Photochemical Transformations. 14. Photochemical Reactions of Ketones with Some Aliphatic Ureas[1]

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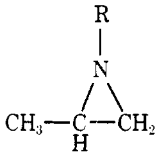
Irradiation of mixtures of aliphatic ureas and ketones led to ureido alcohols, bisureas, or mixtures of these products. Formation of these products is rationalized mechanistically.

Our research group has been interested in the photochemistry of allylic compounds for some time.[2] It has been reported[3] that irradiation of allylamine derivatives 1 gives mixtures of aziridines 2, Schiff bases 3, as well as deallylation products 4, when R is aliphatic or hydrogen, while that of allylanilines (R = Ar) gave deallylation 4 or rearrangement products,[4] presumably via bond-homolysis precursors. The photochemical deallylation reaction seemed of considerable interest to us, particularly if it could be induced by photosensitization, as it offered the possibility of using an allylic group as a protecting group, say in peptide synthesis, with photochemical "deblocking" rather than chemical deblocking.

$CH_2{=}CHCH_2NHR$

1



2

$CH_3CH_2CH{=}NR$

3

RNH_2

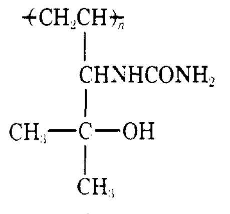
4

$CH_2{=}CHCH_2NHCONH_2$

5

We therefore decided to irradiate allylurea 5 in acetone, as a model system. With a Pyrex light filter a precipitate formed rapidly upon irradiation. Investigation showed that it was not urea, but rather that it was a low molecular weight polymer containing both allylurea- and acetone-derived fragments. Although we did not characterize this product completely, the work we are describing with benzylurea makes it clear that the polymer may be described essentially as 6. We did not find any evidence for an aziridine or imine product, or for urea (cleavage product) itself.

In order to investigate the photochemical reaction in more simple systems, we chose to study a number of other ureas. Irradiation of 0.16 M benzylurea (7) in acetone gave 39% of 1-phenyl-1-ureido-2-methyl-2-propanol (8), with 60% of 7 being recovered. No 1,2-diphenyl-1,2-diureidoethane (9) was detected. On the other hand, irradiation of methylurea (10) in acetone gave a good yield of 1,2-diureidoethane (11), without detectable amounts of the ureido alcohol 12-H being formed. Similarly, *N,N'*-dimethylurea (13) gave 14 and no 12-CH_3. Preliminary results indicated that *n*-propylurea and *n*-butylurea behaved like methylurea.

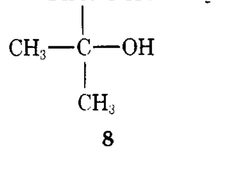


$$\begin{array}{l} \!-\!(CH_2CH)_n\!-\! \\ \quad\;| \\ \quad CHNHCONH_2 \\ \quad\;| \\ CH_3-C-OH \\ \quad\;| \\ \quad CH_3 \end{array}$$

6

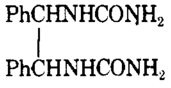
$PhCH_2NHCONH_2$

7



$$\begin{array}{l} \quad PhCHNHCONH_2 \\ \quad\;| \\ CH_3-C-OH \\ \quad\;| \\ \quad CH_3 \end{array}$$

8



$$\begin{array}{l} PhCHNHCONH_2 \\ \;| \\ PhCHNHCONH_2 \end{array}$$

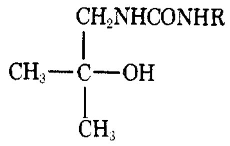
9

$CH_3NHCONH_2$

10

$$\begin{array}{l} CH_2NHCONH_2 \\ | \\ CH_2NHCONH_2 \end{array}$$

11

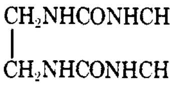


$$\begin{array}{l} \qquad\quad CH_2NHCONHR \\ \qquad\quad\;| \\ CH_3-C-OH \\ \qquad\quad\;| \\ \qquad\quad CH_3 \end{array}$$

12

$CH_3NHCONHCH_3$

13

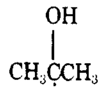


$$\begin{array}{l} CH_2NHCONHCH_3 \\ | \\ CH_2NHCONHCH_3 \end{array}$$

14

Benzylurea (7) was irradiated directly in acetonitrile and in *tert*-butyl alcohol solutions, using either quartz or Vycor tubes, for extended periods of time, and was recovered unchanged. Attempted sensitization with benzonitrile gave largely unchanged 7 with no evidence for cleavage products. Deaeration had little effect on any of the results.

The products of the photoreactions are readily rationalized mechanistically. n-π^* excited states of ketones are reactive hydrogen-atom abstractors,[5] and it seems clear that, instead of the triplet excitation transfer we had hoped for, excited acetone abstracted hydrogen from the α position of the alkyl group of the urea to give a 2-hydroxy-2-propyl radical 15 and a ureidoalkyl radical 16. Combination of 15 and 16 in the benzylurea case gave 8, while combination of two 16 radicals gave the bisureas observed in the other systems. We are unable to rationalize the failure to observe ureido alcohols from the methylureas, propylurea, or butylurea, as one might anticipate that geminate combination of 15 and 16 would occur more readily with R aliphatic or H rather than with the more stable 16 (R = Ph).

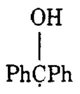


$$\begin{array}{c} OH \\ | \\ CH_3\dot{C}CH_3 \end{array}$$

15

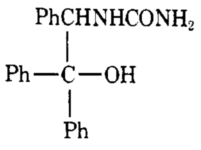
$R\dot{C}HNHCONH_2$

16



$$\begin{array}{c} OH \\ | \\ Ph\dot{C}Ph \end{array}$$

17

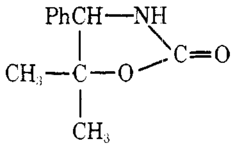


$$\begin{array}{l} \qquad PhCHNHCONH_2 \\ \qquad\;| \\ Ph-C-OH \\ \qquad\;| \\ \qquad Ph \end{array}$$

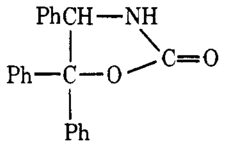
18

As it seemed likely that 8 formed, in large part at least, from geminate combination of 15 and 16 (R = Ph), we thought that use of a ketone which would give a more stable radical might permit the formation of bisurea 9. Indeed when an equimolar solution of benzylurea (7) and benzophenone in acetonitrile was irradiated, besides the ureido alcohol 18, there was formed 10–15% of a mixture of the meso and *dl* isomers of 9, as well as benzopinacol from the dimerization of 17.

The ureido alcohols 8 and 18 were unstable at their melting points and were found to eliminate ammonia and to give the



19



20

known oxazolidones **19**[6] and **20**,[6,7] respectively, in about 80% yield.

Experimental Section

Proton magnetic resonance spectra were obtained with a Varian A-60A spectrometer. Mass spectra were obtained on a Varian MAT Model CH-7 spectrometer. Irradiations were carried out using a Hanovia 450-W mercury arc lamp (Engelhardt-Hanovia, Inc., Newark, N.J., Model L679A-36) inserted into a water-cooled quartz immersion probe.

Ureas used in irradiation experiments were either commercial products or were prepared from potassium cyanate or the corresponding amine.[8]

Irradiation procedure involved irradiating 10 mL of solution in a 25 cm × 10 mm Pyrex tube sealed with a serum stopper and immersed in a water bath. Large-scale irradiations were carried out using 125 mL of solution in a water-jacketed probe immersion well. Reaction temperatures were kept constant at about 15 °C. Analyses were by Galbraith Laboratories.

Irradiation of Benzylurea (7)-Acetone Solutions. A solution of 3.0 g (0.02 mol) of **7** in 125 mL of acetone was irradiated through quartz for 2 h. A precipitate formed (1.65 g, 39%) which was almost pure 1-phenyl-1-ureido-2-methyl-2-propanol (**8**): mp after recrystallization from ethanol 202 °C dec; ^{1}H NMR (Me$_2$SO-d_6) δ 0.97 (s, CH$_3$), 1.10 (s, CH$_3$), 4.48 (s, OH), 4.50 (d, J = 10 Hz, CH), 5.52 (m, NH$_2$), 6.58 (d, J = 10 Hz, NH), 7.25 (s, C$_6$H$_5$).

Anal. Calcd for $C_{11}H_{16}N_2O_2$: C, 63.43; H, 7.75. Found: C, 63.60; H, 7.90.

When the solvent was evaporated from the mother liquor, 1.80 g (60%) of **7** was recovered.

Irradiation of Methylurea (10)-Acetone Solutions. A solution of 1.07 g (0.014 mol) of **10** in 45 mL of acetone was irradiated through Pyrex for 35 h. A precipitate formed (0.434 g, 40%) which was almost pure 1,2-diureidoethane (**11**): mp after recrystallization from propylene carbonate and ethyl acetate 192–195 °C dec (lit.[9] mp 193–194 °C); ^{1}H NMR (Me$_2$SO-d_6) δ 3.0 (m, CH$_2$), 5.45 (m, NH), 5.95 (m, NH$_2$).

The mother liquors were evaporated to dryness and dissolved in Me$_2$SO-d_6. The ^{1}H NMR spectrum had absorption peaks largely attributable to starting material **10** with smaller peaks attributable to **11**. No peaks attributable to **12** were observed.

Irradiation of *N,N'*-Dimethylurea (13)-Acetone Solutions. A solution of 2.3 g (0.026 mol) of **13** in 50 mL of acetone was irradiated through Pyrex for 29 h. A precipitate formed (0.62 g, 27%) which was almost pure 1,2-bis(3-methylureido)ethane (**14**): mp after recrystallization from ethanol 218–219 °C (lit.[10] mp 218–219 °C); ^{1}H NMR (Me$_2$SO-d_6) δ 2.59 (d, J = 5 Hz, CH$_3$), 3.01 (m, CH$_2$), 5.86 (m, 2 NH).

Anal. Calcd for $C_6H_{14}N_4O_2$: C, 41.10; H, 8.05. Found: C, 41.31; H, 7.68.

The mother liquors were evaporated to dryness and dissolved in Me$_2$SO-d_6. The ^{1}H NMR spectrum had peaks largely attributable to **13** and smaller peaks attributable to **14**. Not more than a trace of ureido alcohol could have been present.

Irradiation of Benzophenone and Benzylurea (7) in Acetonitrile. A solution of 3.0 g (0.02 mol) of **7** and 3.64 g (0.02 mol) of benzophenone in 125 mL of acetonitrile was irradiated through quartz for 2 h. A precipitate formed (0.30 g, 12.5%) which was a mixture of *meso*- and *dl*-1,2-diphenyl-1,2-diureidoethane (**9**). The meso and *dl* diastereoisomers were separated on a silica preparative TLC plate (E-M Reagents, F-254) using acetone, eluting three times and drying the plate completely between each elution. The ratio of *rac*- to *meso*-**9** was 2.1:1.0. ^{1}H NMR spectra for these diastereoisomers were obtained on a JEOL 100-MHz spectrometer.

meso-1,2-Diphenyl-1,2-diureidoethane (**9**) hardly moved on the TLC plate. It was recrystallized from ethanol: mp 221–222 °C dec; ^{1}H NMR (Me$_2$SO-d_6) δ 5.01 (s, CH), 5.57 (m, NH$_2$), 7.16 (s, C$_6$H$_5$), NH too broad to detect readily.

Anal. Calcd for $C_{16}H_{18}N_4O_2$: C, 64.36; H, 6.08. Found: C, 64.35; H, 6.06.

dl-1,2-Diphenyl-1,2-diureidoethane (**9**) had been prepared previously.[11] It was recrystallized from ethanol: mp over 360 °C (lit.[11] mp over 360 °C); ^{1}H NMR (Me$_2$SO-d_6) δ 4.86 (s, CH), 5.57 (m, NH$_2$), 7.16 (C$_6$H$_5$).

The solvent was evaporated from the mother liquor and the residue was washed twice with 100-mL portions of boiling water. When the water extract was evaporated 1.2 g (40%) of **7** was recovered. The water-insoluble solid was then washed with two 100-mL portions of diethyl ether. When the ether extract was evaporated 2.2 g (74%) of benzopinacol was recovered. The dried ether-insoluble solid (2.71 g, 50%) was almost pure 1,1,2-triphenyl-2-ureidoethanol (**18**): mp after recrystallization from methanol 193–194 °C dec; ^{1}H NMR (Me$_2$SO-d_6) δ 5.58 (m, CH), 5.75 (s, OH), 6.00 (m, NH), 6.62 (m, NH$_2$), 7.0–7.6 (C$_6$H$_5$).

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88, H, 6.02. Found: C, 75.70; H, 6.17.

Irradiations of Allylurea (5)-Acetone Solutions. A typical experiment was conducted as follows. A solution of 1.20 g of **5**, mp 88–90 °C, in 10 mL of acetone was irradiated for 35 h, following deaeration. A white solid (1.37 g) collected on the sides of the tube. The acetone solution was decanted and evaporated to dryness; an additional 0.48 g of oily solid remained. In various experiments the amounts of acetone-insoluble material varied slightly, but generally represented (in weight) more than the initial allylurea. This material was a granular, hygroscopic solid. It was soluble in water, methanol, ethanol, dimethylformamide, and dimethyl sulfoxide; it was insoluble in acetone, ethyl acetate, acetonitrile, benzene, tetrahydrofuran, and chloroform. Dissolution in methanol and precipitation with acetone led to almost complete recovery of product, but without significant change of properties. It melted over a wide range, beginning to decompose at 70 °C, and giving vigorous evolution of volatile materials at 100 °C. Analysis indicated that the material was an impure substance, which might be largely a low molecular weight polymer having a structure approximating **6**.

Anal. Calcd for $(C_7H_{14}N_2O_2)_n$: C, 53.1; H, 8.9; N, 17.7. Found: C, 51.1; H, 8.1; N, 17.9.

Thermal Cyclization of 1-Phenyl-1-ureido-2-methyl-2-propanol (8). **8** (2.9 g, 0.015 mol) was heated to 210 °C under a nitrogen atmosphere until the evolution of ammonia ceased. After initial purification in a Kugelrohr oven at reduced pressure (4 Torr) the residue formed (1.87 g, 80%) was almost pure 5,5-dimethyl-4-phenyl-2-oxazolidone (**19**): mp after recrystallization from acetone 129.5–130 °C (lit.[6] mp 125–127 °C); ^{1}H NMR (Me$_2$SO-d_6) δ 0.82 (s, CH$_3$), 1.55 (s, CH$_3$), 4.7 (s, CH), 7.4 (s, C$_6$H$_5$), 8.05 (m, NH).

Thermal Cyclization of 1,1,2-Triphenyl-2-ureidoethanol (18). **18** (2.0 g, 0.006 mol) was heated to 200 °C under a nitrogen atmosphere until the evolution of ammonia ceased. After initial purification on a Kugelrohr oven at reduced pressure (4 Torr), the residue formed (1.29 g, 78%) was almost pure 4,5,5-triphenyl-2-oxazolidone (**20**): mp after recrystallization from ethanol–water 230–231 °C (lit.[7] mp 229.5–231 °C); ^{1}H NMR (Me$_2$SO-d_6) δ 5.70 (s, CH), 7.05 (s, C$_6$H$_5$), 7.40 (m, 2 C$_6$H$_5$), 7.90 (m, NH).

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Registry No.—**5**, 557-11-9; **6**, 62183-25-9; **7**, 538-32-9; **8**, 62183-18-0; *meso*-**9**, 62183-19-1; *dl*-**9**, 62183-20-4; **10**, 598-50-5; **11**, 1852-14-8; **13**, 96-31-1; **14**, 62183-21-5; **18**, 62183-22-6; **19**, 33664-93-6; **20**, 62183-23-7; acetone, 67-64-1; benzophenone, 119-61-9.

References and Notes

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