technique to the study of the conformational properties and processes of appropriate macromolecules.

Registry No.—I, 127-19-5; I–Eu(fod)$_3$ complex, 35208-59-4; II, 7103-46-0; II–Eu(fod)$_3$ complex, 35208-60-7; III, 24768-60-3; IV, 18940-57-3; IV–Eu(fod)$_3$ complex, 35238-57-4; V, 35168-21-9; V–Eu(fod)$_3$ complex, 35208-61-8; VI, 35211-97-3; VI–Eu(fod)$_3$ complex, 35208-62-9; VII, 35168-20-8; VII–Eu(fod)$_3$ complex, 35208-63-0; VIII, 35212-03-4; VIII–Eu(fod)$_3$ complex, 35208-64-1; IX, 35212-04-5; IX–Eu(fod)$_3$ complex, 35238-58-5; Eu(fod)$_3$, 17631-68-4.

Acknowledgments.—Part of this work was carried out by G. M. at the Department of Chemistry, University of Michigan—Ann Arbor. The authors wish to express sincere thanks to Dr. C. G. Overberger who provided stimulating discussions and donated some of the samples used in the present work.

Intramolecular Oxygen–Nitrogen Benzoyl Migration of 6-Aroyloxyphenanthridines[1,2]

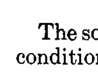
DAVID Y. CURTIN* AND JOHN H. ENGELMANN

Department of Chemistry, University of Illinois, Urbana, Illinois 61801

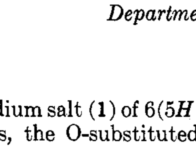
Received March 28, 1972

The sodium salt (**1**) of 6(5*H*)-phenanthridinone reacts with benzoyl chloride to give, under kinetically controlled conditions, the O-substituted product, 6-benzoyloxyphenanthridine (**2a**). When heated alone the *O*-benzoyl compound rearranges to the crystalline *N*-benzoyl isomer, *N*-benzoyl-6(5*H*)-phenanthridinone (**3a**), to the extent of at least 99%. This rearrangement also occurs in hexane or tetrahydrofuran solution but approaches an equilibrium with the ratio **3a**:**2a** of about 5:1. The approach to equilibrium in hexane is first order in **2a** or **3a** and is relatively insensitive to change in solvent polarity. The benzoylations with *p*-methoxybenzoyl chloride and with *p*-chlorobenzoyl chloride have been found to proceed in a similar fashion and the rate and equilibrium constants for reactions of the variously substituted compounds are compared. The effect of the crystalline state on the position of the equilibrium is discussed and other cases are reviewed where crystallization has been utilized to achieve isolation in the pure state of substances which are in mobile equilibrium in solution.

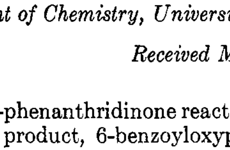
The ready 1,3 rearrangement of acyl groups between oxygen and/or nitrogen atoms[3] may be anticipated to have an important bearing on the chemistry of N- and O-acylated heterocyclic compounds. In a preliminary communication[4] the sodium salt (**1**) of 6(5*H*)-phenanthridinone was reported to undergo O-benzoylation in tetrahydrofuran to give 6-benzoyloxyphenanthridine (**2a**); when heated alone or in methylene chloride solution **2a** was found to rearrange to the *N*-benzoyl isomer **3a**. This paper presents a more detailed study of the equilibrium between **2a** and **3a** as well as rates of isomerization of **2a** and **3a** and their para-substituted analogs.



1



2a, X = H
b, X = CH$_3$O
c, X = Cl



3

Experimental Section

Melting points were determined on a calibrated micro hot-stage melting point apparatus. Infrared spectra were determined with a Perkin-Elmer Model 521 spectrophotometer, uv spectra with a Cary Model 14 spectrophotometer, and nmr spectra by Mr. R. Thrift and his associates with a Varian Model A-56/60 and HA-100 spectrometer. Microanalyses were performed by Mr. J. Nemeth and his associates. Reproductions of the principal spectra are contained in the thesis[1] available from University Microfilms, Ann Arbor, Mich.

Unless otherwise indicated, solvents were purified as follows. Methylene chloride was spectral grade stored over molecular sieves. Pentane and petroleum ether (bp 90–120°) were treated with concentrated H$_2$SO$_4$, then with NaHCO$_3$ solution, dried with molecular sieves, and distilled from NaH. Tetrahydrofuran (THF) was freshly distilled from lithium aluminum hydride for each use. Benzene and toluene were reagent grade and were dried by passage through a column of molecular sieves. Glassware was dried in an oven at 120°.

Benzoylation of the Sodium Salt (1) of Phenanthridone. 6-Benzoyloxyphenanthridine (2a).—The sodium salt **1** was prepared from phenanthridinone (5.12 g) which had been purified by recrystallization from pyridine, washed with dilute HCl and water, and dried in a vacuum desiccator for 8 hr, by treatment in 200 ml of THF with 2.0 g of 57% NaH in mineral oil. After reaction the infrared maxima (THF solution) at 1678 and 1609 cm^{-1} had been replaced by absorptions at 1621, 1584, 1515, and 1474 cm^{-1}. The mixture was cooled in a Dry Ice bath and 3.66 g of benzoyl chloride was added. After several hours at −20° the mixture was filtered and the filtrate was evaporated to dryness. Extraction with pentane at −20° left an insoluble residue which was extracted with 250 ml of toluene at room temperature. Filtration of the toluene solution, evaporation at 0° under reduced pressure of the toluene solution to a volume of 100 ml, addition of 100 ml of pentane, and cooling to −20° gave 2.46 g (32% based on benzoyl chloride) of crude **3** as tan crystals. Three recrystallizations from toluene–pentane gave 0.55 g of white crystals: mp 119° (resolidified almost immediately and remelted at 189–193.5°); ir (CH$_2$Cl$_2$) 1743 (s), 1621 (m), 1593 (m), 1467 cm^{-1} (m); nmr (CDCl$_3$) δ 7.14–8.15 (m); uv (hexane–0.3% THF) λ_{max} 240 nm (ϵ 46,200), 249 (46,300).

Anal. Calcd for C$_{20}$H$_{13}$NO$_2$: C, 80.3; H, 4.4; N, 4.7. Found: C, 80.4; H, 4.3; N, 4.5.

A similar reaction mixture from which aliquots were withdrawn a few minutes after addition of the benzoyl chloride showed, in addition to the absorption at 1656 cm^{-1} attributed to unreacted phenanthridone, the development of the absorption at 1742 cm^{-1} of the benzoyloxyphenanthrene **2**. No absorption was observed at 1733 or 1656 cm^{-1} where the *N*-benzoyl isomer **3** absorbs.

***N*-Benzoyl-6(5*H*)-phenanthridinone (3). A. Room Temperature Benzoylation of the Sodium Salt 1.**—A reaction starting with 4.45 g of phenanthridinone, 1.70 g of 50% NaH, 200 ml of THF, and 6.0 g of benzoyl chloride carried out at room temperature for several minutes was completed by evaporation of the THF, extraction with pentane, and finally with boiling toluene. Filtration and partial evaporation of the toluene extracts gave upon

---

[1] Taken in part from the Ph.D. Thesis of J. H. E., University of Illinois, Urbana, Ill., 1969.

[2] We are very much indebted to the National Science Foundation for a grant which provided substantial support of this work.

[3] D. Y. Curtin and L. L. Miller, *J. Amer. Chem. Soc.*, **89**, 637 (1967).

[4] D. Y. Curtin and J. H. Engelmann, *Tetrahedron Lett.*, 3911 (1968).

TABLE I

KINETICS OF THE EQUILIBRATION OF THE *O*-AROYLPHENANTHRIDINES **2a–c** AND THE *N*-AROYL COMPOUNDS **3a–c**

Starting material	Substituent	Temp, °C	10^5k_e, sec^{-1}	St dev	K_e (3/2)	St dev	$10^5k_1 = [K_e/(K_e + 1)]k_e$, sec^{-1}	$10^5k_{-1} = (k_e - k_1)$, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol		$\Delta G_1^{\ddagger}{}_{44.94°}$, kcal/mol	$\Delta S^{\ddagger}{}_{44.94°}$, cal/deg mol		$\Delta G_{44.94°}$ kcal/mol
									Forward	Reverse		Forward	Reverse	
2a	H	25					$(0.70)^a$	$(0.12)^a$						
		37.50	4.16	0.05^b	5.38	$0.09^{b,c}$	3.51	0.65						
		44.94	10.04	0.15^b	5.25	$0.21^{b,d}$	8.43	1.61	23.4	24.2	24.6	−4.7	−4.5	−1.0
		55.00	32.64	0.26^b	4.91	$0.04^{b,e}$	27.09	5.55						
2b	p-CH_3O	25.00					$(0.364)^a$	$(0.029)^a$						
		25.00	0.497	0.003^f	16.18	$0.28^{f,g}$	0.468	0.029						
		34.95	1.482	0.007^b	11.27	$0.14^{b,h}$	1.362	0.120						
		44.94	5.548	0.030^b	10.00	$0.58^{b,g}$	5.043	0.505	23.9	26.1	24.9	−3.2	−0.9	−1.5
		55.00	17.45	0.10^b	9.01	$0.15^{b,i}$	15.72	1.73						
2c	p-Cl	44.94	10.31	0.13^b	11.17	$0.47^{b,i}$	9.46	0.85						−1.5

[a] Obtained from extrapolation of data at higher temperatures. [b] In hexane solution. [c] Average of data from three equilibrations starting with **2a** and one with **3a**. [d] Average of two values. [e] Average of three values. [f] In tetrahydrofuran solvent. [g] Average of five values. [h] Average of six values. [i] Average of four values.

cooling 6.0 g (88%) of crystals, mp 189–192.5°. Four recrystallizations from toluene–petroleum ether gave 1.49 g of analytically pure **3**: mp 186–190°; ir (CH_2Cl_2) 1733 (s), 1656 (s), 1610 (m), 1600 (m), 1588 (m), 1450 (m), 1440 (m), 1424 cm^{-1} (m); nmr (HMPA) 7.2 (m); uv (hexane–0.3% THF) λ_{max} 236 nm (ϵ 50,400).

Anal. Calcd for $C_{20}H_{13}NO_2$: C, 80.3; H, 4.4; N, 4.7. Found: C, 80.1; H, 4.2; N, 4.6.

B. **Rearrangement of 6-Benzoyloxyphenanthridine (2).**—A sample of **2** heated under an argon atmosphere at 125° for several minutes melted and quickly resolidified. The product was shown by the uv analysis to be discussed to contain about 99% of the *N*-benzoyl compound **3**.

6-(4-Methoxybenzoyloxy)phenanthridine (2b).—4-Methoxybenzoyl chloride [6.08 g, bp 83° (0.3 mm)], was allowed to react for 10 hr at −20° with the sodium salt prepared from 7.58 g of phenanthridinone, 3.5 g of 57% NaH, and 200 ml of THF as above. After extraction with five 125-ml aliquots of toluene an equal volume of pentane was added to each of the toluene solutions at −20°; crystallization occurred. The material from the fourth and fifth extractions was recrystallized by solution in toluene at room temperature and addition of an equal volume of pentane. There was obtained 1 g (9% yield) of the *O*-methoxybenzoyl compound **2b**: mp 134° (with resolidification and remelting at 223–228°); ir (CH_2Cl_2) 1735 (s), 1625 (sh), 1605 (s), 1592 (sh), 1581 cm^{-1} (sh); nmr (pyridine-d_5) δ 7.24–8.69 (m, 12), 3.84 (s, 3); uv (hexane) λ_{max} 250 nm (ϵ 52,100), 256 (55,900).

Anal. Calcd for $C_{21}H_{15}NO_3$: C, 76.6; H, 4.6; N, 4.3. Found: C, 76.8; H, 4.8; N, 4.1.

***N*-(4-Methoxybenzoyl)-6(5*H*)-phenanthridinone (3b). A. By Benzoylation of the Salt 1.**—The first three fractions from the extraction procedure above gave material which was recrystallized three times from boiling toluene, filtered, and diluted with an equivalent volume of petroleum ether. There was obtained 1.0 g (8.5%) of white, crystalline **3b**: mp 226–229°; ir (CH_2Cl_2) 1721 (s), 1654 (s), 1602 (s), 1512 (m), 1335 cm^{-1} (m); nmr (pyridine-d_5) δ 6.98–8.67 (m, 12), 3.77 (s, 3); uv (hexane) λ_{max} 229 nm (ϵ 49,500).

Anal. Calcd for $C_{21}H_{15}NO_3$: C, 76.6; H, 4.6; N, 4.3. Found: C, 76.8; H, 4.8; N, 4.3.

B. **By Rearrangement of the *O*-Methoxybenzoyl Isomer 2b.**—When a sample of **2b** was heated to 150° under an argon atmosphere it melted and quickly recrystallized to give material shown by the uv analysis to be discussed below to be the *N*-benzoyl isomer **3b** in a purity of at least 99%.

6-(4-Chlorobenzoyloxy)phenanthridine (2c).—The reaction of the salt from 5 g of phenanthridinone and 1.5 g of NaH in 200 ml of THF with 4.3 g of *p*-chlorobenzoyl chloride was carried out for 5 hr at −20°, after which the mixture was warmed to room temperature and filtered. Evaporation of the filtrate to dryness and extraction with toluene at room temperature gave on addition of petroleum ether 2.55 g (42% based on unrecovered phenanthridinone) of **2b** as white crystals which were purified by further recrystallization from toluene–petroleum ether. [The toluene-insoluble fraction amounted to 2.55 g (42%) of unreacted phenanthridinone.] There was thus obtained 2.12 g of purified **2c**: mp 135° (resolidified and remelted at 195–200°); ir (CH_2Cl_2) 1742 (s), 1620 (w), 1592 cm^{-1} (m); nmr (pyridine-d_5) δ 7.17–8.67 (m); uv (hexane–0.3% THF) λ_{max} 248 nm (ϵ 61,270).

Anal. Calcd for $C_{20}H_{12}ClNO_2$: C, 72.0; H, 3.6; Cl, 10.6; N, 4.2. Found: C, 72.0; H, 3.7; Cl, 10.9; N, 4.3.

***N*-(4-Chlorobenzoyl)phenanthridinone (3c).**—A 1.0-g sample of analytically pure *p*-chlorobenzoylphenanthridine (**2c**) was recrystallized from boiling toluene to yield 0.82 g of analytically pure **3c**: mp 198–200°; ir (CH_2Cl_2) 1730 (s), 1655 (s), 1612 (m), 1590 cm^{-1} (m); nmr (pyridine-d_5) 7.08–8.67; uv (hexane–0.3% THF) λ_{max} 236 nm (ϵ 47,890).

Anal. Calcd for $C_{20}H_{12}ClNO_2$: C, 72.0; H, 3.6; Cl, 10.6; N, 4.2. Found: C, 72.0; H, 3.6; Cl, 10.8; N, 4.3.

Equilibration of 2a and 3a. A. Spectroscopic Analysis in Hexane Solution.—Solutions of **2a** in hexane were allowed to stand in a constant-temperature bath until no further change in the uv spectrum was observed. They were then analyzed with a least-squares curve-fitting method[5] which determined the concentrations of **2a** and **3a** from absorbancies of the mixture together with standard absorbancies of the pure components at 20 wavelengths with incremental steps from 211–215, 222–225, and 244–254 nm. Application of the method to known mixtures gave average deviations from the theoretical value of 1.3%. The equilibrium constants calculated from these data (K_e = **3a**/**2a**) are given in Table I. A solution of **3a** in hexane on long standing gave the same equilibrium spectrum as **2a**.

B. **Analysis by Thin Layer Chromatography.**—Qualitative confirmation of the uv results was obtained by dissolution of a sample of the more stable isomer **3a** in methylene chloride and heating the solution under reflux for 70 hr. Tlc on Eastman silica gel plates using 20% diethyl ether in benzene as eluent and with standard samples of **2a** and **3a** on the same plate showed the presence of two spots, one (the smaller) with the R_f corresponding to that of **2a** and the other with an R_f corresponding to that of **3a**.

Kinetics of the Rearrangements of the Benzoyloxyphenanthrenes 2a–c to the *N*-Benzoylphenanthridinones 3a–c.—Solutions 2×10^{-5}–10^{-4} *M* of **2a, b,** or **c** in spectral grade hexane were heated in a constant-temperature bath maintained at a temperature controlled to ±0.05°. Temperatures were measured with thermometers calibrated by the National Bureau of Standards. Aliquots were withdrawn after various times and analyzed by the uv method described in method A for the determination of the equilibrium between **2a** and **3a** above.[6] The per cent of starting material present at equilibrium, % C, was the average of several determinations in each case. Plots of ln (% C − % C_e) *vs.* time were linear to greater than 90% approach to equilibrium. Rate constants k_e are reported in Table I. Sample kinetic data are presented in Table II.

Reaction of 6-Benzoyloxyphenanthridine (2a) and *N*-Benzoylphenanthridinone (3a) with Piperidine.—Reaction of 176 mg of **2a** with 55 mg of piperidine in 5 ml of pentane for 24 hr at −20° gave, after removal of the pentane solution from the insoluble

---

(5) D. B. Pendergrass, Jr., Ph.D. Thesis, University of Illinois, Urbana, Ill., 1971, pp 148 ff.

(6) The analyses of mixtures from **2b** and **2c** were made from absorbancies at the even-numbered wavelengths from 222 to 260 nm (20 points) by an otherwise identical method. Average deviations from the correct values of known mixtures were 0.9% for **2b** and 0.67% for **2c**.

TABLE II

RATE OF EQUILIBRATION OF **2a** AND **3a** AT 44.94 ± 0.05

Time, min	**2a**, %	$10^6 k_e$[a]
0	100	
30	85.27	10.70
70	71.04	10.05
110	60.52	9.61
140	51.26	10.32
180	42.53	10.65
192	41.34	10.38
240	35.02	10.29
280	30.13	10.58
300	28.53	10.54
340	26.15	10.32
361	24.85	10.35
415	22.26	10.38
420	22.54	10.08
510	20.16	9.76
600	18.31	9.88
600	18.58	9.58
660	18.10	9.21
690	16.98	10.54
780	16.81	9.70
	Average	10.15

[a] Value calculated by the method of least squares $10^6 k_e$ 10.15. Per cent **2a** at equilibrium, 15.91.

residue followed by extraction with water to remove the piperidine and evaporation to dryness, 74 mg (66% yield) of *N*-benzoylpiperidine, mp 48–49° (lit.[7] mp 48°), identified by comparison of the melting point, mixture melting point, and infrared spectrum with those of an authentic sample.[7] The pentane-insoluble fraction was 97 mg (84%) of phenanthridinone, mp 292–294°.

When 164 mg of **3a** was treated with 46 mg of piperidine and 10 ml of pentane at ambient temperature for 15 hr and then after addition of 40 ml of additional pentane under reflux for 5 hr, there was obtained after work-up as with the reaction of **2a** 24 mg (23%) of benzoylpiperidine, mp 47–49°, characterized by melting point, mixture melting point, and infrared spectrum. The pentane-insoluble residue yielded 123 mg (75%) of recovered **3a**.

Results and Discussion

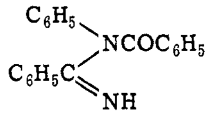
The kinetically controlled aroylation of the sodium salt of phenanthridinone in THF (low temperatures and short reactions times) clearly shows a strong preference for attack at the oxygen atom. However, in hexane solution as well as THF the equilibration of *O*- and *N*-aroylphenanthridinones is readily obtained, the *N*-aroyl species being favored with an equilibrium constant of about 5 (Table I).[8] The solid-state equilibrium favors the *N*-aroyl isomer still more, at least 99% of the mixture being the N-substituted component.

The evidence bearing on the mechanism of the acyl migration in solution can be summarized briefly. Linearity of first-order plots and the observation that a fourfold increase in concentration of starting material gave no change in the rate constant shows that the reactions interconverting **2a** and **3a** are first order. Since the observed rate constant k_e for the approach to equilibrium is the sum of forward and reverse rate constants k_1 and k_{-1}, it has been partitioned to give the values shown in Table I. Comparison of the rates of reaction of **2b** and **3b** in tetrahydrofuran with their rates in hexane (Table I) shows that there is an increase of less than 30% in the more polar solvent.[9] The effects of substituents on the rate and equilibrium constants, shown in Table III, are small, the overall spread of any set of constants being less than a factor of 4. Although the values of k_1 show a reasonable trend, *p*-methoxyl decreasing the rate and *p*-chloro increasing it, a plot of log k_1 *vs.* σ^{11} is not linear. Calculation from pairs of rate constants using the Hammett equation gives values of ρ ranging from 0.22 to 0.88. One source of the nonlinearity is seen when the effect of substituents on the equilibrium constants K_e is considered. Both *p*-methoxy and *p*-chloro substituents increase the equilibrium constant and by amounts which are clearly outside experimental error and are comparable to the magnitudes of the effects on the rate constants. It seems unwise to attempt to draw conclusions about details of mechanism from such small substituent effects on the benzoyl phenanthridinone rearrangements without further data. However, the modest effect of substituents and solvent change on k_1 is reminiscent of the behavior of other 1,3-acyl migrations which are compared in Table IV. It may be noted also that a ρ of +0.518 has been reported[12] for the reaction of meta- and para-substituted methyl benzoates with aniline in nitrobenzene to form benzanilides. In short, the interconversion of **2** and **3** seems to belong to a group of re-

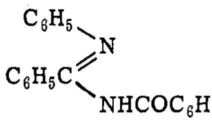
TABLE III

RELATIVE VALUES OF THE RATE AND EQUILIBRIUM CONSTANTS FOR THE EQUILIBRATION OF THE N- AND O-PARA-SUBSTITUTED BENZOYLPHENANTHRIDINONES **2** AND **3** IN HEXANE AT 44.94°

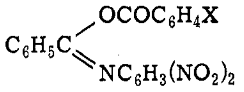
Compd	Substituents	k_1 (rel)	k_{-1} (rel)	K_e (rel)
2b, 3b	*p*-CH_3O	0.60	0.31	1.90
2a, 3a	H	1.00	1.00	1.00
2c, 3c	*p*-Cl	1.12	0.53	2.12



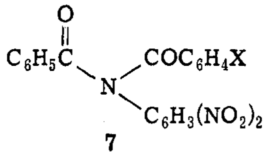
4



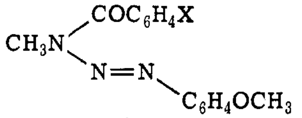
5



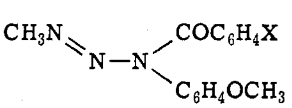
6



7



8



9

---

[7] C. Schotten, *Ber.*, **17**, 2545 (1884); **21**, 2238 (1888).

[8] At the time of publication of the preliminary report[4] of this work the presence of a minor component of the solution equilibrium had not been recognized.

[9] If the assumption is made that the *Z* value for hexane is the same as that for isooctane [E. M. Kosower, *J. Amer. Chem. Soc.*, **80**, 3253 (1958)] and it is employed to calculate k_1 with eq 6 of Smith, Fainberg, and Winstein,[10] the rate constants for the reaction of **2b** in hexane and in tetrahydrofuran (Table I) lead with the Smith–Fainberg–Winstein equation (eq 7)[10] to an "*a*" value for the rearrangement of **2b** to **3b** of 0.17.

[10] S. G. Smith, A. H. Fainberg, and S. Winstein, *J. Amer. Chem. Soc.*, **83**, 618 (1961); S. G. Smith, *Tetrahedron Lett.*, 979 (1962).

[11] L. P. Hammett, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1970, pp 355 ff.

[12] N. T. Vartak, N. L. Phalnikar, and B. V. Bhide, *J. Indian Chem. Soc.*, **24**, 131A (1947).

TABLE IV

1,3-ACYL MIGRATIONS BETWEEN NITROGEN AND/OR OXYGEN ATOMS

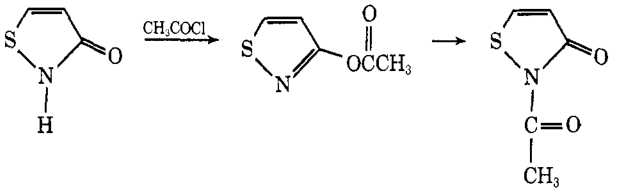
Reaction	Change	Solvent	Temp range studied, °C	Rate of compd (X = H) 10^5k_1, sec^{-1}	Temp, °C	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal/mol deg	ρ
$4^a \rightarrow 5^a$	N → N	Toluene	45–80	1.3	45.00	20.2	−17	
$6^b \rightarrow 7^b$	N → O	Benzene	42–64	6.1	42.86	23.8	−2	0.6
2a → **3a**[c]	O → N	Hexane	37–55	10.0	44.94	23.14	−5	0.6
3a → **2a**[c]	N → O	Hexane	37–55	1.6	44.94	24.2	−5	0.0 ± 2
8 → **9**[d]	N → N	Diphenyl ether	148–185	2×10^{-5}	43[e]	33.6	−3	0.6

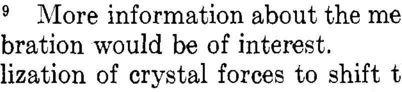
[a] D. A. R. Thompson, Ph.D. Thesis, University of Illinois, Urbana, Ill., 1970; H. L. Wheeler, T. B. Johnson, and D. F. McFarland, *J. Amer. Chem. Soc.*, **25,** 787 (1903); D. A. Peak, *J. Chem. Soc.*, 215 (1952). [b] Reference 4. [c] This paper. [d] C. L. Mampaey, Ph.D. Thesis, University of Illinois, Urbana, Ill., 1968; see also D. Y. Curtin and J. D. Druliner, *J. Org. Chem.*, **32,** 1552 (1967). [e] Data extrapolated to this temperature.

actions whose mechanism is essentially an intramolecular nucleophilic replacement at a carbonyl group, as discussed previously.[3] As is seen in Table IV, these proceed under mild conditions (with the exception of the rearrangement of the benzoyltriazene **8**) in nonpolar solvents in spite of the fact that a strained four-membered cyclic transition state is involved.

The interconversion of *N*- and *O*-acyl derivatives of heterocycles could be expected to be a general reaction and to proceed under mild conditions. The aroylation of the sodium salt of 2-pyridone suspended in benzene was shown in a preliminary study[13] to yield what appeared to be a mixture of *N*- and *O*-aroylpyridones, the N isomer disappearing on standing. Furthermore, acetylation of the thallous salt of 2-pyridone in chloroform at −40° has been reported[14] to produce a solution whose nmr spectrum strongly suggests that a mixture of *N*- and *O*-acetyl products is formed in a ratio (N:O) of 2:3, the *N*-acetyl compound being converted to O-acetyl on standing at room temperature. It is not certain just how far toward the *O*-acyl derivatives the equilibria lie in the case of the acylpyridones. It is somewhat surprising that an *N*-oxalyl derivative of 2-pyridone has been reported to show no tendency to rearrange to the O-substituted derivative.[15] The equilibria between hydroxy pyridine and pyridone isomers with proton transfer and with methyl transfer have been studied in considerable detail.[16] However, as was pointed out by Chan and Crow[17] in their study of the positions of equilibria of *N*- and *O*-acyl-3-hydroxyisothiazoles, acyl equilibria differ from equilibria involving proton or alkyl migration not only because of polar effects but also due to steric effects arising from the preference for a planar conformation of the ester and amide functional groups.

The study[17] of the acyl-3-hydroxyisoxazoles is of interest in another connection. Acylation of the parent isoxazole with acetyl chloride and triethylamine in benzene (the kinetically controlled reaction) favored the *O*-acetyl compound by a factor of at least 9:1. The O compound could be made subsequently to rearrange to the N-substituted isomer, but not by an intramolecular path. It seems likely that the intramolecular 1,3-acyl migration is slower in the case of five-membered heterocycles because of the increased N–C–O bond angle of the five-membered ring; a competing intermolecular reaction can then predominate. A reaction which may be related is the rearrangement of the *O*- to *N*-carbalkoxylbenzisoxazoles recently reported.[18]





As a further example of what seems to be an intermolecular rearrangement, 4-pyridone on acetylation gives the *N*-acetyl derivative as the stable crystalline product which on solution in methylene chloride rearranges to an equilibrium mixture of 4-acetoxypyridine and *N*-acetyl-4-pyridone in nearly equal amounts.[19] More information about the mechanism of this equilibration would be of interest.

The utilization of crystal forces to shift the equilibrium between **2** and **3** from one balanced in solution to an equilibrium essentially completely one-sided in the crystalline state deserves further emphasis. Numerous examples have been recently reported of the use of the great selectivity inherent in the crystallization process to obtain in pure form one or more isomeric species which are known to be in equilibrium in solution. These include crystallization of rotational conformers,[20] equilibrium asymmetric transformers,[21] cis–trans iso-

---

[13] Reference 3, footnote 23.

[14] A. McKillop, M. J. Zelesko, and E. C. Taylor, *Tetrahedron Lett.*, 4945 (1968).

[15] L. J. Bollyky, B. G. Roberts, R. H. Whitman, and J. E. Lancaster, *J. Org. Chem.*, **34,** 836 (1969).

[16] P. Beak, T. S. Woods, and D. S. Mueller, *Tetrahedron*, in press; A. R. Katritsky, *Chimia*, 134 (1970).

[17] A. W. K. Chan and W. D. Crow, *Aust. J. Chem.*, **21,** 2967 (1968).

[18] H. Büshagen and W. Geiger, *Chem. Ber.*, **103,** 123 (1970).

[19] I. Fleming and D. Philippides, *J. Chem. Soc. C*, 2426 (1970).

[20] S.-I. Mizushima, "Structure of Molecules and Internal Rotation," Academic Press, New York, N. Y., 1954; J. W. Barsch, *J. Chem. Phys.*, **43,** 3473 (1965); P. Klaeboe, *Acta Chem. Scand.*, **23,** 2641 (1969); F. R. Jensen and C. H. Bushweller, *J. Amer. Chem. Soc.*, **91,** 3223 (1969); T. Fujiyama, *Bull. Chem. Soc. Jap.*, **44,** 3317 (1971); T. Miyazawa, *ibid.*, **42,** 3021 (1969).

[21] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, pp 58–60, 63–65; R. E. Pincock and K. R. Wilson, *J. Amer. Chem. Soc.*, **93,** 1291 (1971); S. A. Chawdhury, A. Hargreaves, and R. A. L. Sullivan, *Acta Crystallogr., Sect. B*, **24,** 1222 (1968).

mer,[22] proton-transfer tautomers,[23] ring–chain tautomers,[24] and diastereoisomeric hemiacetals,[25] as well as the isomers related by 1,3-acyl migration discussed above. In many of the cases cited it is not clear whether the selectivity observed is due to preferential nucleation of one isomer or to a thermodynamic preference for one isomer in the crystalline state.

(22) I. R. Gault, W. D. Ollis, and I. O. Sutherland, *Chem. Commun.*, 269 (1970); N. A. Bailey and S. E. Hull, *ibid.*, 960 (1971); D. Y. Curtin and J. W. Hausser, *J. Amer. Chem. Soc.*, **83**, 3474 (1961); E. F. Schoenwaldt, R. B. Kinnel, and P. Davis, *J. Org. Chem.*, **33**, 4270 (1968); M. Raban and E. Carlson, *J. Amer. Chem. Soc.*, **93**, 685 (1971); A. G. Sanchez, A. M. Valle, and J. Bellanato, *J. Chem. Soc. B*, 2330 (1971); F. Sondheimer, *Accounts Chem. Res.*, **3**, 81 (1972); A. Rieker and H. Kessler, *Chem. Ber.*, **102**, 2147 (1969); A. J. Bellamy and R. D. Guthrie, *J. Chem. Soc. C*, 2090 (1968).

(23) B. H. Chase and J. Walker, *J. Chem. Soc.*, 3518 (1953); J. W. Schulenberg, *J. Amer. Chem. Soc.*, **90**, 1367 (1968); E. M. Peresleni, M. Y. Uritskaya, V. A. Loginova, Y. N. Sheinker, and L. I. Yakontov, *Dokl. Akad. Nauk SSSR*, **183**, 1102 (1968); G. A. Newman and P. J. S. Pauwels, *Tetrahedron*, **25**, 4605 (1969); E. Spinner and G. B. Yeh, *J. Chem. Soc. B*, 279 (1971); T. Shono, Y. Hayashi, and K. Shima, *Bull. Chem. Soc. Jap.*, **44**, 3179 (1971); D. Hadzi, *J. Chem. Soc.*, 2143 (1956); G. T'oth, I. T'oth, and L. Toldy, *Tetrahedron Lett.*, 5299 (1969); W. Walter and K. J. Reubke, *Chem. Ber.*, **102**, 2117 (1969).

(24) P. R. Jones and P. J. Desio, *J. Org. Chem.*, **30**, 4203 (1965); W. Flitsch, *Chem. Ber.*, **103**, 3205 (1970); A. F. McDonagh and H. E. Smith, *J. Org. Chem.*, **33**, 1 (1968); W. Schaefer and H. Schlude, *Tetrahedron Lett.*, 2161 (1968); H. Alper, E. C. Keung, and R. A. Partis, *J. Org. Chem.*, **36**, 1352 (1971), and earlier papers.

(25) M. C. Tanret, *Bull. Soc. Chim. Fr.*, **33**, 337 (1905); C. S. Hudson and E. Yanovsky, *J. Amer. Chem. Soc.*, **39**, 1013 (1917); R. W. King, C. F. Murphey, and W. C. Wildman, *ibid.*, **87**, 4912 (1965); J. Karle, J. A. Estlin, and I. L. Karle, *ibid.*, **89**, 6510 (1967).

Differential thermal analysis in which **2a** was heated at a rate of 10°/min showed an endotherm (partial melting) interrupted by an exotherm (heat of reaction and recrystallization of the **3a** which had been formed) and then a melting endotherm corresponding to the melting of the product **3a**.[26] From the areas of these peaks the thermal changes were estimated to be 4.7 kcal/mol for the first endotherm and −6.9 kcal/mol for the exotherm. At the end of those changes, if melting, reaction, and recrystallization had taken place, the net change for the process **2a** (solid) → **3a** (solid) was 4.7 + (−) 6.9 = 2.2 kcal/mol. These data are not of high accuracy but the result is reasonable. The final melting endotherm had an area which gave a value for the heat of fusion of 12 kcal/mol for the **3a** which had been formed. The value of the heat of fusion obtained with recrystallized **3a** was 9.3 kcal/mol. The reason for the greater stabilization of **3a** by crystal packing forces must await information about the crystal structures of these compounds.

Registry No.—**1**, 20178-62-5; **2a**, 20178-63-6; **2b**, 35454-86-5; **2c**, 35356-68-4; **3a**, 20178-64-7; **3b**, 35427-28-2; **3c**, 35356-69-5.

(26) We are indebted to Dr. S. R. Byrn for these results. The method employed has been described: D. Y. Curtin, S. R. Byrn, and D. B. Pendergrass, Jr., *J. Org. Chem.*, **34**, 3345 (1969).

Carbon-13 Nuclear Magnetic Resonance Spectroscopy. Conformational Analysis of Methyl-Substituted Cycloheptanes, Cycloheptanols, and Cycloheptanones[1]

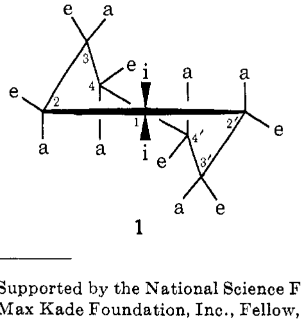
MANFRED CHRISTL[2] AND JOHN D. ROBERTS*

Contribution No. 4417 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109

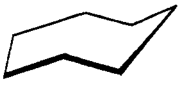
Received February 8, 1972

The ^{13}C chemical shifts were determined of the carbons in 12 cycloheptanes, 21 cycloheptanols, and 8 cycloheptanones. In some cycloheptanols and cycloheptanones, the assignments have been obtained unambiguously by the synthesis of deuterated derivatives and the use of paramagnetic-shift reagents. Substituent effects for the different types of groups have been calculated. The most informative data about the cycloheptane conformations were provided by the relatively well understood γ effects. The results are generally in good agreement with predictions based on the twist-chair form, which has been predicted by Hendrickson to be the most stable conformation. Pairs of cis–trans isomers are found to have rather characteristic differences in their ^{13}C spectra. This fact was used to assign the resonances found for cis–trans mixtures of methyl-substituted cycloheptanols to specific isomers.

In contrast to the many published studies of cyclohexane conformations, the results of relatively few experimental investigations of the cycloheptane conformations have been reported.[3] One reason is complexity. The twist–chair conformation (**1**) of cycloheptane is predicted to be most stable,[4] and this form has three different equatorial (e) and axial (a) positions besides two identical isoclinal (i) or axis positions. Substituents at the i and the various *e* positions are calculated to have pretty much the same conformational energy.[4d] To add to the complexities, and, in contrast to the rather rigid cyclohexane chair form, the cycloheptane twist form is quite flexible and an unsubstituted twist form can transform to another one by "pseudorotation" in which the axis of symmetry has moved by one carbon. The barrier to pseudorotation is estimated to be 1.4 kcal/mol[4e] and the highest point of energy along the interconversion pathway is the chair form **2**, which has a plane of symmetry.[4e] The twist-boat (**3**) and the boat (**4**) are other cycloheptane con-



1



2

---

[1] Supported by the National Science Foundation.

[2] Max Kade Foundation, Inc., Fellow, 1970–1971.

[3] For a review see W. Tochtermann, *Fortschr. Chem. Forsch.*, **15**, 378 (1970).

[4] (a) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 4537 (1961); (b) *ibid.*, **84**, 3355 (1962); (c) *ibid.*, **89**, 7036 (1967); (d) *ibid.*, **89**, 7043 (1967); (e) *ibid.*, **89**, 7047 (1967).