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Preparation and reactions of 2,4,6-tris(trifluoromethyl)phenylamine

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Abstract

Starting from R_fH (**1**) [R_f = 1,3,5-tris(trifluoromethyl)phenyl] R_fNH_2 (**6**) is obtained in a four-step synthesis. The amine **6** reacts with chlorotrimethylsilane in the presence of DBU (1,8-diazabicyclo(5,4,0)undec-7-ene) forming the monosilylated and the bissilylated amines **7** and **8**. The potassium salt of **7** reacts with $SiCl_4$ yielding $R_fN(SiCl_3)_2$ (**10**). The single crystal X-ray structure of **10** is reported. © 1998 Elsevier Science S.A.

Keywords: Aromatic fluorides; Fluorinated amines; Silicon derivatives

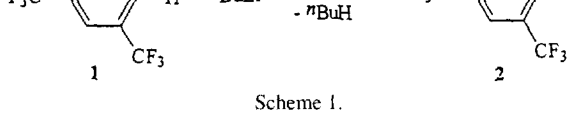
1. Introduction

We recently reported the synthesis and structural characterisation of a wide variety of R_f [R_f = 2,4,6-tris(trifluoromethyl)phenyl] substituted metal and non-metal compounds [1–7]. It has been shown that in many of these systems, the 2,4,6-tris(trifluoromethyl)phenyl substituent plays an important role in stabilizing unusual coordination numbers in compounds such as $R_fP = PR_f$. Herein, we describe a facile synthesis for the preparation of R_fNH_2 (**6**). The known published method started from 2,4,6-trimethylbenzoic acid and its oxidation by potassium permanganate to form the corresponding $C_6H_2(COOH)_4$ [8,9]. The acid is recrystallised from hot concentrated nitric acid to obtain an anhydrous product. Treatment of $C_6H_2(COOH)_4$ with SF_4 resulted in the formation of R_fCOF. Finally, the corresponding amide R_fCONH_2 (**5**) reacts under a Hofmann rearrangement yielding R_fNH_2 (**6**). The new synthetic route to **6** starts from R_fH and uses standard organic reactions.

2. Results and discussion

In contrast to the known procedure [2,10] for the preparation of LiR_f (**2**) starting from R_fH (**1**), the reaction is conducted at −5°C using a 1.5-fold excess of ^nBuLi. Under these conditions, a yellow reaction mixture is obtained rather than a brown solution. The complete conversion of **1** to **2** is followed by ^{19}F NMR and moreover, the addition of ^nBuLi to the solution has to be fast. (Scheme 1). Immediately after the addition of ^nBuLi is complete, a stream of gaseous carbon dioxide is bubbled into the solution of R_fLi. After 2 h, the addition of CO_2 is stopped and the resulting R_fCOOLi is hydrolysed using 6 M hydrochloric acid, followed by usual work-up procedures and isolation of R_fCOOH (**3**). Compound **3** is a colourless crystalline substance. Its ^1H NMR spectrum shows a singlet of the aromatic protons (8.17 ppm) and a broad signal at 4.94 ppm (carboxylate proton). The shift and the intensity of a second signal make it plausible that additional water is bound to the carboxylate group of **3**. Two singlets are observed in the ^{19}F NMR spectrum (−59.9 and −63.5 ppm) for the *o*-CF_3 and *p*-CF_3 groups respectively. (Scheme 2).

Previous studies in our laboratory used $SOCl_2$ for converting R_fCOOH (**3**) to R_fCOCl (**4**). However, the yield of compound **4** is rather poor (38%) [10]. If PCl_5 is used as a chlorinating agent, compound **4** is isolated in nearly quantitative yield. For this reaction, it is necessary to use an excess of PCl_5 due to the small amount of water in **3**. (Scheme 3).



Scheme 1.

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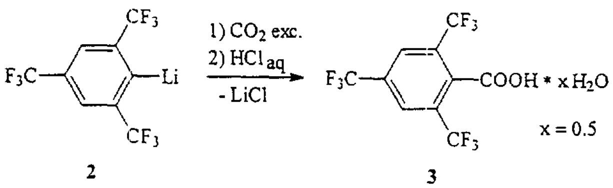
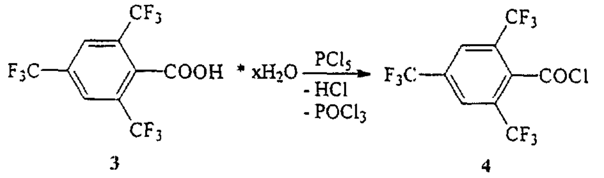
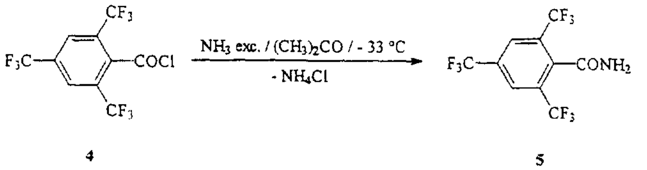


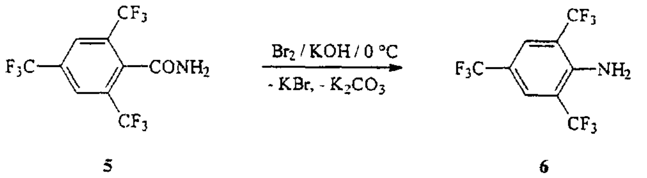
Scheme 2.



Scheme 3.



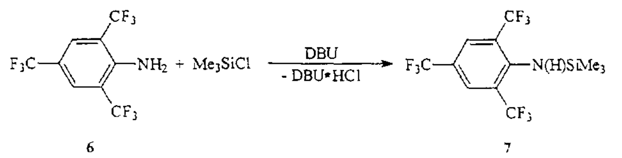
Scheme 4.



Scheme 5.

After the HCl evolution has ceased, all volatiles are removed in vacuo. Compound **4** is separated by distillation from unreacted PCl_5. The resulting liquid crystallises on standing. The ^1H NMR spectrum exhibits only one signal (8.21 ppm, aromatic protons). The ^{19}F NMR spectrum shows two singlets (−59.1 ppm and −64.3 ppm) for the *o*-CF_3 and *p*-CF_3 groups respectively.

The literature method uses aqueous ammonia for preparing R_fCONH_2 (**5**) from R_fCOCl (**4**). The reaction is carried out in a stainless steel cylinder at 150°C. However, the product forms a stone-like block at the bottom of the cylinder and it is not easy to remove this from the cylinder. (Scheme 4). We used instead liquid ammonia and added acetone as solvent to prepare compound **5**. In a glass apparatus equipped with a dry ice reflux condenser, compound **4** is reacted at −33°C. After filtration and removing the solvent in vacuo, colourless R_fCONH_2 (**5**) is obtained without further purification. In the ^1H NMR spectrum, the R_f protons are observed at 8.18 ppm, while the NH protons resonate at 6.05 and 5.82 ppm due to the hindered rotation. The ^{19}F NMR spectrum shows two singlets (−59.7 (*o*-CF_3) and −63.8 ppm (*p*-CF_3)). According to the literature method [8], compound **5** is converted to **6**. Pure **6** was obtained after steam distillation and recrystallisation from hot hexane. (Scheme 5) Finally, **6** is sublimed over CaO to remove traces of moisture. The ^1H NMR spectrum exhibits a singlet of the aromatic protons (7.84 ppm) and a broad signal (5.04 ppm) of the NH protons. The ^{19}F NMR spectrum exhibits two singlets (−62.7 and −64.3 ppm fluorine *o*-CF_3 and *p*-CF_3, respectively).



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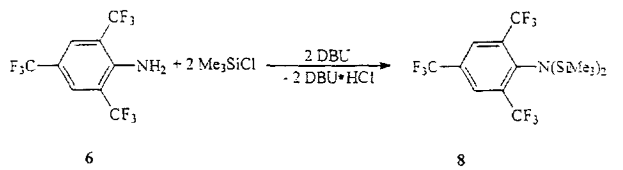
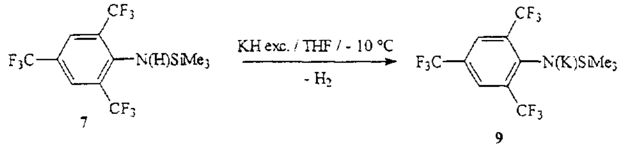
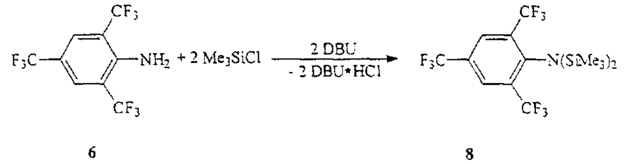


Scheme 7.



Scheme 8.



Scheme 9.

The monolithium salt of compound **6** is not suitable for the synthesis of $R_fN(H)SiMe_3$ (**7**) [11]. However, compound **6** reacts in the presence of 1,8-diazabicyclo(5,4,0)undec-7-ene with one equivalent of Me_3SiCl to yield compound **7**. (Scheme 6). The ^1H NMR spectrum of **7** exhibits singlets at 7.96 ppm (R_f protons), 3.78 ppm (NH proton) and 0.20 ppm ($SiMe_3$ protons), respectively. The ^{19}F NMR spectrum shows singlets at −61.9 ppm (*o*-CF_3) and −63.5 ppm (*p*-CF_3). In the ^{29}Si NMR spectrum, the signal of the $SiMe_3$ group is observed at 13.5 ppm. The synthesis of $R_fN(SiMe_3)_2$ (**8**) is analogous to that of the monosilylated amine **7**. (Scheme 7). Sublimation of the crude product yields colourless **8**. In contrast to **7**, compound **8** is stable towards moisture and air. The ^1H NMR spectrum exhibits a singlet (7.95 ppm) of the aromatic protons and a septet (0.07 ppm $^7J(H,F)$ = 0.07 Hz) of the $SiMe_3$ protons. In the ^{19}F NMR spectrum, two singlets are obtained (−57.7 and −62.8 ppm for *o*-CF_3 and *p*-CF_3). The ^{29}Si NMR spectrum displays the signal of both silicon atoms at 10.5 ppm.

The reaction of $R_fNH(SiMe_3)$ (**7**) with KH results in the thermally unstable $R_fNK(SiMe_3)$ (**9**). (Scheme 8). Conversion of the potassium salt **9** using $SiCl_4$ does not form $R_fN(SiMe_3)(SiCl_3)$ [12,13]. Independently of the molar ratio of the starting materials, compound $R_fN(SiCl_3)_2$ (**10**) is formed. The colourless product **10** is recovered from the reaction mixture. (Scheme 9).

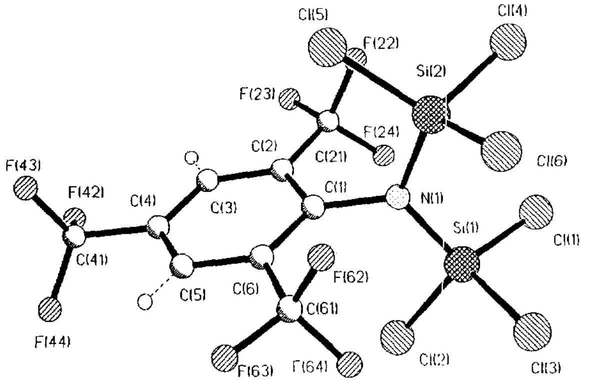


Fig. 1. Molecular structure of **10**; selected bond distances [pm] and angles [°]: N(1)–Si(1) 174.1(3), N(1)–Si(2) 173.9(3), N(1)–C(1) 146.1(4), Si(1)–Cl(1) 200.5(2), Si(1)–Cl(2) 201.19(14), Si(1)–Cl(3) 200.58(14), Si(2)–Cl(4) 201.1(2), Si(2)–Cl(5) 200.58(14), Si(2)–Cl(6) 201.69(14); C(1)–N(1)–Si(1) 118.0(2), C(1)–N(1)–Si(2) 118.3(2), Si(1)–N(1)–Si(2) 123.7(2), N(1)–Si(1)–Cl(1) 113.28(11), N(1)–Si(1)–Cl(2) 108.01(10), N(1)–Si(1)–Cl(3) 111.79(10), N(1)–Si(2)–Cl(4) 111.81(11), N(1)–Si(2)–Cl(5) 108.47(11), N(1)–Si(2)–Cl(6) 108.90(7), Cl(1)–Si(1)–Cl(2) 109.11(7), Cl(1)–Si(1)–Cl(3) 105.25(7), Cl(1)–Si(1)–Cl(2) 109.11(7), Cl(2)–Si(1)–Cl(3) 109.33(7), Cl(1)–Si(1)–Cl(2) 109.11(7), Cl(4)–Si(2)–Cl(5) 110.53(7), Cl(4)–Si(1)–Cl(6) 104.90(7), Cl(5)–Si(1)–Cl(6) 109.90(7).

In the ^{1}H NMR spectrum, the signal of the R$_f$ protons appear at 8.21 ppm. The ^{19}F NMR spectrum exhibits two singlets (-61.2 ppm (o-CF$_3$) and -62.9 ppm (p-CF$_3$)). In the ^{29}Si NMR spectrum, both silicon atoms resonate as a singlet (13.4 ppm). Crystals of **10** suitable for an X-ray structural analysis are obtained by slow cooling of a hot saturated hexane solution. Compound **10** crystallises in a monoclinic system [14–17]. Selected bond lengths, angles and numbering scheme for **10** are given in the caption of Fig. 1. The observed differences of the N–Si bond lengths are within the experimental errors [174.2(3) pm (N(1)–Si(1)) and 173.9(3) pm (N(1)–Si(2))]. The N–Si bond lengths are compared with a trichlorosilane [$\{(Me_2CH)_2N\}_2SiFN(SiCl_3)C_6H_2Me_3$] structurally characterised by Schütte et al. [18] (N–Si 169.8(4) ppm). The Si–Cl bond distances are in the range from 200.5(2) (Si(1)–Cl(1) to 201.69(14) pm (Si(2)–Cl(6)). In the cited compound, the average Si–Cl bond length is 202.6 pm. The geometry at the nitrogen atom is trigonal planar, the angles around it add to 360°. The angles at both Si atoms vary between 104.90(7)° (Cl(4)–Si(2)–Cl(6)) and 113.28(11)° (Cl(1)–Si(1)–Cl(1)). The differences from the ideal tetrahedral angle are possibly the result of packing effects in the solid state. The crystals were measured at 213 K, however, the CF$_3$ groups at this temperature are still rotational disordered.

3. Conclusion

In summary, it has been shown that the 2,4,6-tris(trifluoromethyl)phenylamine is easily accessible and a valuable starting material for preparing interesting new compounds.

4. Experimental details

Reactions were performed and worked up using standard Schlenk techniques, and products were handled under dry oxygen-free nitrogen. Solvents were dried, distilled and stored using standard procedures. Infrared spectra were obtained using a Bio-Rad FTS7 spectrometer, NMR spectra on Bruker AM 250, WP 80SY and MSL 400 spectrometers (standards ^{1}H NMR: TMS, ^{19}F NMR: CFCl$_3$, ^{29}Si NMR: TMS) and mass spectra on Finnigan MAT 8230, MAT 95 and Varian CH 5 spectrometers. Microanalyses were performed by the analytical laboratories of the University of Göttingen. The spectroscopic data of the known compounds **3**–**5** are listed for comparison reasons.

4.1. Preparation of LiR$_f$ (2) and R$_f$COOH (3)

A solution of ^{n}BuLi (225 ml, 532 mmol, 2.36 M in hexane) is added as fast as possible to a solution of R$_f$H (**1**), 100 g dissolved in ether (100 ml). The temperature of the reaction mixture should not exceed -5°C. The end-point of the reaction is determined by ^{19}F NMR spectroscopy. Then CO$_2$ is bubbled through the reaction mixture for 2 h. The resulting slurry is quenched using 6 M HCl (100 ml) and extracted with ether. The extract is dried over Na$_2$SO$_4$. All volatiles are removed in vacuo. The residue is suspended in hexane, filtered off and washed with the same solvent to yield 86.7 g (75%) of colourless **3**. Mp. 182°C. ^{1}H NMR (250 MHz, CDCl$_3$): δ 8.17 (s, 2 H, H$_{aryl}$), 4.94 (s, br, 2 H, COOH $*$ 0.5 H$_2$O) ppm. ^{19}F NMR (188 MHz, CDCl$_3$): δ -59.9 (s, 6 F, o-CF$_3$), -63.5 (s, 3 F, p-CF$_3$) ppm. IR (Nujol): ν 3113 st, br (OH $*$ 0.5 H$_2$O), 1731 sst, 1280 sst, 1157 sst, 915 st cm^{-1}.

4.2. Preparation of R$_f$COCl (4)

An ice-cold mixture of R$_f$COOH (**3**) (50 g, 153 mmol) and PCl$_5$ (40 g) is suspended in CCl$_4$ (30 ml). After the HCl evolution has ceased, the reaction is refluxed for 1 h. The volatiles are removed in vacuo. The crude product is distilled in vacuo to yield 45 g (85%) **4**. Mp. 35°C. ^{1}H NMR (200 MHz, CDCl$_3$): δ 8.21 (s, H$_{aryl}$) ppm. ^{19}F NMR (188 MHz, CDCl$_3$): δ -59.1 (s, 6 F, o-CF$_3$), -64.3 (s, 3 F, p-CF$_3$) ppm.

4.3. Preparation of R$_f$CONH$_2$ (5)

At -196°C NH$_3$ (20 g 1.2 mol) is condensed into a solution of **4** (40 g, 116 mmol) in acetone (50 ml). The reaction mixture is allowed to warm to -33°C and finally refluxed for 12 h. Afterwards, the excess of NH$_3$ is removed. The resulting slurry is filtered. Removing the solvent in vacuo yielded 34 g (90%) of colourless **5**. Mp. 205°C. ^{1}H NMR (200 MHz, CDCl$_3$): δ 8.18 (s, 2 H, H$_{aryl}$), 6.05 (s, br, 1 H, NH), 5.82 (s, br, 1 H, NH) ppm. ^{19}F NMR (188 MHz, CDCl$_3$): δ -59.7 (s, 6 F, o-CF$_3$), -63.8 (s, 3 F, p-CF$_3$) ppm.

4.4. Preparation of R_fNH_2 (**6**)

A solution of KOBr is prepared at 0°C using KOH (34.4 g, 614 mmol), Br_2 (20.5 g) and water (300 ml). Compound **5** (32.5 g, 100 mmol) is added over a period of 2 h. The reaction mixture is stirred for 12 h. The resulting R_fNH_2 (**6**) is separated by steam distillation and extraction with ether. The organic layer is dried over Na_2SO_4. The solvent is distilled off in vacuo and the residue recrystallised from hexane (20 ml). Compound **6** is sublimed over CaO (bath temperature 40°C, $1 * 10^{-1}$ bar) to remove traces of moisture. Yield: 22.2 g (75%). Mp. 58°C. ^1H NMR (250 MHz, $CDCl_3$): δ 7.84 (s, 2 H, H_{aryl}), 5.04 (s, br, 2 H, NH) ppm. ^{19}F NMR (235 MHz, $CDCl_3$): δ −62.7 (s, 3 F, p-CF_3), −64.3 (s, 6 F, o-CF_3) ppm. IR (Nujol): ν 3556 m (NH), 3462 m (NH), 1651 st, 1375 sst, 1261 sst, 1177 st, 917 sst, 668 st cm^{-1}. MS (EI, m/z (%)): 297 (M, 100), 277 ($C_9H_3F_8N$, 50), 257 ($C_9H_2F_7N$, 40).

4.5. Synthesis of $R_fN(H)SiMe_3$ (**7**)

To a solution of **6** (10 g, 33.7 mmol) and Me_3SiCl (3.7 g, 33.7 mmol), hexane (50 ml) is added dropwise DBU (5.1 g, 33.7 mmol) at 0°C. The reaction mixture is stirred for 3 h. The DBU * HCl is filtered off and the filtrate concentrated to dryness in vacuo. The crude product is distilled using a 10 cm Vigreux column. The colourless liquid **7** is obtained between 36–39°C (5×10^{-6} bar) in 78% yield (9.6 g). ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 2 H, H_{aryl}), 3.78 (s, br, 1 H, NH), 0.20 (s, 9 H, $Si(CH_3)_3$) ppm. ^{19}F NMR(376 MHz, $CDCl_3$): δ −61.9 (s, 6 F, o-CF_3), −63.5 (s, 3 F, p-CF_3) ppm. ^{29}Si NMR (79 MHz, $CDCl_3$): δ 13.5 (s, $SiMe_3$) ppm. IR (Film): ν 3335 m (NH), 3104 s, 1633 sst, 1273 sst, 1135 sst, 917 st, 696 st cm^{-1}. MS (EI, m/z (%)): 369 (M, 10), 354 (M–Me, 50), 258 ($C_9H_3F_7N$, 100). Analysis: Calc. for $C_{12}H_{12}F_9NSi$ (M = 369.32 g/mol): C, 39.03; H, 3.27; N, 3.79; F, 46.31%. Found: C, 38.5; H, 2.9; N, 3.9; F, 46.1%.

4.6. Preparation of $R_fN(SiMe_3)_2$ (**8**)

R_fNH_2 (**6**) (10.0 g, 33.7 mmol) and Me_3SiCl (7.4 g, 67.4 mmol) are dissolved in hexane (50 ml). At 0°C, DBU (10.2 g, 67.4 mmol) is added dropwise. After stirring for 3 h, the DBU * HCl is filtered off and the filtrate evaporated to dryness. The residue is sublimed in vacuo to give 12.2 g (82%) **8**. Mp. 67°C. ^1H NMR (250 MHz, C_6D_6): δ 7.95 (s, 2 H, H_{aryl}), 0.07 (sept, 18 H, $^7J(H,F) = 0.7$ Hz, $Si(CH_3)_3$) ppm. ^{19}F NMR (235 MHz, C_6D_6): δ −57.7 (s, 6 F, o-CF_3), −62.8 (s, 3 F, p-CF_3) ppm. ^{29}Si NMR (49 MHz, C_6D_6): δ 10.5 (s, $SiMe_3$) ppm. IR (Nujol): ν 3106 s, 1629 sst, 1296 sst, 1237 sst, 1143 sst, 919 st, 697 st cm^{-1}. MS (EI, m/z (%)): 441 (M, 10), 426 (M–Me, 20), 334 (M–Me_3SiF–Me, 100). Analysis: Calc. for $C_{15}H_{20}F_9NSi_2$ (M = 441.50 g/mol): C, 40.81; H, 4.57; N, 3.17; Si, 12.68%. Found: C, 40.4; H, 4.6; N, 3.5; Si, 12.7%.

4.7. Synthesis of $R_fN(K)SiMe_3$ (**9**) and $R_fN(SiCl_3)_2$ (**10**)

To a slurry of KH (0.43 g, 10.8 mmol) in THF (10 ml) is added dropwise a solution of **8** 2.00 g in THF (10 ml) at −10°C. The colourless mixture turned to yellow. After the addition is complete, the mixture is stirred for 1 h at the same temperature. The excess of KH is removed by filtration and finally, the filtrate is added to a solution of $SiCl_4$ (1.83 g, 10.8 mmol) in THF (10 ml). The reaction is completed by stirring the mixture for an additional hour. Volatiles are removed in vacuo. The residue is treated with refluxing hexane (15 ml), filtered and washed a few times with the same solvent. The solution is allowed to cool to room temperature to yield 2.28 g (75%) of colourless **10**. Mp. 108°C. ^1H NMR (200 MHz, $CDCl_3$): δ 8.21 (s, H_{aryl}) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −61.2 (s, 6 F, o-CF_3), −62.9 (s, 3 F, p-CF_3) ppm. ^{29}Si NMR (79 MHz, $CDCl_3$): δ 13.4 (s, $SiCl_3$) ppm. IR (Nujol): ν 3107 s, 1631 st, 1277 sst, 1155 sst, 933 st, 842 st cm^{-1}. MS (EI, m/z (%)): 563 (M, 100), 528 (M–Cl, 40), 133 ($SiCl_3$, 80). Analysis: Calc. for $C_9H_2Cl_6F_9NSi_2$ (M = 564.00 g/mol): C, 19.17; H, 0.36; N, 2.48; F, 30.32; Cl, 37.72%. Found: C, 20.0; H, 0.6; N, 2.6; F, 30.0; Cl, 37.2%.

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