ether–hexane gave 190 mg (VIII), mp 205-206°C. IR spectrum (ν, cm^{-1}, KBr): 3590, 3480, 1720, 1250. PMR spectrum (δ, ppm): 0.79, 0.88 s (6H, 18-CH_3, 19-CH_3), 1.28 t (3H, OCH_2CH_3, J = 7 Hz), 1.37 s (3H, 21-CH_3), 4.18 q (2H, OCH_2CH_3, J = 7 Hz), 5.02 m (1H, 3-H), 5.42 t (1H, 16-H).

3β-Acetoxy-6-keto-24-nor-5α-cholan-16α-ol-23-oic Acid 23 → 16-δ-Lactone (16-Isothiogralactone Acetate) (X). A sample of 0.06 ml $SOCl_2$ was added to a solution of 120 mg (V) in 3 ml pyridine at 0°C. After 20 min at 0°C and 30 min at 20°C, the mixture was diluted by water and extracted by ethyl acetate. The extract was washed with 2% aq. HCl and water, dried over $MgSO_4$, and evaporated to yield 110 mg (IX), R_f 0.5 (from 9:1 benzene–acetone). IR spectrum (ν, cm^{-1}, $CHCl_3$): 1725, 1690, 1635, 1245. UV spectrum (λ_{max}, nm): 239 (ε 4440). PMR spectrum (δ, ppm): 0.8 s (3H, 18-CH_3), 1.02 s (3H, 19-CH_3), 1.09 d (3H, 21-CH_3, J = 7 Hz), 2.08 s (3H, acetate), 4.49 m (1H, 16-H), 5.34 m (1H, 3-H), 6.12 br. s (1H, 4-H). Mass spectrum (m/z): 414 M^+, 354 $[M - 60]^+$. A sample of 20 mg (IX) in 10 ml ethyl acetate was hydrogenated over 20 mg 5% Pd/C until there was no further hydrogen absorption. The catalyst was filtered off and the filtrate was evaporated. Column chromatography with 15:3 ether–hexane eluent gave 7.5 mg (X), mp 138-140°C (from ether). IR spectrum (ν, cm^{-1}, KBr): 1730, 1710, 1240. PMR spectrum (δ, ppm): 0.74 s (3H, 18-CH_3), 0.78 s (3H, 19-CH_3), 1.05 d (3H, 21-CH_3, J = 6.5 Hz), 2.03 s (3H, acetate), 4.49 m (1H, 16-H), 4.69 m (1H, 3-H). Mass spectrum (m/z): 356 $[M - 60]^+$, 341 $[M - 60 - 15]^+$, 328 $[M - 60 - 28]^+$.

CONCLUSIONS

Syntheses are reported for 16-isochiogralactone, its 5α-hydroxy analog, and 5α-hydroxy-6-ketosteroids with unsaturated lactone E rings.

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SUBSTITUENT EFFECTS ON THE RATE OF CYCLIZATION OF N-PHENYL-N'-(o-CYANOPHENYL)UREA IN SOLUTION

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The isomerizational cyclization of N-phenyl-N'-(o-cyanophenyl)urea (PCPU) to give 2-oxo-3-phenyl-4-imino-1,2,3,4-tetrahydroquinazoline is a model for the polycyclization of polycyanourea to give heat-resistant polyiminoquinazolines.

In our previous work [1], we showed that the cyclization of PCPU is a first-order reaction subject to Brönsted base catalysis and inhibition by protic acids. We proposed that by analogy with the cyclization of o-cyanobenzaniline [2], this reaction involves proton abstraction by the catalyst and subsequent intramolecular cyclization of intermediate anion (II).

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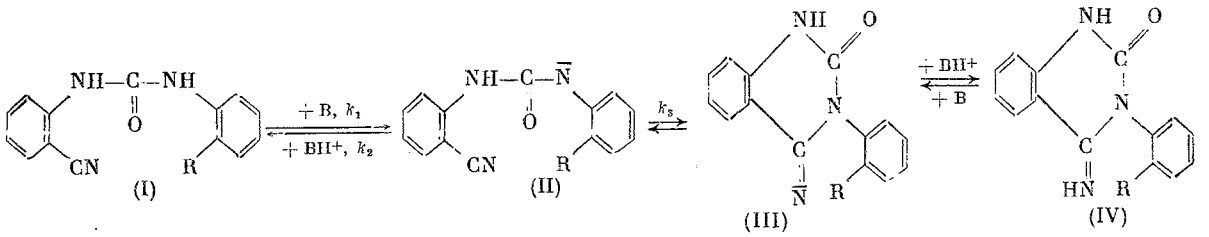
TABLE 1. Elemental Analysis Data and IR Spectra of N-(R-Phenyl)-N'-(o-cyanophenyl)ureas and the Effective Rate Constants for Their Isomerizational Cyclization

Substituent R	mp, °C	Calculated/Found, %			IR spectra (cm^{-1}, KBr)				$k_{ef} \cdot 10^5$, sec^{-1}	pK_a^a
		C	H	N	νC≡N	νC=O	νN–H	δN–H		
p-NO_2	314–316 [b]	59,57 / 59,31	3,55 / 4,02	19,86 / 19,73	2225	1695	3330	1570	39,0±3	15,7
p-CH_3OOC	212–213	65,08 / 65,98	4,41 / 4,23	14,24 / 13,83	2230	1715	3290	1580	22,8±0,1	18,7[c]
m-Cl	170	61,89 / 62,06	3,71 / 3,78	15,47 / 15,13	2240	1690	3330	1570	32,0±1	18,4
p-Br	233–235	53,16 / 53,82	3,16 / 3,21	13,29 / 13,54	2230	1685	3340	1580	35,5±2,4	18,8
H	167	70,87 / 70,10	4,67 / 5,12	17,71 / 18,07	2230	1715	3350	1570	8,9±0,3	19,9
m-CH_3	170–172	71,70 / 71,84	5,21 / 5,25	16,72 / 15,89	2230	1645	3300	1570	9,8±0,5	19,8
p-CH_3	188–189	71,70 / 72,20	5,21 / 4,89	16,72 / 16,99	2230	1645	3300	1570	11,3±0,8	20,5
p-OCH_3	196–197	67,41 / 67,53	4,81 / 4,32	15,73 / 15,32	2230	1640	3300	1580	17,0±0,9	20,5

a) The pK_a values of the corresponding substituted N,N'-diphenyl-N-methylureas were taken from our previous work [3]; the pK_a value for PCPU could not be measured due to cyclization during the determination.
b) The melting point of 2-oxo-3-(p-nitrophenyl)-4-imino-1,2,3,4-tetrahydroquinazoline formed during the determination.
c) The pK_a value was calculated using our previous equation [3].



In order to support this hypothesis, we studied the polar substituent effect on the rate constant for the cyclization of PCPU. The reaction was carried out at 40°C in 9:1 DMSO--H_2O in the presence of acetate buffer (0.01 M AcOH, 0.1 M AcONa). The PCPU concentration was found relative to the optical density of the nitrile group IR band.

Using the steady-state principle for the rate of formation and disappearance of (II), assuming that $k_2 > k_1$ (the basicity of (II) is significantly greater than for B), assuming that $k_3 < k_2$, we obtain the following expression for the effective rate constant for the cyclization of PCPU:

$$k_{ef} = (k_1/k_2)k_3 = K_{eq}k_3.$$

Electron-withdrawing substituents which increase the NH acidity of PCPU (and enhance K_{eq}) should also lower the basicity of (II) (decrease k_3). Electron-donor substituents should have the opposite effect. Thus, we might expect a mutually compensating substituent effect. The nature of the dependence of k_{ef} on the Hammett constant of the substituents is a factor of the ratio of the contributions of K_{eq} and k_3 to the cyclization kinetics.

A satisfactory linear equation was found between the logarithm of the cyclization rate constant and the Hammett rate constants of the substituents R with $\rho \sim 0.3$. The linear nature of the dependence indicates the predominant effect of one of the steps on the kinetics. Table 1 shows that the cyclization rate constant of substituted PCPU in going from electron-donor to electron-withdrawing substituents is directly related to the change in the NH acidity of these compounds. The positive sign of ρ indicates that the reaction is facilitated by a decrease in the electron density at the reaction site. Thus, proton abstraction is the rate-determining step for the cyclization.

There is a significant change in electron density at the reaction site in each step of the reaction upon the introduction of substituents R, but the absolute value of the constant ρ for the cyclization reaction is low. This may be a reflection of the compensation of the effects of K_{eq} and k_3 on the reaction rate. Such low values for ρ have been found for other reactions proceeding by similar mechanisms [4]. The presence of two NH-acid sites, one of which bound to the o-cyanophenyl group has greater acidity than the other (pK 14.8 and 20.6 in DMSO, respectively [3, 5]) may make a significant contribution to the low sensitivity of the reaction to the nature of the substituent. Thus, we may assume that the basic catalyst reacts initially with the more acidic NH group and the reactivity of the NH group participating in the cyclization is largely a function of the negative charge on the nitrogen atom and not of the nature of the substituent, which should also lead to a low value of the ρ constant observed experimentally.

EXPERIMENTAL

Anthranilonitrile was obtained according to Kost and Stankevichus [6].

o-Cyanophenyl Isocyanate. A mixture of 6 g (37 mmoles) isatin-β-oxime and 60 ml (835 mmoles) $SOCl_2$ was heated for 1 h at 65-75°C with a condenser equipped with a calcium chloride tube. The excess $SOCl_2$ was distilled off. The residue was distilled at 150-155°C (1 mm) and recrystallized from abs. hexane to give 2.88 g (53%) product, mp 60-61°C.

N-(R-phenyl)-N'-(o-cyanophenyl)urea, RPCPU with R = p-CH_3O_2C, p-CH_3, p-OCH_3, p-Br, and p-NO_2 were obtained by the reaction of o-cyanophenyl isocyanate with the correspondingly substituted aniline. Typical preparative procedure: A solution of 2.09 g (195 mmoles) p-toluidine in 10 ml abs. benzene was added in an argon atmosphere to a solution of 3.1 g (215 mmoles) o-cyanophenyl isocyanate in 30 ml abs. benzene at 20°C and stirred for 3 h. The precipitate was filtered off and recrystallized from 20:1 benzene–ethanol. The product yield was 3.28 g (67%), pm 170-172°C.

R-PCPU with R = H, m-Cl, and m-CH_3 were obtained by the reaction of anthranilonitrile with the corresponding substituted phenyl isocyanate according to Breukink and Verkade [7] and recrystallized from 3:1 benzene–ethanol.

The structures of the compounds synthesized and their purity were monitored by elemental analysis and IR spectroscopy. The IR spectra of the PCPU solutions during the cyclization were taken on a UR-10 spectrometer.

CONCLUSIONS

The isomerizational cyclization of N-phenyl-N'-(o-cyanophenyl)urea in solution in the presence of bases is a one-step reaction with an equilibrium step involving proton abstraction as the rate-limiting step.

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PERFLUOROAZOMETHINES WITH FLUOROSULFATE GROUPS

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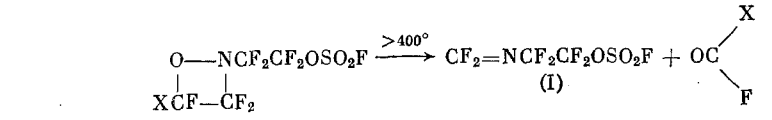
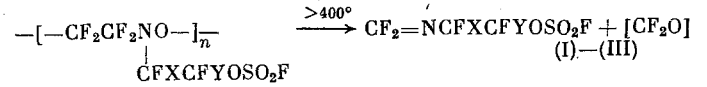
The pyrolysis of the adducts of fluoroolefins and nitrosofluoroalkanes is commonly used for the preparation of perfluoroazomethines [1]. An example of the pyrolysis of a copolymer of trifluoronitrosomethane with trifluoroacrylyl fluoride has also been reported [2].

In the present work, we studied the pyrolysis of adducts of 2-nitrosoperfluoroalkyl fluorosulfates with fluoroolefins containing fluorosulfate groups in the side chain. The pyrolysis of 1,2-oxazetidines with a fluorosulfonyloxytetrafluoroethyl group at N-2 proceeds with retention of the fluorosulfate group.



X = Cl, CF_3O.

Perfluoroazomethines with fluorosulfate groups were also obtained in the pyrolysis of the corresponding nitrosofluoro polymers.



X = Y = F (I); X = Cl, Y = F (II); X = F, Y = CF_3O (III).

Analogous results were obtained from the pyrolysis of "mixed" nitrosofluoro polymers.

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