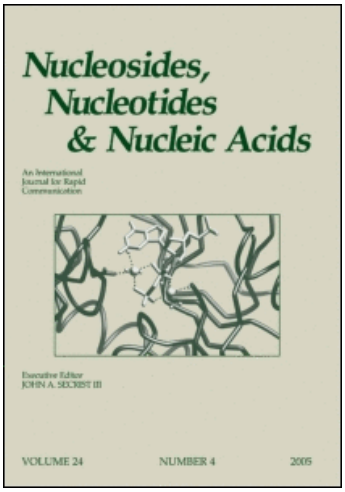

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Synthetic Approaches to 5:8-Fused Heterocyclic Systems. A Novel Rearrangement During the Synthesis of Imidazo[4,5-*e*][1,2,4]triazocine Ring System

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SYNTHETIC APPROACHES TO 5:8-FUSED HETEROCYCLIC SYSTEMS. A NOVEL REARRANGEMENT DURING THE SYNTHESIS OF IMIDAZO[4,5-*e*][1,2,4]TRIAZOCINE RING SYSTEM.

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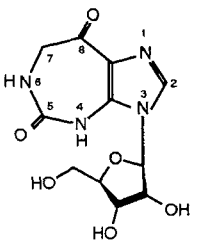
ABSTRACT

*The attempted ring-closure of 4-amino-1-benzyl-5-[(N^2-benzyl-N^2-methoxycarbonyl)hydrazinomethylenecarbonyl]imidazole (**5b**) in sodium hydride/dimethyl sulfoxide at 50-60 °C afforded 1,7-dibenzylxanthine (**6**) instead of the anticipated 5:8-fused heterocycle **4b**. A tentative reaction pathway has been proposed for the observed transformation.*

INTRODUCTION

We have recently reported the synthesis and investigation of structural, chemical, biochemical, as well as biophysical properties of a number of ring-expanded ("fat") nucleosides and nucleotides containing the 5:7-fused heterocyclic ring systems, *e.g.*, **1**, **2**, and **3**.[1] We now report on a novel rearrangement that we encountered during our synthetic endeavors toward a 5:8-fused ring system **4**. The attempted synthesis of **4b** via ring-closure of **5b** in sodium hydride/DMSO at 50-60 °C gave only



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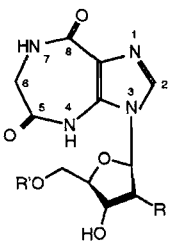

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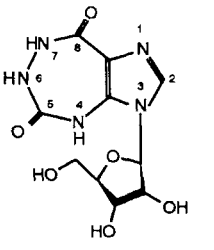
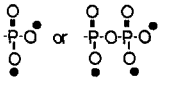
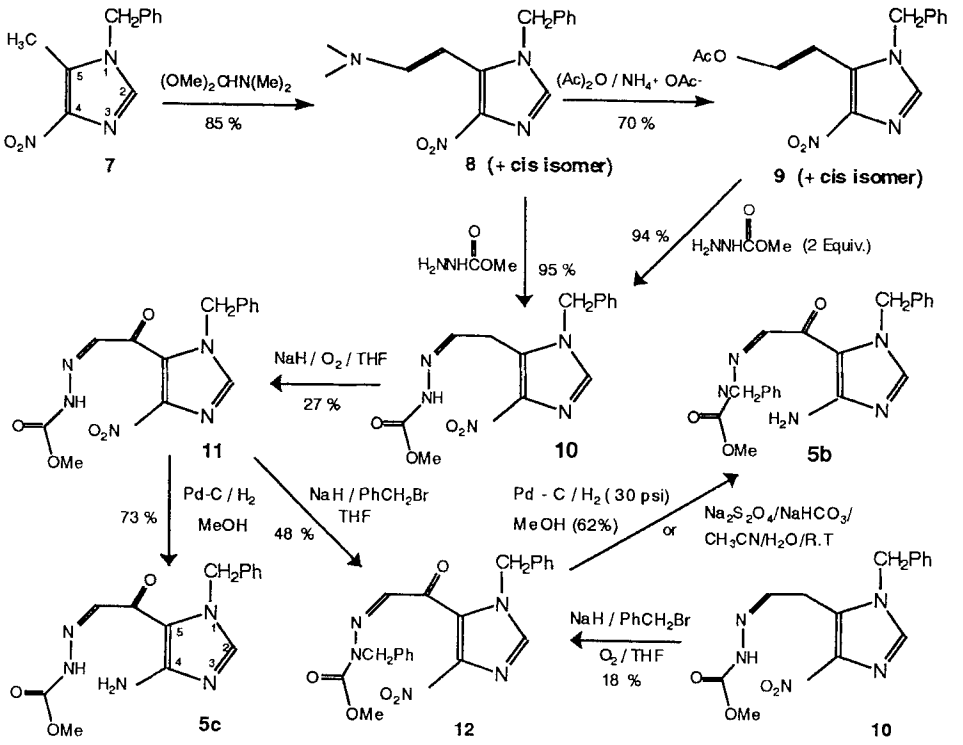


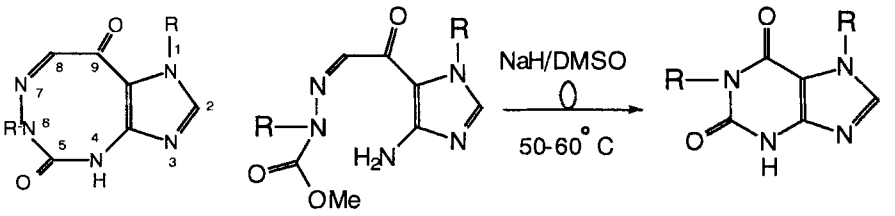
3

R = H or OH; R' = 



SCHEME I

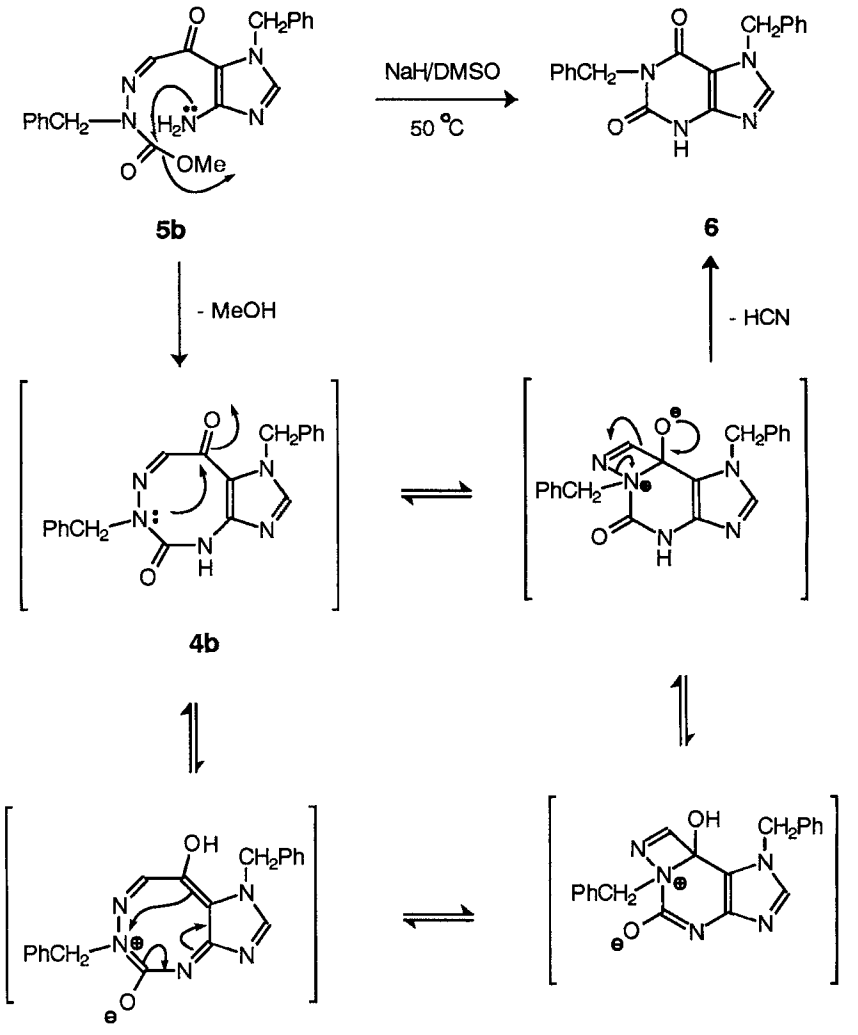
the 5:6-fused xanthine derivative (**6b**). The synthesis of the precursor **5b** from **7**[4] is outlined in **Scheme I**. The structures of **6b**, **5c**, and the precursor to **5b** were confirmed by single-crystal X-ray diffraction analyses.



4 **5** **6**

a, R = R' = H; b, R = R' = CH_2Ph; c, R = CH_2Ph, R' = H; d, R = H, R' = CH_2Ph

Syntheses of large ring heterocycles are often plagued with undesired, opportunistic rearrangements,[2] and we have indeed uncovered a few such



SCHEME II

rearrangements while attempting to synthesize **3**.[3] A tentative reaction pathway for the transformation of **5b** to **6** is outlined in **Scheme II**.

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