BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 39 1765—1767 (1966)

The Reaction of 2-Cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline

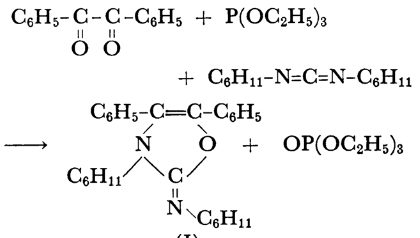
By Takanobu KUMAMOTO, Takenori NAGAOKA and Teruaki MUKAIYAMA

Laboratory of Organic Chemistry, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo

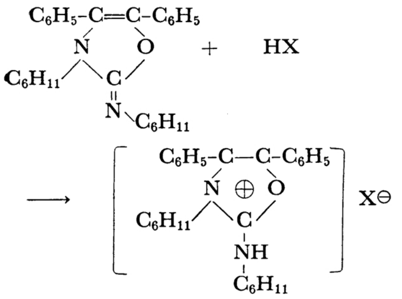
(Received December 9, 1965)

The reaction of 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline with isocyanate or isothiocyanate was studied. When the oxazoline was treated with isocyanate, an exchange reaction took place, thus forming new 2-imino-oxazoline and cyclohexyl isocyanate. Similarly, the reaction of the oxazoline with carbon disulfide resulted in the formation of 3-cyclohexyl-4, 5-diphenyl-4-oxazoline-2-thione and cyclohexyl isothiocyanate. Further, cyclohexyl isothiocyanate was obtained by the reaction of dicyclohexylcarbodiimide or cyclohexyl isocyanate with carbon disulfide.

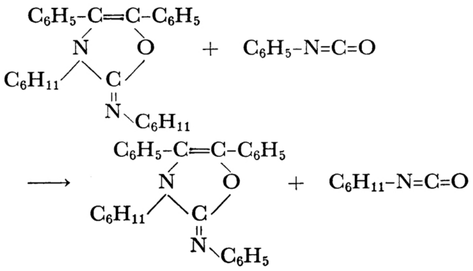
It has recently been found[1] that 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline was obtained in a good yield, along with triethyl phosphate, when a toluene solution of benzil, triethyl phosphite and dicyclohexylcarbodiimide was refluxed in the presence of copper powder. Further, it has been shown that the oxazoline gave the stable salts with protonic acids:



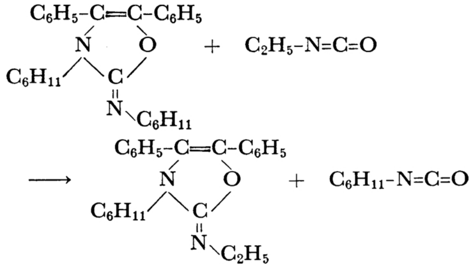
(I)



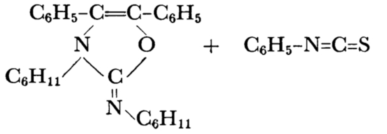
In the present study, it was found that the reactions of the oxazoline with isocyanate, isothiocyanate and carbon disulfide resulted in the formation of new oxazolines and oxazoline-2-thione. When a mixture of 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline and phenyl isocyanate was stirred in petroleum ether at room temperature for 3 hr., 2-phenylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline and cyclohexyl isocyanate were obtained in 72% and 69% yields respectively. These results show that the *exo*-imino group of the oxazoline is replaced by the phenylimino group of phenyl isocyanate:



The same exchange reaction was expected to occur in the case of ethyl isocyanate, which is considered to have a more enhanced reactivity than the cyclohexyl isocyanate produced. Indeed, when oxazoline (I) and ethyl isocyanate were heated at 120°C for 4 hr. in a sealed tube, 2-ethylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline was obtained in a 24% yield:

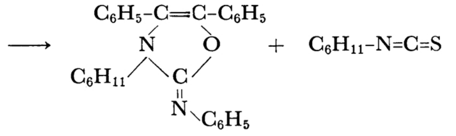


Further, when a solution of oxazoline (I) and phenyl isothiocyanate was stirred in petroleum ether at room temperature for 4 hr., 2-phenylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline (80% yield) and cyclohexyl isothiocyanate (92% yield) were obtained:

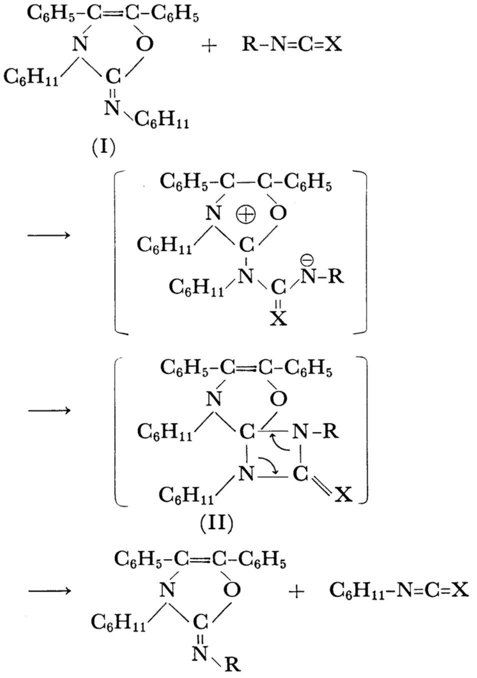


---

[1] T. Mukaiyama, T. Kumamoto and T. Nagaoka, Part XVIII: Annual Meeting of The Chemical Society of Japan, Preliminary Issue (1965), p. 248.



The above-mentioned exchange reactions are considered to proceed through the initial formation of an unstable four-membered intermediate (II) which is formed by the electrophilic attack of isocyanate or isothiocyanate on the *exo*-imino group of the oxazoline (I). By the transfer of electrons, II in turn changes into new 2-imino-oxazoline and cyclohexyl isocyanate or isothiocyanate:

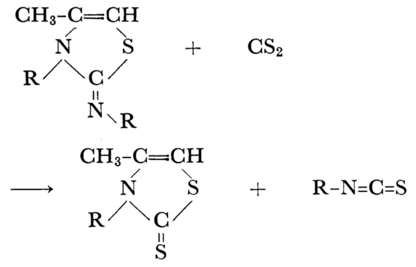


(I)

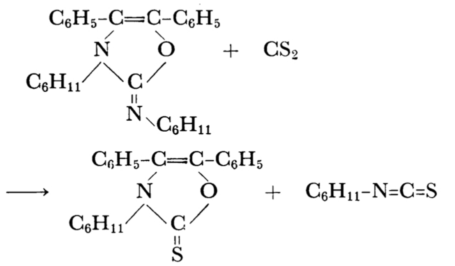
(II)

(X=O, S)

Concerning this type of exchange reaction, Bartoszewski and Jerzmanowska have already reported that[2] thiazoline-2-thione is produced by the reaction of 2-imino-thiazoline, the sulfur isomer of the oxazoline, with carbon disulfide:



It was also established by the present experiment that the treatment of the oxazoline (I) with excess carbon disulfide at 150°C resulted in the formation of 3-cyclohexyl-4, 5-diphenyl-4-oxazoline-2-thione (90% yield) and cyclohexyl isothiocyanate (83% yield):



However, when 2-phenylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline and carbon disulfide were heated under the same conditions, the expected products, 3-cyclohexyl-4, 5-diphenyl-4-oxazoline-2-thione and phenyl isothiocyanate, could not be obtained, only the starting materials were recovered.

Next, the reaction of dicyclohexylcarbodiimide and carbon disulfide was attempted in expectation that cyclohexyl isothiocyanate would be formed in a way similar to that described in the above exchange reaction. When they were heated at 150°C for 10 hr., cyclohexyl isothiocyanate was obtained in a 25% yield, and 55% of the dicyclohexylcarbodiimide was recovered:

$$C_6H_{11}\text{-}N{=}C{=}N\text{-}C_6H_{11} + CS_2 \longrightarrow 2C_6H_{11}\text{-}N{=}C{=}S$$

Further, it was established that cyclohexyl isothiocyanate was obtained in a 41% yield when a mixture of cyclohexyl isocyanate and carbon disulfide was heated under the same conditions in the presence of triethylamine:

$$C_6H_{11}\text{-}N{=}C{=}O + CS_2 \xrightarrow{N(C_2H_5)_3} C_6H_{11}\text{-}N{=}C{=}S + COS$$

Experimental

The Reaction of 2-Cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline with Phenyl Isocyanate.—A solution of 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline (2.00 g., 0.005 mol.) and phenyl isocyanate (0.60 g., 0.005 mol.) in petroleum ether was stirred for 3 hr. at room temperature. After the petroleum ether, had been removed, a white precipitate was obtained. It was recrystallized from ethyl acetate to give 2-phenylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline, 1.98 g. (72%); m. p. 182—183°C.

Found: C, 81.82; H, 6.65; N, 7.34. Calcd. for $C_{27}H_{26}N_2O$: C, 82.20; H, 6.64; N, 7.10%.

The residue was distilled in vacuo, giving cyclohexyl isocyanate, 0.42 g. (63%); b. p. 62—67°C/20 mmHg.

The Reaction of 2-Cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline with Ethyl Isocyantate.—A mixture of 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline (1.00 g., 0.0025 mol.) and an excess of ethyl isocyanate (0.71 g., 0.01 mol.) was heated at

---

[2] J. Bartoszewski and Z. Jerzmanowska, *Roczniki. Chem.*, **37**, 11 (1963); *Chem. Abstr.*, **59**, 7510 (1963).

120°C for 4 hr. in a sealed tube. The removal of the excess ethyl isocyanate gave a white precipitate. It was then recrystallized from ethyl acetate, giving 2-ethylimino-3-cyclohexyl- 4, 5 - diphenyl - 4 - oxazoline, 0.21 g. (24%); m. p. 112—114°C.

Found: C, 79.42; H, 7.82; N, 8.30. Calcd. for $C_{23}H_{26}N_2O$: C, 79.73; H, 7.56; N, 8.09%.

The Reaction of 2-Cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline with Phenyl Isothiocyanate.—A solution of 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline (2.00 g., 0.005 mol.) and phenyl isothiocyanate (0.68 g., 0.005 mol.) in petroleum ether was stirred at room temperature for 4 hr. After the solvent had been removed, a white crystalline solid was obtained. This was then filtered and recrystallized from ethyl acetate, giving 2-phenylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline, 1.58 g. (80%); m. p. 183—184°C.

The fractional distillation of the residue gave cyclohexyl isothiocyanate, 0.51 g. (72%); b. p. 102—103°C/10 mmHg.

The Reaction of 2-Cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline with Carbon Disulfide.—A mixture of 2-cyclohexylimino-3-cyclohexyl-4, 5-diphenyl-4-oxazoline (4.00 g., 0.01 mol.) and an excess of carbon disufide (4 ml.) was heated at 150°C for 5 hr. in a sealed tube. The removal of the excess carbon disulfide gave a white precipitate. This was then recrystallized from ethanol, giving 3-cyclohexyl-4, 5-diphenyl-4-oxazoline-2-thione, 3.03 g. (90%); m. p. 201°C.

Found: C, 75.17; H, 5.96; N, 4.09. Calcd. for $C_{21}H_{22}NOS$: C, 75.00; H, 6.53; N, 4.19%.

The distillation of the residue under reduced pressure gave cyclohexyl isothiocyanate, 1.17 g. (83%); b. p. 101—104°C/10 mmHg.

The Reaction of Dicyclohexylcarbodiimide and Carbon Disulfide.—A mixture of dicyclohexylcarbodiimide (2.06 g., 0.01 mol.) and carbon disulfide (5 ml.) was heated at 150°C for 10 hr. in a sealed tube. After the excess carbon disulfide had been removed, cyclohexyl isothiocyanate, 0.75 g. (27%); b. p. 100—105°C/10 mmHg, was obtained, and 1.14 g. of dicyclohexylcarbodiimide (55%), b. p. 149—151°C/10 mmHg, was reccovered.

When dicyclohexylcarbodiimide (2.06 g., 0.01 mol.) and carbon disulfide (5 ml.) were heated in the presence of triethylamine (0.1 ml.) in a sealed tube at 150°C for 5 hr., cyclohexyl isothiocyanate, 0.36 g. (13%); b. p. 108—110°C/12 mmHg was obtained, and dicyclohexylcarbodiimide, 1.24 g. (60%); b. p. 152—154°C/12 mmHg, was recovered.

When a catalytic amount of boron trifluoride etherate was used in the above experiment, cyclohexyl isothiocyanate 0.20 g. (7%); b. p. 115—117°C/13 mmHg, was obtained, and 1.35 g. of dicyclohexylcarbodiimide (66%), b. p. 152—155°C/12 mmHg, was recovered.

The Reaction of Cyclohexyl Isocyanate with Carbon Disulfide in the Presence of Triethylamine.—A mixture of cyclohexyl isocyanate (2.50 g., 0.01 mol.), carbon disulfide (2 ml.) and triethylamine (2 ml.) was heated at 150°C for 5 hr. in a sealed tube. Distillation in vacuo gave cyclohexyl isothiocyanate, 1.17 g. (42%); b. p. 95—97°C/10 mmHg.