[CONTRIBUTION FROM THE LABORATORIES OF LION OIL DIVISION OF THE MONSANTO CHEMICAL CO. AND MIDWEST RESEARCH INSTITUTE]

# A New Synthesis of Ureas. II. The Reaction of Primary Aliphatic Amines with Carbon Monoxide and Sulfur

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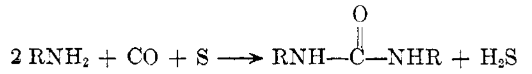
The reaction of primary amines with sulfur and carbon monoxide is shown to produce high yields of 1,3-dialkylureas.

We have previously described[3] a new method for the preparation of urea by the reaction of sulfur, carbon monoxide, and ammonia at temperatures of about 100°. The present paper shows that this reaction is widely applicable to aliphatic amines, and high yields of 1,3-disubstituted ureas are obtained. The following equation describes the net results of this reaction. More complex reactions



$$2\,RNH_2 + CO + S \longrightarrow RNH-\overset{\overset{\displaystyle O}{\|}}{C}-NHR + H_2S \quad (1)$$

where cyclic, polymeric, or other types of products are produced will be discussed in subsequent papers.

The reactants were generally mixed in a two-liter steel oxygen bomb and then heated for one to two hours.

The products were obtained easily in the case of aliphatic amines with yields ranging from 50 to 90% even though most yields were measured in single runs with no attempt to optimize conditions. Using a selected procedure described in the experimental portion of this paper, a number of 1,3-dialkylureas were prepared and the data of interest are shown in Table I.

In this group of ureas structural proofs rest on comparisons with reported melting points, a few mixed melting points with authentic samples, and elemental analysis for those ureas not previously reported.

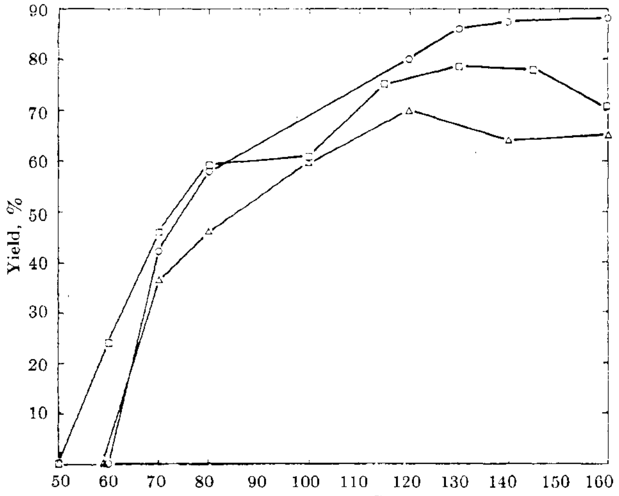


Fig. 1. The effect of temperature on yields of 1,3-dialkylureas

○ 1,3-Diisobutylurea, △ 1,3-didecylurea, □ 1,3-diethylurea

*The effects of reaction conditions on yields.* In order to learn more about the nature of this reaction, the effects of temperature, time, pressure, solvent, and the amount of sulfur on the yields were investigated. Figure 1 shows that the reaction had a threshold temperature between 50 and 70° for various amines. Below this temperature, no hydrogen sulfide was detected and no urea was found. The yield rose rapidly with temperature to a plateau at about 120° in runs of two hours. This effect was similar for ethyl-, isobutyl-, and decylamine.

The yields as a function of time are shown in Fig. 2 for isobutyl amine at 70 and 130°. At 70°, the yield leveled off at about 70% in four hours. At 130°, maximum yields near 90% were obtained in less than twenty minutes.

It should be noted that the reaction time is not a precise value in these experiments since it was impossible to obtain instantaneous heating and cooling in a batch reactor. The actual reaction time would include a short heating period (up to six minutes) and less than a minute for blow-down time. Of the six minutes heating period, only three minutes would actually affect the results since about

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TABLE I

1,3-DIALKYLUREAS

| Compound Prepared | Yield, % | Melting Point |  | Ref. | Carbon |  | Hydrogen |  | Nitrogen |  | Recrystallized from |
|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  | Obsvd. | Lit. |  | Calcd. | Anal. | Calcd. | Anal. | Calcd. | Anal. |  |
| 1,3-Dimethylurea | 88 | 101–103 | 106 | 4 |  |  |  |  |  |  | Benzene-Skellysolve B[a] |
| 1,3-Diethylurea | 75 | 111 | 112 | 4 |  |  |  |  |  |  | Water |
| 1,3-Diisopropylurea | 51 | 192 | 192 | 5 |  |  |  |  |  |  | Water |
| 1,3-Di-*n*-propylurea | 69 | 102–103 | 105 | 6 |  |  |  |  |  |  | Hot water |
| 1,3-Diisobutylurea | 80 | 128–130 | 134 | 4 |  |  |  |  |  |  | Skellysolve B |
|  |  |  | 128 | 7 |  |  |  |  |  |  |  |
| 1,3-Di-*n*-butylurea | 81 | 67–69 | 71 | 4 |  |  |  |  |  |  | Skellysolve F[b] |
| 1,3-Di-*sec*-butylurea | 71 | 135 | 137–138 | 8 | 62.74 | 63.10 | 11.70 | 11.70 | 16.28 | 16.52 | Skellysolve F |
| 1,3-Di-*tert*-butylurea | 54 | 245 | 242 | 9 |  |  |  |  |  |  | Methanol |
| 1,3-Di-*n*-amylurea | 71 | 79–81 | 88 | 10 |  |  |  |  |  |  | Skellysolve F |
| 1,3-Dicyclohexylurea | 68 | 229–230 | 230 | 11 |  |  |  |  |  |  | Methanol |
| 1,3-Di-*n*-hexylurea | 71 | 73–74 |  |  | 68.37 | 68.39 | 12.36 | 12.46 | 12.28 | 12.43 | Methanol |
| 1,3-Di-*n*-octylurea | 84 | 89–90 |  |  | 71.77 | 72.11 | 12.75 | 12.78 | 9.86 | 9.81 | Methanol |
| 1,3-Di-*tert*-octylurea | 29 | 145–147 | 153 | 12 |  |  |  |  |  |  | Petroleum ether[c] |
| 1,3-Di-*n*-decylurea | 70 | 99–100 |  |  | 74.05 | 74.18 | 12.93 | 13.05 | 8.25 | 8.53 | Methanol |
| 1,3-Di-*n*-dodecylurea | 80 | 105–106 | 105.5 | 13 |  |  |  |  |  |  | Benzene |
| 1,3-Di-*n*-tetradecylurea | 61 | 106–107 |  |  | 76.92 | 76.90 | 13.35 | 13.41 | 6.19 | 6.19 | Propanol-2 |
| 1,3-Di-*n*-octadecylurea | 71 | 110–111 | 113–114 | 14 |  |  |  |  |  |  | Benzene |
| 1,3-Bis(2-acetamidoethyl)urea | 60 | 200–202 |  |  | 46.97 | 47.02 | 7.87 | 7.74 | 24.34 | 24.41 | Methanol |
| 1,3-Bis(3-methoxypropyl)urea | 60 | 47–49 |  |  | 52.92 | 52.69 | 9.87 | 9.45 | 13.72 | 13.09 | Ether-Skellysolve B |
| 1,3-Difurfurylurea | 73 | 126–129 | 124–127 | 15 |  |  |  |  |  |  | Water |
| 1,3-Bis(2-*N*-morpholinoethyl)urea | 60 | 109–111 |  |  | 54.52 | 54.35 | 9.15 | 8.74 | 19.56 | 19.12 | Benzene |
| 1,3-Bis(3-isopropoxypropyl)urea | 72 | 37–39 |  |  | 59.96 | 59.85 | 10.84 | 10.56 | 10.76 | 10.88 | Skellysolve B |
| 1,3-Dibenzylurea | 60 | 169–171 | 169 | 16 |  |  |  |  |  |  |  |
| 1,3-Bis(α-methylbenzyl)urea | 39 | 121–122 |  | 17 | 76.08 | 76.13 | 7.51 | 7.81 | 10.45 | 10.60 | Water |
|  |  | 141–148 |  |  |  |  |  |  |  |  |  |
| 1,3-Bis(4-methoxybenzyl)urea | 64 | 176–177 | 178–179 | 18 | 67.98 | 68.03 | 6.67 | 6.52 | 9.33 | 9.34 |  |

[a] Boiling range 60–71° [b] Boiling range 35–60°. [c] Boiling point 80–110°.

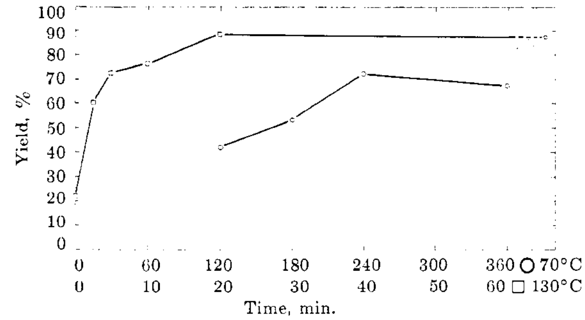

Fig. 2. The effect of time on yields of 1,3-dialkylureas at 70 and 130°

three minutes are required to reach the threshold temperature of 60°.

At temperatures near the optimum, no effect of carbon monoxide pressure was noticeable. However, at lower temperatures (70°), higher pressure did produce considerable increases in the yields of 1,3-diisobutylurea, see Table II. In this study the concentration in ethylene glycol and the reactants mole ratios were held constant (2:1:1.2 for amine:sulfur:carbon monoxide) while the carbon monoxide pressure was varied by increasing the batch size, thus reducing the free space in the vessel.

TABLE II

EFFECT OF CO PRESSURE ON YIELD OF 1,3-DIISOBUTYLUREA AT 70°[a]

| P.s.i.a. at 30° | Yield, % |
|---|---|
| 17 | 0 |
| 33 | 5 |
| 73 | 24 |
| 266 | 23 |

[a] Time—2 hr.

The amount of sulfur limited the yields of urea as predicted by Equation 1, but no beneficial effect was found for excess sulfur.

The products were easily obtained in pure form. Most of the compounds were white crystalline materials easily purified by a single recrystallization from a suitable solvent. Melting points agreed well with reported compounds.

The *tert*-octyl and *tert*-butyl group decreased the yield with only 29 and 54% of the corresponding ureas being obtained. Large amounts of unchanged amine were recovered. This lack of reactivity was apparently a steric effect which could also be observed in the yields of the series of butylureas. The yields under similar conditions were: *n*-butyl-, 80%; isobutyl, 79%; *sec*-butyl, 71%, and *tert*-butyl-, 52%. Attempts to obtain high yields from *tert*-butyl- and *tert*-octyl- amines were not successful. It was shown, however, that by increasing the concentration of *tert*-octylamine (omitting solvent) the yields were raised to 50%.

## EXPERIMENTAL

All the reactions were run in 2-l., Army surplus oxygen bombs with heating and shaking arrangements as described earlier.[3]

In a typical synthesis, powdered sulfur (0.16 mole), isobutyl amine (0.32 mole), and methanol (200 ml.) were placed in the reactor. The reactor was evacuated to 30 or 40 mm. (depending on the volatility of the amine), then pressurized with carbon monoxide to 70 p.s.i.g. and the reactants heated to 120° for 2 hr. The gases were released, and the product was rinsed out with methanol. The mixture was refluxed for 10 or 15 min. during which time the hydrogen sulfide was volatilized, and small amounts of sulfur precipitated.

When methanol was a satisfactory solvent for recrystallization, the solution was concentrated to saturation, cooled, and filtered. In some cases the methanol was evaporated and the product recrystallized from a more suitable solvent.

The ureas with alkyl groups containing twelve or more carbon atoms were very insoluble in methanol, and it was necessary to separate them from sulfur by dissolving the product in benzene.

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