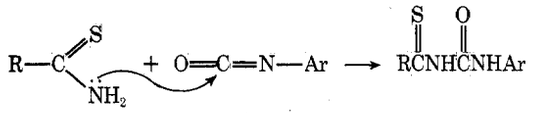
Table I

No.	R	Ar	C=S	C=O	Mp, °C	Crystn solvent	Reflux time, min	Yield, %	Reflux solvent	Formula[a]
1	CH_3	α-$C_{10}H_7$	1240	1702	233	Xylene	1	60	Xylene	$C_{13}H_{10}N_2OS$
2	C_6H_5	C_6H_5	1215	1705	218[b]	1-Butanol	15	70	Xylene, toluene	$C_{14}H_{12}N_2OS$
3	C_6H_5	p-ClC_6H_4	1212	1702	248	1-Butanol	1	65	Xylene	$C_{14}H_{11}ClN_2OS$
4	C_6H_5	α-$C_{10}H_7$	1210	1700	232	Xylene	2	75	Xylene	$C_{18}H_{14}N_2OS$
5	p-$CH_3C_6H_4$	C_6H_5	1215	1700	218	1-Butanol	15	81	Toluene	$C_{15}H_{14}N_2OS$
6	p-$CH_3C_6H_4$	p-ClC_6H_4	1210	1690	262	Anisole	1	70	Xylene	$C_{15}H_{13}ClN_2OS$
7	p-$CH_3C_6H_4$	α-$C_{10}H_7$	1205	1700	232	Methyl ethyl ketone	2	85	Xylene	$C_{19}H_{16}N_2OS$
8	α-$C_{10}H_7$	C_6H_5	1228	1690	233	1-Butanol	5	52	Toluene	$C_{18}H_{14}N_2OS$
9	α-$C_{10}H_7$	p-ClC_6H_4	1220	1690	238	Methyl ethyl ketone	1	48	Xylene	$C_{18}H_{13}ClN_2OS$
10	α-$C_{10}H_7$	α-$C_{10}H_7$	1220	1695	211	1-Butanol	1	84	Toluene, xylene	$C_{22}H_{16}N_2OS$

[a] Analyzed within ±0.4% for C, H, N, and S, except 6. Calcd for 6: C, 59.11; H, 4.29; N, 9.18; S, 10.49. Found: C, 58.75; H, 4.17; N, 9.89; S, 9.25. [b] J. Goerdeler and H. Schenk[5] report mp 214°.

We have now found that in the presence of Cu_2O, the reaction of thioamides and aryl isocyanates provides a satisfactory preparation of thioacylureas for which we propose the following scheme. Cu_2O is specific catalyst for this reaction—perhaps because of its ability to form complex with thioamide C=S bond and permit nitrogen unshared electron pair attack at carbon isocyanate C=N bond.



R = alky or aryl

The spectra of the thioacylureas (Table I) showed a thiocarbonyl absorption band at 1240–1205 cm^{-1} and carbonyl absorption at 1700–1690 cm^{-1}; the intensity ratio $\nu_{C=O}/\nu_{C=S}$ is ~1.4. The related disubstituted ureas show carbonyl absorption at 1650–1610 cm^{-1}.

The reaction of aryl isothiocyanates with alkyl- and arylthioamides provides a general method for preparing substituted thioacylureas. Previous preparation have involved the addition of amines to thiobenzoyl isocyanate[5] or less direct methods.[6-8]

Experimental Section

General. Melting points were measured on a Köfler hotbench apparatus. A Beckman IR-20A spectrophotometer was used for ir spectra, which were run in KBr. Microanalyses were performed by CNRS (Service Central de Microanalyse; 2, rue Henry-Dunant, 94-Thiasis, France).

Commercially available aryl isocyanates and thioacetamide were used as received. Arylthioamides were prepared by established procedures.[9] Useful solvents for the reaction are benzene, toluene, and xylene; 100 mg of Cu_2O as catalyst was used per mole of reactant. To avoid side reactions, dry solvents should be used for reflux and recrystallization. In a typical example a solution of 0.75 g (0.01 mmol) of thioacetamide, 1.6 g (0.01 mol) of α-naphthyl isocyanate, and 10 mg of Cu_2O in 10 ml of anhydrous xylene was heated under reflux for 1 min. The reaction was filtered. Recrystallization from anhydrous xylene gave thioacetyl-3-α-naphthylurea(60%), mp 233°.

Acknowledgment. The author is grateful to Dr. N. Mojdehi the chancellor of the Meshed University for his constant encouragements.

Registry No. **1,** 51933-47-2; **2,** 3553-47-7; **3,** 51933-48-3; **4,** 51933-49-4; **5,** 51933-50-7; **6,** 51933-51-8; **7,** 51933-52-9; **8,** 4875-18-7; **9,** 51933-53-0; **10,** 51933-54-1; $RC(S)NH_2$ (R = CH_3), 62-55-5; $RC(S)NH_2$ (R = C_6H_5), 2227-79-4; $RC(S)NH_2$ (R = p-$CH_3C_6H_4$), 2362-62-1; $RC(S)NH_2$ (R = α-$C_{10}H_7$), 20300-10-1; OCNAr (Ar = α-$C_{10}H_7$), 86-84-0; OCNAr (Ar = C_6H_5), 103-71-9; OCNAr (Ar = p-ClC_6H_4), 104-12-1.

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Pyrolysis of a Tropane Analog of Pethidine. A Novel 7-Azabicyclo[4.2.1]nonane Derivative

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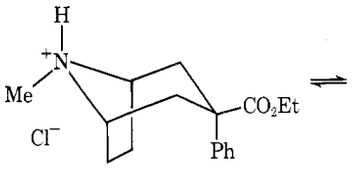
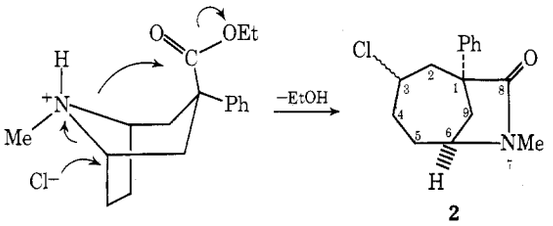
Received May 13, 1974

We recently undertook a conformational analysis of 3-β-carbethoxy-3-α-phenyltropane hydrochloride (1),[1] a tropane analog of pethidine, as part of our interest in the stereochemistry of narcotic analgesics based on 4-phenylpiperidine.[2] The ethyl ester hydrochloride **1,** prepared from 3-tropinone,[3] melted within the reported range (192.5–193.5°) but with evolution of gas, behavior not originally described. Pyrolysis of 1 was therefore investigated on a larger scale and a nonbasic solid isolated from the thermolysate. This product is assigned the structure 7-aza-3-chloro-7-methyl-1-phenyl-8-oxobicyclo[4.2.1]nonane (2) on the following grounds: (i) elemental analysis; (ii) the M^+ (263) and $M^+ + 2$ (265) ions in its mass spectrum had the

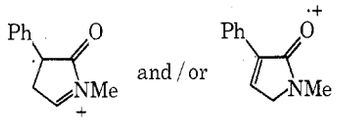
relative abundance ratio of 3:1 characteristic of chlorine-containing derivatives—probable assignments to the base (*m/e* 42) and second most abundant peak (*m/e* 173, 78%) are $H_2C{=}N^+{=}CH_2$ and (3), respectively; (iii) its ir spectrum (Nujol mull) displayed amide carbonyl bands (1670, 1678 cm^{-1}); and (iv) its 100-MHz ^1H nmr spectrum in $CDCl_3$ (TMS reference) showed 1-proton multiplets assigned to methine hydrogens at C-3 and C-6, and an *N*-methyl resonance (s, δ 2.88) typical of an *N*-methyl cyclic amide (*cf.* δ_{NMe} 2.82 for 1-methyl-2-pyrrolidone).[4] The stereochemistry at C-3 is unestablished. Pyrolysis of the amino acid hydrochloride corresponding to 1 gave the same bicyclononane.



1



2



3

The reaction 1 to 2 represents the interconversion of 8-azabicyclo[3.2.1]octane and 7-azabicyclo[4.2.1]nonane derivatives through nucleophilic attack by chloride, and the gas observed when (1) melts must therefore be ethanol vapor.[5]

Experimental Section

Pyrolysis of 3-β-Carbethoxy-3-α-phenyltropane Hydrochloride. The hydrochloride 1 (0.96 g) was heated for 15 min in an oil bath kept at 190–200°. The thermolysate in chloroform was washed with water, and the organic phase dried (Na_2SO_4) and evaporated to leave 7-aza-3-chloro-7-methyl-1-phenyl-8-oxobicyclo[4.2.1]nonane (0.59 g): mp 132–137° (142–144° from benzene–hexane); ^1H nmr δ ($CDCl_3$) 7.46 and 7.22 (2 m, 2 H, 3 H, aryl protons), 4.00 (m, 1 H, $W_{1/2}$ = 22 Hz, 3 CH or 8 CH), 3.70 (m, 1 H, $W_{1/2}$ = 8 Hz, 3 CH or 8 CH), 2.88 (s, 3 H, NMe); 2.86–1.64 (m, 8 H, 2, 4, 5 and 9 CH_2).

Anal. Calcd for $C_{15}H_{18}ClNO$: C, 68.30; H, 6.88; Cl, 13.44; N, 5.31. Found: C, 68.39; H, 7.01, Cl, 13.44; N, 5.09.

Similar treatment of the amino acid hydrochloride corresponding with 1 gave a comparable yield of 2.

Acknowledgment. We thank the Medical Research Council for Canada for financial support.

Registry No.—1, 52123-58-7; 2, 52123-59-8.

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Synthesis of 1-(6-Aminopurin-9-yl)-2,5-anhydro-1,2-dideoxy-DL-ribitol, a New "Reversed" Amino Nucleoside[1]

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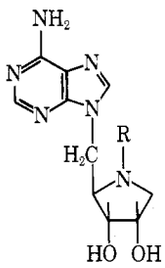
Received April 16, 1974

Many nucleosides which are effective agents in inhibiting the growth of malignant cells become ineffective *in vivo* because they are rapidly destroyed by enzymatic cleavage into a purine or pyrimidine and a carbohydrate moiety.[2,3] A reversed nucleoside, however, does not possess the normal linkage between the nitrogen of the base and the anomeric carbon of the sugar, and is more stable with respect to hydrolytic cleavage. A number of reversed nucleosides have already been synthesized.[4–9] Some have elicited interest in connection with cytokinin activity.[10,11] Recently, two patents have been filed which list several reversed nucleosides as antiviral and anticancer drugs.[12,13]

Our research interests in the area of amino and aminoacyl nucleosides prompted the synthesis of 1, the first example of a reversed amino nucleoside. Central to any of the several possible chemical strategies for obtaining 1 is the synthesis of the pyrrolidine sugar 4. The biologically active and synthetic imino acid dehydroproline can be modified by reduction and hydroxylation to give 4 in high yields.[14] Conversion of the amino sugar 4 to 7, subsequent coupling with the sodium salt of adenine, and removal of the isopropylidene group with formic acid gave **1b** as a stable, white, crystalline compound, mp 212–213°. The detosylated com-



1a, R = H
b, R = tosyl