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**Synthesis and Analgesic Activity of Novel Heterocycles, [1]Benzothio-
pyrano[3,4-*b*]pyrrole Derivatives.**

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In order to develop analgesic compounds possessing a sulfur atom in the alicyclic ring, novel *cis*-fused heterocycles, [1]benzothio-pyrano[3,4-*b*]pyrrole derivatives were synthesized *via* a unique cyclization reaction starting from 4-(4-methoxyphenylthio)-2-butanone (1) or 6-methoxy-3,4-dihydro-2*H*-1-benzothio-pyran-4-one (2). The analgesic effects of benzothio-pyranopyrroles (3, 4) were measured by means of the writhing test. The phenolic derivative 4 completely inhibited the appearance of writhing at the dose of 50mg/kg, but the methoxy derivative 3 had no analgesic effect.

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**Facile Synthesis of 8-Benzoylthio-2,6-methano-3-benzazocines and 3-
Benzoylthiomorphinans Having Small-Ring Substituents.**

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Synthesis of 3-cyclopropylmethyl-, 3-cyclobutylmethyl, and 3-methyl-8-benzoylthio-2,6-methano-3-benzazocines (1*j*-1) was performed by regio-selective chlorosulfonation of non-narcotic 8-deoxy derivatives (1*a*-*c*) followed by reduction and benzylation. 3-Benzoylthiomorphinans (2*h*-*j*) were also obtained by the same method. Compounds having small-ring substituents (1*k*, 1*l*, 2*i*, 2*j*) were found to be weak but pure μ - and δ -opioid antagonists. The analgetic activity of 1*k* was almost equal to that of pentazocine.

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Formation of a Novel Bicyclic γ -Lactam with Isopenicillin *N* Synthase.

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Previous articles have documented that incubation of isopenicillin *N* synthase (IPNS) with analogues of the natural substrate for IPNS, [(5*S*)-5-amino-5-carboxypentanoyl]-L-cysteinyl-D-valine (L, D-ACV), can provide a wide range of bicyclic β -lactam structures.

Incubation of [(5*S*)-5-amino-5-carboxypentanoyl]-L-homocysteinyl-D-cysteine with IPNS in the presence of Fe²⁺, ascorbate, and O₂ resulted in the formation of a novel bicyclic γ -lactam containing an intramolecular disulphide linkage. The present result provided a strong evidence supporting the mechanism proposed for the non-hemin catalysed oxidative double-cyclisation of L, L, D-ACV leading to isopenicillin *N* in penicillin biosynthesis.