidic conditions in 1.8—6.6% yields.

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[Lab. of Pharm. Synthetic Chemistry]

**Remote Asymmetric Induction in Lewis Acid Catalyzed Diels–Alder Reaction of
 α,β -Unsaturated Enones Having a Chiral Sulfinyl-substituted,
5-Membered Aromatic Heterocycle**

Yoshitsugu ARAI,* Tsutomu MASUDA and Yukio MASAKI

Two types of chiral sulfoxides as Diels–Alder dienophiles were synthesized and high levels of diastereoselectivity were observed in cycloadditions. 2-Furyl and 2-thienyl α,β -enones, bearing a chiral sulfinyl group in the heterocycle, served as efficient dienophiles in Diels–Alder reactions, where the catalytic use of aluminium chloride or a lanthanide triflate effected the cycloaddition with cyclopentadiene affording the *endo* adduct with high diastereoselectivity, ranging from 91% to 98%.