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Synthesis and Analgesic Activity of Novel Heterocycles, 〔1〕Benzothiopyrano〔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〕benzothiopyrano〔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-benzothiopyran-4-one (**2**). The analgesic effects of benzothiopyranopyrroles (**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 (**1j-l**) was performed by regio-selective chlorosulfonation of non-narcotic 8-deoxy derivatives (**1a-c**) followed by reduction and benzoylation. 3-Benzoylthiomorphinans (**2h-j**) were also obtained by the same method. Compounds having small-ring substituents (**1k**, **1l**, **2i**, **2j**) were found to be weak but pure μ- and δ-opioid antagonists. The analgetic activity of **1k** 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, 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 Fe^{2+}, ascorbate, and O_2 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 catalised oxidative double-cyclisation of L, L, D-ACV leading to isopenicillin *N* in penicillin biosynthesis.