Table I

R in RLi	Solvent, temp, °C	Reaction time, days	Product	Yield, %
n-C_4H_9	Hexane–THF, −30	1	n-$C_5H_{11}NHCH_3$	50
sec-C_4H_9	Hexane–THF, −30	4	$C_2H_5CH(CH_3)CH_2NHCH_3$	68
C_6H_5	7:3 benzene–ether and THF, 0	3	$C_6H_5CH_2NHCH_3$	75

ric triamide in a 2:1 ratio, gave the homologous *N*-methylamines in 50–75% yield, as summarized in Table I.

In addition to being of potential synthetic value, these findings show that HMPTA in the presence of an alkyllithium is an *in situ* source of the very unstable species $CH_3N{=}CH_2$. Although this compound has been prepared[4,5] and studied spectroscopically,[5,6] it polymerizes[4,7] near its boiling point of −35°. Our findings also constitute a *caveat* to investigators who wish to use HMPTA as a solvent for organoalkali reagents, although we must emphasize that the less reactive lithium compounds **1** and **2** are stable in HMPTA for prolonged periods of time at 0°C and room temperature, respectively.

Experimental Section

***N*-Methyl-*N*-(2-methyl)butylamine.** A dry 200-ml round-bottom flask containing a Teflon-coated magnetic stirring bar was capped with a rubber septum and flushed with dry nitrogen using hypodermic needles; then *sec*-butyllithium (50 ml, 0.8 *M* in hexane, 0.04 mol) was introduced into the flask with a syringe. The solution was cooled by immersion in a cooling bath at −30° and diluted with 25 ml of tetrahydrofuran (THF). A solution of 3.6 g (0.02 mol) of HMPTA in 15 ml of THF was then similarly added slowly with cooling and vigorous stirring. The mixture was placed in the deep freeze at −30° for 4 days and then quenched by the addition of several ml of water with continued cooling. The product was extracted from the solution with ether using continuous liquid-liquid extraction. The ether layer was dried over magnesium sulfate, the solvents were removed with a fractionating column, and the residue was distilled, bp 107°, to yield 1.7 g of material of 80% purity (glpc) (68% yield). The material was purified by preparative gas chromatography (10 ft × ⅜ in. 20% SE-30 on 60–80 mesh Chromosorb A): ir 745 cm^{-1} (s, broad), 1110 (m), 1140 (m), 1160 (m), 1385 (m), 1470 (s), 2800 (s), 2885 (s), 2940 (s), 2965 (s), 3290 cm^{-1} (w); nmr 0.65–1 (m, 7 H, reduced to 6 H by D_2O exchange), 0.9–1.7 (m, 3 H), 2.48 ppm (s, and overlapping m, total 5 H). The picrate melted at 102–103° after three recrystallizations from benzene.

Anal. Calcd for $C_{12}H_{18}N_4O_7$: C, 43.64; H, 5.49. Found: C, 43.43; H, 5.55.

An authentic sample of the amine was prepared by treating 2-methylbutanoyl chloride with aqueous methylamine and sodium hydroxide[8] to give the *N*-methylamide, bp 70° (1 mm) [lit.[9] 70° (1 mm)] in 85% yield; reduction of the amide with ethereal lithium aluminum hydride[10] gave *N*-methyl-*N*-(2-methyl)butylamine in 80% yield, bp 107°. The nmr and ir spectra of this sample were identical with those described above.

***N*-Methyl-*N*-amylamine** was similarly prepared from 0.1 mol butyllithium (50 ml, 2*M* in hexane) in 25 ml of THF and 8.95 g (0.05 mol) of HMPTA in 25 ml of THF. The product collected on distillation weighed 2.72 g (50%): bp 116–118° (lit.[11] bp 116–118°); picrate mp 123.5–125.5° (lit.[11] mp 119–120°); nmr 0.6 (s, 1 H, disappears upon D_2O exchange), 0.75–1.08 (m, 3 H), 1.16–1.5 (m, 6 H), 2.38 (s, 3 H), 2.4–2.72 ppm (m, 2 H).

***N*-Methyl-*N*-benzylamine** was prepared from 0.06 mol of phenyllithium (33.3 ml of 1.8 *M* solution in 7:3 benzene–ether) diluted with 20 ml of THF and 5.38 g (0.03 mol) of HMPTA in 20 ml of THF to give 3.2 g of 85% pure material (75% yield): bp 80° (25 mm) [lit.[12] bp 184–185° (749 mm)]; ir (material purified by glpc) identical with that of an authenic sample;[13] nmr 1.38 (s, 1 H, disappears upon D_2O exchange), 2.44 (s, 3 H), 3.74 (s, 2 H), 7.4 ppm (s, 5 H).

***r*-2-Methylaminomethyl-2,*cis*-4,*cis*-6-trimethyl-1,3-dithiane (4).** *r*-2, *cis*-4, *cis*-6-Trimethyl-1,3-dithiane (243 mg, 1.5 mmol) was dissolved in 10 ml of a THF–HMPTA mixture (2:1) contained in a 25-ml round-bottom flask capped with a rubber septum and flushed with nitrogen as described above. Butyllithium (1.3 ml, 2.4 *M* solution in *n*-hexane, 3 mmol) was added and the mixture kept at −30° for 20 hr and then added to rapidly stirred D_2O. The product was extracted three times with 10 ml of hexane, the combined extracts were washed twice with 10-ml portions of water and dried over sodium sulfate, and the solvent was evaporated at water aspirator pressure. The product appeared homogenous upon gas chromatography on a 25 ft × ⅛ in. 25% QF-1 on Chromosorb W column at 120°: ir 730 (m), 780 (m), 1025 (m), 1065 (m), 1105 (m), 1145 (m), 1245 (s), 1370 (m), 1440 (s), 2780 (m), 2860 (s), 2910 (s), 2950 (s), 3300 cm^{-1} (w, broad); nmr 1.25 (d, J = 7 Hz) and 0.83–1.5 (B part of AB, total of foregoing peaks, 7 H), 1.84 (s, 3 H), 2–2.35 (A part of AB) and 2.23 (s) (total of these two peaks 3 H), 2.59 (s, 3 H), 3.0 (s, 2 H), 2.83–3.5 ppm (m, 2 H). The picrate melted at 180.5–182°.

Anal. Calcd for $C_{15}H_{22}N_4O_7S_2$: C, 41.47; H, 5.07. Found: C, 41.42; H, 5.10.

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Registry No.—4, 51932-18-4; **4** picrate, 52019-82-6; HMPTA, 680-31-8; *N*-methyl-*N*-(2-methyl)butylamine, 22431-10-3; *N*-methyl-*N*-(2-methyl)butylamine picrate, 51932-20-8; *N*-methyl-*N*-amylamine, 25419-06-1; *N*-methyl-*N*-amylamine picrate, 51932-21-9; *N*-methyl-*N*-benzylamine, 103-67-3; *r*-2, *cis*-4, *cis*-6-trimethyl-1,3-dithiane, 22452-27-3.

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Novel Synthesis of Substituted Thioacylureas. Reaction of Aryl and Alkyl Thioamides with Aryl Isocyanates

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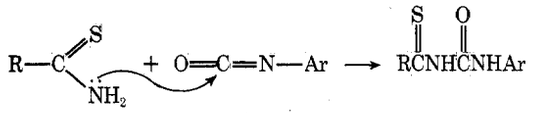
The preparation of acylureas from amides and aryl and alkyl isocyanates has been described by B. Kühn,[1,2] and extended by P. F. Wiley.[3] However, when aliphatic or aromatic thioamides are refluxed with aryl isocyanate in benzene or toluene, loss of H_2S from the thioamide occurs and symmetrical diarylurea is obtained from the reaction of isocyanate and H_2S.[4]

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°.

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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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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