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THE REACTION OF PERFLUORO(N-ALKYL-CYCLIC AMINES) WITH OLEUM. THE FORMATION AND CHARACTERIZATION OF PERFLUOROLACTAMS

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SUMMARY

Treatment of several kinds of perfluoro(N-alkyl-cyclic amines)(-pyrrolidines, -morpholines, -piperidines and -hexahydroazepin) with oleum at 140~170 °C afforded the corresponding perfluorolactams in fair yields. The reaction conditions and the properties of perfluorolactams are described.

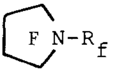
INTRODUCTION

Perfluorotertiary amines are known to be thermally and chemically inert compounds which have become used as inert liquids mainly in the electronic industry [1]. That is why the study of their synthetic utility has been limited only to several reactions involving thermolysis [2] and reactions with $AlCl_3$ [3] and SO_3 [4].

On the other hand, there are relatively few synthetic routes to perfluorolactams, though there has been considerable interest in perfluoroheterocyclic compounds. Such reports include: the formation of perfluoro(N-methyl pyrrolidone) by photolysis of tetrafluoroformaldehyde azine with perfluoro(glutaryl fluoride) [5], and by pyrolysis of perfluoro(tetrahydro-2-methyl-2H-1,2-oxazine) [6], and heptafluoroazacyclopentane-2-one from base catalyzed decomposition of 1-difluoroamino-2-fluorosulfato-hexafluorocyclobutane [7] and perfluoro(N-methyl-3-oxo-morpholine) from hydrolysis of perfluoro(N-methyl-3-sulfato-morpholine) [4].

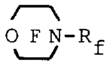
We have found that α-CF_2 of the ring of perfluoro(N-alkylcyclic amines) could be hydrolyzed with oleum to give directly perfluorolactams in fair yields, this providing a new route to them by one step [8]. In this paper, we wish to report the full account of this reaction, which is a convenient synthetic method for various perfluorolactams from the view point of the simplicity of the procedure.

Perfluorocyclic amines used for this investigation were various kinds of perfluoro-N-alkyl-substituted perfluoropyrrolidines (1a), perfluoromorpholines (2a), perfluoropiperidines (3a), and a perfluoro(N-ethyl hexahydroazepin)(4a), viz.



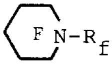
(R_f=CF_3, C_2F_5, $ClCF_2CF_2$, n-C_3F_7, c-C_5F_9)

1a



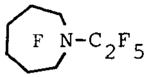
(R_f=C_2F_5, $ClCF_2CF_2$, n-C_3F_7, c-C_5F_9, $FSO_2CF_2CF_2CF_2$)

2a



(R_f=CF_3, C_2F_5, $ClCF_2CF_2$),

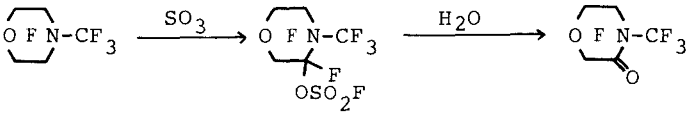
3a



4a

RESULTS AND DISCUSSION

The introduction of a nitrogen atom into a saturated perfluorocarbon skeleton increases the reactivity of C-F bonds at α-positions to it; this makes it possible to enter into reaction with such powerful electrophilic reagents as SO_3. For example, it is known that perfluoro(N-methyl-3-fluorosulfatomorpholine)(II) is formed by the reaction of perfluoro(N-methyl morpholine)(I) and SO_3, and the corresponding perfluoro(N-methyl-3-oxomorpholine)(III) is obtained by a subsequent hydrolysis of II with dilute sulfuric acid [4].

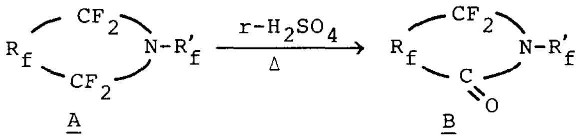


I II III

Scheme 1

As a general method for the preparation of perfluorolactams, however, this process suffers from handling of anhydrous SO_3 and subsequent controlled hydrolysis of II, which limits the easy access to other perfluorolactams.

It was found possible to effect hydrolysis of α-CF_2 groups of perfluoro(N-alkyl-cyclic amines) A directly by the action of oleum by heating the reaction mixture at 140~170 °C preferably in the presence of catalysts like $HgSO_4$ and $MoCl_5$. Hydrolysis occurred exclusively at an α-CF_2 of the ring affording a lactam B as the sole product.



$$\left[\begin{array}{l} R_f = -(CF_2)_n-,\ \text{where } n=2,3 \text{ or } 4,\ -CF_2OCF_2- \\ R'_f = \text{perfluoroalkyl group} \end{array}\right]$$

Scheme 2

In Table 1, are shown the details of the experiments which were conducted in order to find the optimum reaction conditions with 1a(R_f=C_2F_5) and 1a(R_f=CF_2CF_2Cl), using different molar ratios of amine to SO_3 and reaction temperatures of 120~170 °C. From these results it was found that the use of a large excess of oleum reduced both the yield of B and the amount of A recovered [Runs 2 and 3]. In the reaction of 1a(R_f=CF_2CF_2Cl), substitution of the Cl atom did not occur, but the α-CF_2 of the ring was converted into a carbonyl group giving 1b(R_f=CF_2CF_2Cl) (1) [Runs 5 and 6]. Though the use of catalyst($HgSO_4$) is not indispensable, it could improve slightly the yield and the purity of B.

TABLE 1

Reactions of 1a(R_f=C_2F_5) and 1a(R_f=CF_2CF_2Cl) with oleum at several reaction conditions[a]

Run	Sample (mmol)	Amine/SO_3 ratio	Reaction conditions Temp (°C)/time (hr)	Lactam (Yield%)[b]	Sample recovered (%)
1	1a(R_f=C_2F_5) (5.35)	1/3.8	145/24	1b(R_f=C_2F_5) (2) (73.9)	45.5
2	1a(R_f=C_2F_5) (5.05)	1/7.6	145/24	2 (43.9)	9.0
3	1a(R_f=C_2F_5) (5.20)	1/8.3[c]	145/24	2 (0)	0
4	1a(R_f=C_2F_5) (5.20)	1/4.2	170/23	2 (71.5)	19.8
5	1a(R_f=CF_2CF_2Cl) (5.06)	1/4.3	145/24	1b(R_f=CF_2CF_2Cl) (1) (64.6)	trace
6	1a(R_f=CF_2CF_2Cl) (2.09)	1/3.7	120/24	1 (60.3)	49.4

[a] Reaction were conducted using 30% oleum unless otherwise stated in a Pyrex ampule (135 cm long x 14 mm wide) and adding catalytic amount of $HgSO_4$.

[b] Yields were determined by GLC based on the sample consumed.

[c] Oleum (60%) was used.

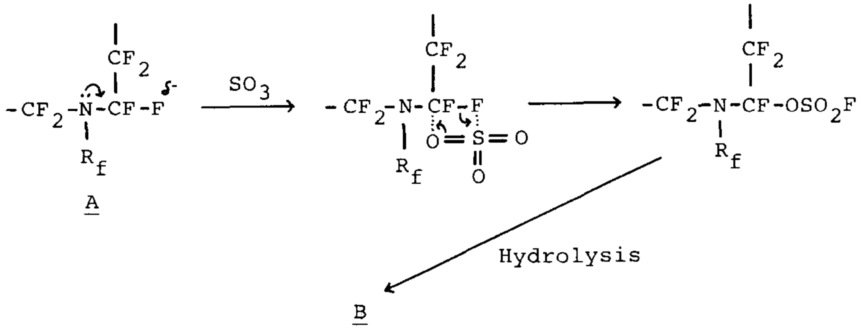
For other amines, the reaction conditions were fixed applying the reaction temperature of 170 °C, except for those containing R_f=CF_2CF_2Cl [1a(R_f=CF_2CF_2Cl), 2a(R_f=CF_2CF_2Cl) and 3a(R_f=CF_2CF_2Cl)], for which a temperature of 145 °C was used. A reaction time of 24 hrs, and SO_3/amine molar ratio of

1 : 4.0 ~ 4.7 in the presence of small quantities of catalyst ($HgSO_4$) was employed. Further optimization of these reactions was not attempted.

The results of these reactions are tabulated in Table 2, and the physical properties of perfluorolactams (B) obtained from reactions are summarized in Table 3.

Generally, with respect to the relationship between the kind of amines and the reactivity toward SO_3, good reactivity was observed for 1a and 2a compared with 3a and 4a. When the same kinds of amine were used, no systematic variations of the reactivity could be recognized for the types of perfluoro-N-alkyl groups, except for the 2-chlorotetrafluoroethyl group. Such amines (1a, 2a and 3a) carrying $R_f = CF_2CF_2Cl$ reacted easily compared with those carrying $R_f = CF_2CF_3$, respectively.

The reaction mechanism between A and oleum seems to be rather complex and has not yet been clarified. Though ^{19}F nmr measurements of the sulfuric layer obtained from the reaction of 1a($R_f = C_2F_5$) were made during the reaction, the only fluoro-compound detected was fluorosulfonic acid, other than 1b($R_f = C_2F_5$)(2). However, the reaction seems to proceed via a fluorosulfato-compound as an intermediate which was formed by an electrophilic attack, presumably involving a four-membered transient species from attack of SO_3 on an α-CF_2 of A.



Scheme 3

TABLE 2

Summary of reactions of perfluoro(N-alkyl cyclic amines) with oleum[a]

Sample (mmol)	Lactam (Yield %)	Sample recovered (%)
1a(R_f=CF_3) (5.87)	1b(R_f=CF_3) (3) (41.2)	14.5
1a(R_f=n-C_3F_7) (4.57)	1b(R_f-n-C_3F_7) (4) (77.0)	trace
1a(R_f=c-C_5F_9) (4.25)	1b(R_f=c-C_5F_9) (5) (84.6)	57.1
2a(R_f=C_2F_5) (5.01)	2b(R_f=C_2F_5) (6) (51.2)	8.0
2a(R_f=CF_2CF_2Cl)[b] (4.84)	2b(R_f=CF_2CF_2Cl) (7) (74.4)	7.9
2a(R_f=n-C_3F_7) (4.54)	2b(R_f=n-C_3F_7) (8) (64.5)	30.4
2a(R_f=c-C_5F_9) (4.91)	2b(R_f=c-C_5F_9) (9) (79.5)	48.4
2a[R_f=$(CF_2)_3SO_2F$] (4.10)	2b[R_f=$(CF_2)_3SO_2F$] (10) (62.0)	47.4
3a(R_f=CF_3) (5.29)	3b(R_f=CF_3) (11) (31.6)	22.7
3a(R_f=C_2F_5) (4.65)	3b(R_f=C_2F_5) (12) (54.6)	39.9
3a(R_f=CF_2CF_2Cl)[b] (4.51)	3b(R_f=CF_2CF_2Cl) (13) (58.7)	33.9
4a (4.32)	4b (14) (44.3)	49.2

[a] Reactions were conducted in the presence of small amounts of $HgSO_4$ under the following conditions unless otherwise stated: amine/SO_3 ratio; 1 : 3.5~4.5; 170 °C, and reaction time; 24 hrs.

[b] Temp; 145 °C.

TABLE 3

Physical properties and IR data of perfluorolactams

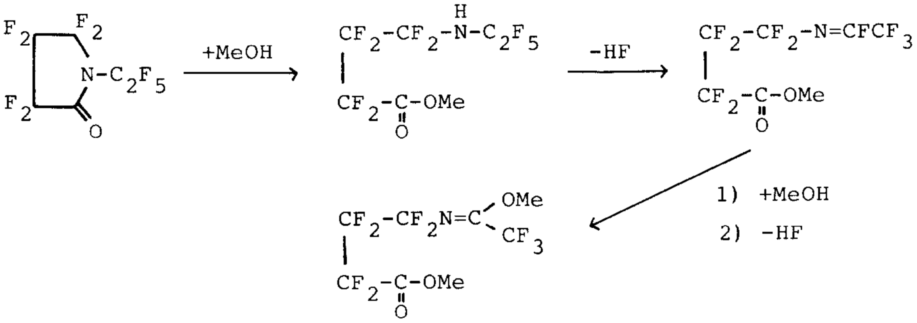
Compd	bp[a]	n_D^{20}	d_4^{20}	IR: ν(C=O)	Elemental Analysis/ C(%)
1	98.5 ~ 99.5	1.3203	1.7273	1833	21.87 (22.00)[b]
2	69.0 ~ 70.5	1.2895	1.7018	1835	23.00 (23.15)
3	52.5 ~ 53.0	1.2865	1.6698	1840	22.89 (22.99)
4	90.0 ~ 91.0	1.2915	1.7354	1836	23.19 (23.27)
5	132.5 ~ 133.0	1.3173	1.8408	1840	25.45 (25.53)
6	77.5 ~ 78.0	1.2913	1.7268	1896	21.90 (22.02)
7	106.5 ~ 107.0	1.3212	1.7475	1807	20.79 (22.98)
8	98.5 ~ 99.0	1.2941	1.7542	1794	22.21 (22.28)
9	139.5 ~ 140.0	1.3174	1.8490	1814	24.52 (24.60)
10	157.0 ~ 157.5	1.3278	1.8450	1801	18.84 (19.06)
11	77.0 ~ 77.5	1.2972		1840	23.03 (23.15)
12	92.0 ~ 93.0	1.2983	1.7797	1836	23.22 (23.27)
13	118.5 ~ 119.5	1.3252	1.7921	1834	22.15 (22.27)
14	113.0 ~ 114.5	1.3032	1.8318	1791	23.32 (23.36)

[a] Boiling points are not corrected.

[b] Calculated values in parentheses.

Failure to detect the expected intermediate may be attributed to facile hydrolysis of the fluorosulfato-compound [4].

Perfluorolactams (B) are fuming liquids in air, and showed strong reactivity towards nucleophiles. Thus, with CH_3OH, 2b(R_f=C_2F_5) (2) gave 2-methoxy-6-methoxycarbonyl-nonafluoro-3-aza-hexene-2 as the main product in a low yield according to the following scheme.



Scheme 4

This reaction which involves a sequence of addition-elemination mechanism is analogous to that between 1a(R_f=CF_3) and H_2O reported in the literature [4].

EXPERIMENTAL

Starting materials and apparatus

The perfluorocyclic amines used were all made by the electrochemical fluorination of the appropriate cyclic amines. Except perfluoro(N-cyclopentyl morpholine), these amines were known compounds. Perfluoro(N-cyclopentyl morpholine) had bp 141~142 °C, n_D^{20}1.3087 and d_4^{20}1.9007. Fuming sulfuric acid (30%) [Nakarai Chemicals Ltd], fuming sulfuric acid (60%)[Nakarai Chemicals Ltd]and mercury sulfate [Wako Chemicals Ltd] were used as received.

Pyrex ampules (135 mm long x 14 mm wide) were used for the reaction throughout the experiments.

^{19}F nmr spectra were recorded on a Hitachi R-20 spectrometer at 56.4 MHz using $CFCl_3$ as an internal reference, while ^1H nmr spectra were recorded using internal TMS as a standard on a Hitachi R-22 spectrometer at 90 MHz.

IR spectra were measured on a Hitachi EPI-G3 spectrometer using a gas cell equipped with KBr optics and mass spectra on a Shimadzu GC/MS-7000 instrument at 70 eV.

General procedure of the reaction of perfluorocyclic amines with oleum

To illustrate the general procedure of this reaction, the reaction of 1a($R_f=C_2F_5$) will be described.

Reaction of 1a($R_f=C_2F_5$) with oleum

In a Pyrex ampule, a mixture of 1.72 g(5.20 mmol) of 1a($R_f=C_2F_5$), 5.9 g of oleum (30%), and a small amount of $HgSO_4$ was held at 170 °C for 24 hrs.

The product consisted of two layers, an upper transparent clear liquid and a lower oily viscous liquid. The upper layer consisting of fluorocarbons was carefully separated from the lower one using a small separating funnel. Gas chromatographic separation of the upper layer (1.26 g) yielded 1b($R_f=C_2F_5$)(2) (0.92 g) and 1a($R_f=C_2F_5$)(0.34 g). The yield of 2 was 71.5% based on the amine consumed.

Perfluoro(N-ethyl pyrrolidone)(2)(nc) had bp 52.5~53.0 °C n_D^{20}1.2865 and d_4^{20}1.6698. IR (cm^{-1}): 1834 ν(C=O)(s), 1382(m), 1345 (s), 1323 (s), 1275 (vs), 1241 (vs), 1218 (s), 1194 (vs), 1165 (m), 1143 (m), 1074 (s), 1055 (s), 993 (ms), 835 (w), 822 (m), 747 (m), 732 (m), 674 (w), 650 (w), 628 (w), 585 (w), 533 (w). Mass: 311 [M^+](17.5), 292 $[M\text{-}COF]^+$(6.8), 264 $C_5F_{10}N^+$(16.5), 242 $C_5F_8NO^+$(18.4), 164 $C_3F_6N^+$(22.3), 150 $C_3F_6{}^+$(78.6), 131 $C_3F_5{}^+$ (14.9), 119 $C_2F_5{}^+$(68.9), 114 $C_2F_4N^+$(24.3), 100 $C_2F_4{}^+$(100), 92 $C_2F_2NO^+$(7.3). Found: C, 23.00%. Calculated for $C_6F_{11}NO$: C, 23.15%. Its ^{19}F nmr data are given in Table 4.

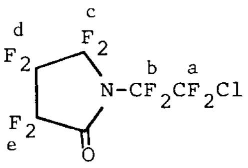
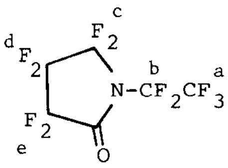
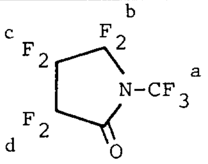
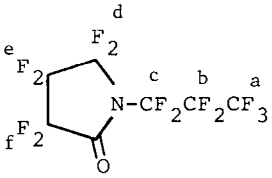
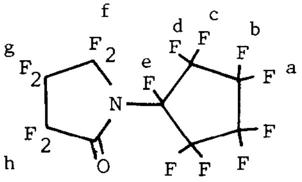
Except 1b($R_f=CF_3$)(3), perfluorolactams (B) synthesized in this work were all new compounds. Physical properties and IR data, and ^{19}F nmr data of these lactams are shown together with those of 1 and 3 in Tables 3 and 4, respectively.

Reaction of 2 with CH_3OH

In a 50 ml flask, 1.55 g(4.98 mmol) of 2, 2 ml of Daiflon S-3 (equivalent to Freon 113) and 0.32 g of CH_3OH were charged and agitated by magnetic stirrer during 3 hrs at room temperature. GLC analysis of the reaction mixture showed that the product

TABLE 4

^{19}F nmr spectra of perfluorolactams

Compd	Formula	Chemical shift[a,b]		J (Hz)[b]
1		a	-70.8	a-c=7.6
		b	-97.5	b-c=12.6
		c	-93.3	c-d=2.8
		d	-135.9	d-e=6.8
		e	-127.7	
2		a	-84.5	a-c=5.0
		b	-101.0	b-c=12.9
		c	-94.9	b-d=2.2
		d	-135.5	b-e=1.4
		e	-127.7	d-e=6.4
3		a	-58.0	a-b=8.5
		b	-96.5	b-d=1.7
		c	-134.6	b-c=2.0
		d	-127.5	c-d=6.5
4		a	-81.8	
		b	-126.3	
		c	-96.9	
		d	-94.8	
		e	-135.7	
		f	-127.8	
5		a	-127.5] J_{AB}	a-b=256
		b	-131.6	c-d=262
		c	-119.1] J_{AB}	e-f=13.3
		d	-127.9	f-h=2.2
		e	-141.5	f-g=2.5
		f	-94.2	g-h=7.4
		g	-135.8	
		h	-127.8	

(Continued)

TABLE 4 (cont.)

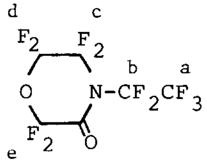
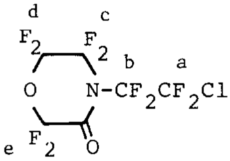
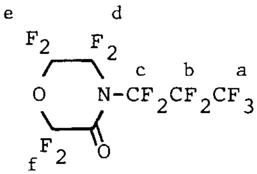
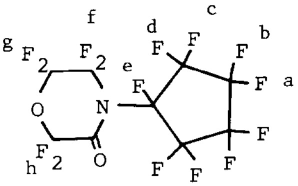
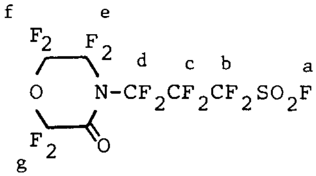
6		a	-82.9		a-c=6.8
		b	-97.3		b-c=17.8
		c	-93.3		d-e=4.8
		d	-90.5		
		e	-72.5		
7		a	-69.0		d-e=4.3
		b	-93.2		
		c	-90.3		
		d	-90.0		
		e	-72.1		
8		a	-81.9		e-f=4.5
		b	-124.2		
		c	-92.9		
		d	-92.9		
		e	-90.3		
		f	-72.4		
9		a	-130.3	J_{AB}	a-b=260
		b	-132.7		c-d=262
		c	-119.4	J_{AB}	g-h=4.2
		d	-123.6		
		e	-140.2		
		f	-92.1		
		g	-90.3		
		h	-73.4		
10		a	46.1		a-c=6.5
		b	-108.8		e-f=4.2
		c	-117.9		f-g=4.8
		d	-92.4		
		e	-91.6		
		f	-90.1		
		g	-72.1		

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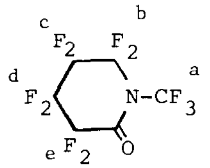
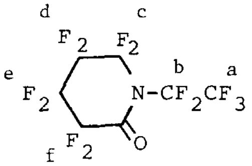
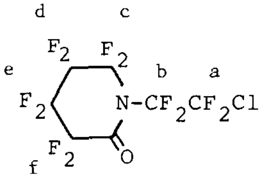
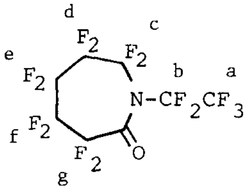
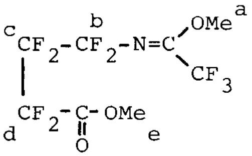
TABLE 4 (cont.)

11		a	-56.2	a-b=13.5
		b	-91.2	
		c	-133.1	
		d	-135.8	
		e	-118.8	
12		a	-81.4	
		b	-95.1	
		c	-89.2	
		d	-132.9	
		e	-135.0	
		f	-117.7	
13		a	-67.8	a-c=8.7
		b	-91.3	b-c=22.3
		c	-88.8	c-f=9.6
		d	-132.7	d-f=9.6
		e	-134.9	
		f	-117.5	
14		a	-81.0	a-c=9.9
		b	-93.5	b-c=24.6
		c	-88.6	
		d	-127.5	
		e	-130.2	
		f	-128.7	
		g	-113.7	

[a] ^{19}F chemical shifts in ppm relative to internal CCl_3F (negative shifts are upfield).

[b] Only obvious chemical shifts and coupling constants are given.

consisted of three components, of which one was major (85.3%). The main product was isolated by semi-preparative GLC giving 0.24 g of clear liquid. This compound was determined to be 2-methoxy-6-methoxycarbonyl-nonafluoro-3-azahexene-2 by spectroscopic evidence: IR (capillary film) (cm^{-1}): 1785 ν(C=O) (s), 1700 ν(N=C) (s). Mass: 335 M^+(1.0), 316 $[M-F]^+$(23.8), 305 $[M-OCH_2]^+$(9.8), 304 $[M-OCH_3]^+$(8.0), 276 $[M-CO_2CH_3]^+$(6.9), 266 $[M-CF_3]^+$(37.1), 176 $C_4F_6N^+$(100), 142 $C_2F_4NCO^+$(40.5), 119 $C_2F_5^+$ (36.8), 100 $C_2F_4^+$(24.5), 92 CF_2NCO^+(35.8), 81 $C_2F_2OH_3^+$ (31.4), 69 CF_3^+(27.5), 59 $CO_2CH_3^+$(75.1).



^1H nmr: $\delta(CH_3^a)$ 3.96, $\delta(CH_3^e)$ 3.92.
^{19}F nmr: $\phi(CF_3)$ -44.1, $\phi(CF_2^b)$ -92.5, $\phi(CF_2^c)$ -119.4, $\phi(CF_2^d)$ -115.0 $[J(CF_2^b-CF_2^d)=23.1$ Hz].

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