

STRUCTURES OF CYCLOHEXANONE-UREA CONDENSATION PRODUCTS¹

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Received March 9, 1962

ABSTRACT

A new series of urea derivatives was prepared by condensing cyclohexanone with urea, thiourea, and their monosubstituted derivatives.

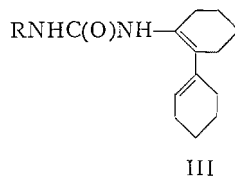
A new series of urea derivatives was prepared by condensing urea, thiourea, and their monosubstituted derivatives with cyclohexanone in the presence of acid. The derivatives formed by the condensation of 2 mole equivalents of cyclohexanone with the ureas and thioureas were formed also by condensing 2-cyclohexylidene-cyclohexanone with the same ureas and thioureas. The new compounds prepared in this study are described in Table I.

Two structures (I and II) were considered for the product from the condensation of



cyclohexanone with urea. If one assumes the substituted N atom to be equivalent to carbon for calculating the ultraviolet λ maxima of these unsaturated structures then the calculated values for structures I and II are 239 $m\mu$ and 326 $m\mu$ respectively (1). The observed λ_{\max} of 238.5 $m\mu$ given in Table II is in good agreement with the calculated value for structure I. This structure was confirmed by an n.m.r. spectrum of the compound. The vinylic proton peak at 4.67 p.p.m. definitely excluded structure II from consideration. A peak at 7.99 p.p.m. is assigned to the four hydrogens of the methylene groups which are unshielded by the diene system. The rest of the hydrogen atoms of the remaining methylene groups gave a peak at 8.4 p.p.m.²

The infrared spectra listed in Table III show that all of the urea and thiourea derivatives possess this same general structure III. The bands between 3060 and 3080 cm^{-1} are



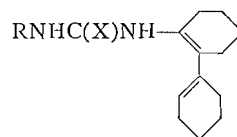
R = hydrogen, aryl, cyclohex-1-enyl, or alkyl

assigned to C—H stretching vibration of the $-\text{C}=\text{C}-\text{H}$ group. The strong absorption band between 1673 and 1685 cm^{-1} is tentatively assigned to the stretching vibrations

¹Contribution No. 36.

²Sixty-megacycle n.m.r. spectrum was measured with Varian model HR-60 high-resolution spectrometer.

TABLE I
Urea and thiourea derivatives



R	X	M.p. (°C)	Yield	Formulae	C		H		N	
					Calc.	Found	Calc.	Found	Calc.	Found
Hydrogen	O	234-235 ^a	16.3 ^e	C ₁₃ H ₂₀ N ₂ O	70.95	71.10	9.16	9.18	12.73	12.56
Hydrogen	S	274-276 ^a	67.0 ^f	C ₁₃ H ₂₀ N ₂ S	66.05	66.01	8.53	8.46	11.86	11.74 ^g
Ethyl	O	164-166 ^b	88.0 ^f	C ₁₅ H ₂₄ N ₂ O	72.53	72.48	9.74	9.76	11.28	11.56
Allyl	O	154-155 ^b	85.5 ^f	C ₁₆ H ₂₄ N ₂ O	73.80	73.97	9.29	9.29	10.76	11.05
Phenyl	O	233 ^c	31.2 ^f	C ₁₉ H ₂₄ N ₂ O	76.99	76.78	8.16	8.24	9.45	9.49
Phenyl	S	195 (decomp.) ^c	37.5 ^f	C ₁₉ H ₂₄ N ₂ S	73.03	73.32	7.74	7.93	8.97	9.13 ^h
4-Chlorophenyl	O	241-243 ^c	42.4 ^f	C ₁₉ H ₂₃ ClN ₂ O	68.97	68.94	7.01	6.99	8.47	8.66 ⁱ
4-Chlorophenyl	S	211 (decomp.) ^a	62.0 ^f (18.4 ^e)	C ₁₉ H ₂₃ ClN ₂ S	65.78	65.76	6.68	6.66	8.08	8.35 ^j
4-Hydroxyphenyl	O	268-269 ^a	68.3 ^f	C ₁₉ H ₂₄ N ₂ O ₂	73.05	73.02	7.74	7.71	8.97	8.96
3,4-Dichlorobenzyl	O	243-244 ^d	86.8 ^f (73.3 ^e)	C ₂₀ H ₂₄ Cl ₂ N ₂ O ₂	63.32	63.13	6.38	6.24	7.39	7.48 ^k
3,4-Dichlorophenyl	O	228-229 ^a	31.0 ^e	C ₁₉ H ₂₂ Cl ₂ N ₂ O ₂	62.47	62.75	6.07	6.25	7.67	7.92 ^l
α-Naphthyl	O	257 ^a	37.6 ^f	C ₂₃ H ₂₆ N ₂ O	79.73	79.65	7.56	7.52	8.09	8.14

^aCrystallized from ethanol.

^bFrom aqueous ethanol.

^cFrom benzene-ethanol (1:1).

^dFrom butyl cellosolve.

^eMethod B.

^fMethod A.

^gS calc. 13.56%, found 13.29%.

^hS calc. 10.26%, found 9.96%.

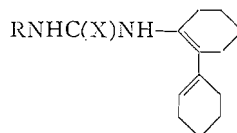
ⁱCl calc. 10.72%, found 10.80%.

^jCl calc. 10.22%, found 10.00%; S calc. 9.24%, found 8.92%.

^kCl calc. 18.69%, found 19.01%.

^lCl calc. 19.41%, found 19.60%.

TABLE II
Ultraviolet absorption^a



R	X	λ_{max} (m μ)	ϵ_{max}
Hydrogen	O	238.5	3,865
Cyclohex-1-enyl	O	233	6,670
Phenyl	O	247 ^b	5,850
		220	End absorption
Hydrogen	S	275	9,020
		256	9,580
		220	End absorption
Phenyl	S	305 ^b	10,280
		220	End absorption

^aThe ultraviolet spectra were determined on ethanolic solutions of the compounds with a Beckman DK-1 recording spectrophotometer.
^bThese absorption bands were broad and unsymmetrical. The phenyl groups contribute to the general absorption in the region covered by these broad bands.

of the —NH—C=C—C=CH or —NH—C=C— group. The CRR=CHR group gives an absorption band around 1670 cm⁻¹ (2). This absorption is generally weak. Conjugation in a diene system shifts the absorption some 30 cm⁻¹ to a lower frequency but the intensity of the band is generally increased considerably. In aliphatic conjugation of C=C bonds splitting of the two double-bond absorption bands usually occurs (2). In most of the compounds in Table III the band assigned to the —C=O group appears as a strong, separate band while in 2-cyclohex-1-enyl cyclohex-1-enyl-urea, 1-(cyclohex-1-enyl)-3-(2-cyclohex-1-enyl cyclohex-1-enyl)-urea, and 1-(4-hydroxyphenyl)-3-(2-cyclohex-1-enyl cyclohex-1-enyl)-urea the C=O absorption band has coalesced with the strong band tentatively assigned to the conjugated unsaturated group.

During this study 1,2-dicyclohexylisourea was prepared. This compound gave a strong, broad infrared absorption band at 1630 cm⁻¹ which includes the C=N stretching and N—H bending modes.

EXPERIMENTAL³

2-Cyclohexylidene-cyclohexanone

2-Cyclohexylidene-cyclohexanone (b.p. 153–155° at 20 mm) was prepared in 69% yield by the method of Gault *et al.* (3).

3,4-Dichlorobenzylurea

3,4-Dichlorobenzylurea (m.p. 164–165°) was prepared in 82% yield from 3,4-dichlorobenzylamine hydrochloride and sodium cyanate by the general procedure described by Vogel (4). Anal. Calc. for C₈H₈Cl₂N₂O: C, 43.86; H, 3.68; Cl, 32.37; N, 12.79%. Found: C, 44.04; H, 3.77; Cl, 32.38; N, 12.55%.

Ethylenediurea

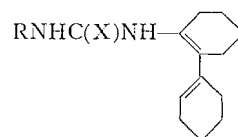
Ethylenediurea (m.p. 199° decomp.) was prepared in 73% yield by a modification of Volhard's (5) method. Sodium cyanate was used in place of silver cyanate.

Preparation of 2-Cyclohex-1-enyl cyclohex-1-enyl Derivatives of Ureas and Thioureas

The compounds described in Table I were prepared by either of the processes given in detail below for the preparation of 1-(3,4-dichlorobenzyl)-3-(2-cyclohex-1-enyl cyclohex-1-enyl)-urea.

³All melting points were determined on samples sealed in evacuated capillary tubes. This technique was essential in obtaining reproducible melting points. Microanalyses were determined by Micro-Tech Laboratories, Skokie, Illinois.

TABLE III
Infrared absorption band (cm^{-1}) assignments^a



R	X	Stretching modes		Other bands
		N—H		
Hydrogen	O	3350, 3250, 3200	1675	3080 (C=CH)
Allyl	O	3330, 3240	1683, 1672 (C=O)	3060 (C=CH), 1620 (C=C)
Cyclohex-1-enyl	O	3250	1673	3070 (C=CH), 1623 (C=C)
Phenyl	O	3350, 3215	1685, 1668 (C=O)	3075 (C=CH), 1623 (C=C), 1595 (aryl)
4-Chlorophenyl	O	3345, 3235, 3105	1688, 1670 (C=O)	1623 (C=C), 1593 (aryl)
3,4-Dichlorophenyl	O	3315, 3250	1683, 1651 (C=O)	3070 (C=CH), 1623 (C=C), 1586 (NH)
α -Naphthyl	O	3192	1681, 1661 (C=O)	3059 (C=CH), 1594 (aryl)
4-Hydroxyphenyl	O	3360, 3270, 3170	1677	3080 (C=CH), 1628 (C=C), 1592 (aryl)
3,4-Dichlorobenzyl	O	3310, 3250	1683, 1651 (C=O)	3060 (C=CH), 1610 (aryl)
1-(2-Cyclohex-1-enyl cyclohex-1-enyl)-ureidoethylene	O	3330, 3190	1678, 1650 (C=O)	3060 (C=CH)
Hydrogen	S	3370, 3225, 3175	1685	3060 (C=CH), 1553 (NH), 1366 (C=S)
4-Chlorophenyl	S	3345, 3200, 3115	1674	1610 (aryl), 1366 (C=S)

^aAbsorption spectra on Nujol mulls of the crystalline compounds.

Method A

A mixture of 3,4-dichlorobenzylurea (10.25 g, 0.047 mole), cyclohexanone (49 g, 0.5 mole), and concentrated hydrochloric acid (5 g, 0.05 mole) was refluxed for 30 minutes. Crystals separated from the solution during the refluxing period. These were separated and washed with ethanol, yield 15.4 g (86.8%). The melting point (243–244°) was not altered by further crystallization.

Method B

This procedure was the same as given in Method A with the exception that 2-cyclohexylidene-cyclohexanone (17.8 g, 0.1 mole) was used instead of cyclohexanone. The yield of product (m.p. 243–244°) was 13 g (73.3%).

1,2-Dicyclohexylisourea

A solution of bromocyanogen (5.3 g, 0.05 mole) in ether (50 ml) was added dropwise over a period of 35 minutes to a cold (–5 to 0°) solution of freshly distilled cyclohexylamine (9.9 g, 0.1 mole) in ether (50 ml). After the mixture was stirred for an additional 30 minutes, the precipitate of cyclohexylamine hydrobromide was removed by filtration and the filtrate at 0° was treated with cyclohexanol (50 g, 0.5 mole). The solution was stirred for 90 minutes, after which dry HCl gas (5.7 g) was added. This solution was allowed to stand at room temperature for 5 days and then the ether and excess cyclohexanol were removed *in vacuo*. The residue was suspended in water (20 ml) and the pH of the suspension was adjusted to 10 with sodium hydroxide solution. A crystalline suspension was obtained after the mixture had remained at room temperature for 4 days. The crystals (m.p. 78°) were recovered by filtration, yield 11.2 g (100%). Two crystallizations from petroleum ether (b.p. 65–110°) (5 ml/g) raised the melting point to 96°, yield 73.3%. Anal. Calc. for C₁₃H₂₃N₂O: C, 69.60; H, 10.78; N, 12.49%. Found: C, 69.80; H, 10.76; N, 12.51%.

1,1'-Bis-(2-cyclohex-1-enyl cyclohex-1-enyl)-ethylenediurea

Ethylenediurea (14.6 g, 0.1 mole), cyclohexanone (58.8 g, 0.6 mole), and concentrated hydrochloric acid (0.2 mole) were heated under reflux for 75 minutes. The crystals were removed from the cool solution by filtration, yield 35.1%. These crystals did not melt below 300° and they were very insoluble in the common organic solvents. Anal. Calc. for C₂₃H₄₂N₄O₂: C, 72.05; H, 9.07; N, 12.00%. Found: C, 72.18; H, 9.06; N, 12.32%.

1-(Cyclohex-1-enyl)-3-(2-cyclohex-1-enyl cyclohex-1-enyl)-urea

Urea (60 g, 1 mole), cyclohexanone (98 g, 1 mole), and concentrated hydrochloric acid (100 g, 1 mole) were heated under reflux for 90 minutes. After cooling of the mixture to room temperature the organic layer was separated and the unreacted cyclohexanone, together with some water, was removed *in vacuo*. The oily residue was diluted with ethanol (25 ml) and the solution poured into water (400 ml). This mixture was neutralized with aqueous sodium hydroxide, after which the oil solidified. The product (m.p. 180–200°) was separated by filtration and washed with water, yield 98 g (98%). Two crystallizations from ethanol-benzene (1:1) raised the melting point to a constant value of 221–223°. In some preparations a crystalline modification melting at 238° was obtained. The infrared spectra of these two crystalline modifications were identical. Anal. Calc. for C₁₉H₂₈N₂O: C, 75.96; H, 9.39; N, 9.33%. Found: C, 75.62; H, 9.40; N, 9.14%.

ACKNOWLEDGMENT

The infrared and ultraviolet spectra were determined by Dr. C. Sandorfy of the University of Montreal, Montreal, Quebec.

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