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Syntheses and Properties of Novel Liquid Crystals Containing a Trifluoromethylamino Group

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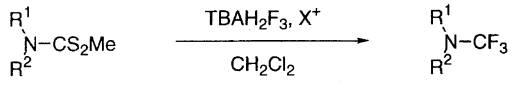
Liquid crystals (LCs) containing a trifluoromethylamino group are prepared by the cross-coupling reaction of *p*-bromo-substituted-(hetero)aryl(trifluoromethyl)amines that are derived from the corresponding dithiocarbamates through oxidative desulfurization–fluorination. The novel LCs are shown to exhibit mainly a smectic phase over a wide range of temperatures. Their electro-optical properties as a component of nematic LCs are compared with those of the corresponding methylamines.

Liquid crystals (LCs) having a fluorine-functional group show high polarity, high thermal and chemical stability, and low viscosity because of the most electronegative fluorine atom and the strong C–F bond.[1] Accordingly, various types of fluorinated LCs have been synthesized,[2] and their phase transition behaviors and electro-optical properties as an additive for LC materials have been shown to be superior to those of the corresponding cyano-substituted ones that are employed widely for twisted nematic displays at present.[3] Such fluorinated compounds are synthesized, in general, using highly toxic reagents such as hydrogen fluoride, metal fluorides, and/or elemental fluorine gas under harsh conditions.[4] Because of the operational difficulties in the syntheses, exploitation of novel fluorinated LCs has been hampered. To assist the development of LC materials, mild, efficient, and selective novel methods have been needed for the fluorination of organic substrates.

We have recently found that *the oxidative desulfurization–fluorination reaction* using an *N*-haloimide and a fluoride source is a convenient fluorination method.[5] This reaction allows us to replace C–S bonds with C–F bonds under extremely mild conditions. For example, when the reaction is applied to methyl dithiocarbamates $R^1R^2NC(S)SMe$, trifluoromethylamines $R^1R^2NCF_3$ are readily prepared in high yields.[6]

The Oxidative Desulfurization-Fluorination of Dithiocarbamates



(1)

All of the preparative methods for trifluoromethylamines reported[7] so far involve the use of highly toxic and corrosive reagents under harsh conditions, and desired products are isolated usually in low yields. The inaccessibility has hampered the systematic studies on trifluoromethylamines, in spite of their unique properties such as resistance against oxidation,[6e] low basicity and nucleophilicity[8] as compared with the corresponding methylamines. Thus, trifluoromethylamines are expected to show low viscosity, and high thermal and chemical stabilities, properties essential for LC materials. Herein we report experimental details of the syntheses, phase transition behaviors, and electro-optical properties of unprecedented LCs containing a trifluoromethylamino group.[6d]

Results and Discussion

Synthesis of Trifluoromethylamino-Substituted LCs with a Heterobiaryl Core. The oxidative desulfurization–fluorination of methyl *N*-methyl-*N*-2-pyridinyldithiocarbamate easily gives 5-bromo-2-[methyl(trifluoromethyl)amino]pyridine (**1**).[6c] We first treated **1** with butyllithium (*n*-BuLi) and then with zinc chloride ($ZnCl_2$)·tetramethylethylenediamine complex ($ZnCl_2$·TMEDA) to give a zinc reagent, which was reacted with 1-halo-4-methoxybenzene in the presence of a [$Pd(PPh_3)_4$] catalyst. Contrary to our expectation, the desired cross-coupled heterobiaryl **5** was not obtained in high yield, due probably to the instability of the zinc reagent (see Experimental).

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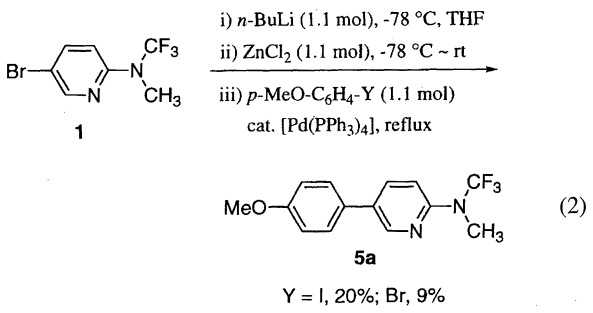
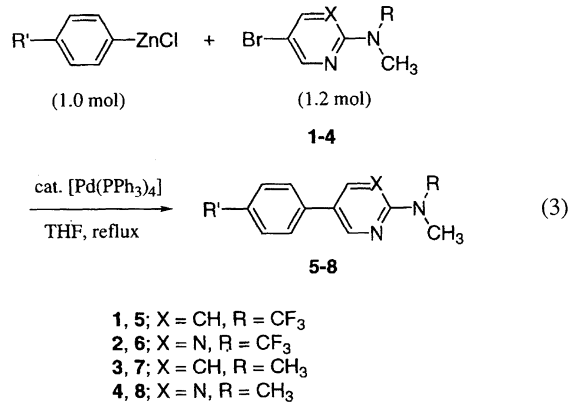
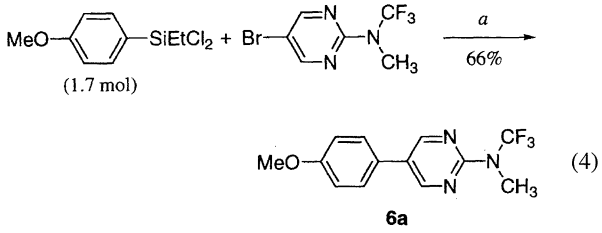


We next examined the reaction of **1** with a 4-alkyl(oxy)-substituted arylzinc reagent prepared in the manner described above from 1-alkoxy-4-bromobenzene. Yields and phase transition temperatures of the resulting heterobiaryls are summarized in Table 1. As one readily sees, 5-(4-alkyloxyphenyl)-2-[methyl(trifluoromethyl)amino]pyridines **5** and -pyrimidines **6** were obtained in moderate yields. In a similar way, corresponding 2-dimethylamino derivatives **7** and **8** were also prepared, but in lower yields (Entries 5, 6, 12, and 13). When a Grignard reagent was used in lieu of the zinc reagent, only a trace amount of the desired heterobiaryl was obtained. Furthermore, a zinc reagent generated from $ZnCl_2$·TMEDA was more effective than that from $ZnCl_2$·Et_2O (compare Entry 2 with 4). The coupling reaction was not applicable to the synthesis of 4-[alkyl(trifluoromethyl)amino]-4′-alkyloxybiphenyls, because these were easily hydrolyzed upon exposure to moisture.



Phase transition temperatures and textures of trifluoromethylamines **5** and **6** as well as the corresponding methylamines **7** and **8** are listed in Table 1. Methyl(trifluoromethyl)amino-substituted pyridines **5** exhibited smectic A (S_A) phase, whereas 2-(dimethylamino)pyridines **7** lost the LC phase. Thus, a trifluoromethylamino group appears to promote liquid crystallinity. This is the first example of LC compounds containing a trifluoromethylamino moiety.[6c,6d] The corresponding pyrimidines **6** and **8** showed melting points only. In addition, melting points of pyridines **5** and pyrimidines **7** turned out to be lower than those of **6** and **8**, respectively (compare Entries 6 with 9; 10 with 13).

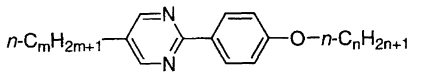
The cross-coupling reaction of dichloro(ethyl)(4-methoxyphenyl)silane[9] with **3** using a $Pd(OAc)_2$ catalyst, tri(*o*-tolyl)-phosphine, and KF in excess gave rise to heterobiaryl **6a** in 66% yield. This procedure was also effective for the preparation of trifluoromethylamino-substituted LCs.



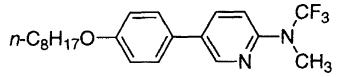
a: i) KF (9 mol), DMF, 60 °C, 3 h,
ii) $Pd(OAc)_2$ (8 mol%), P(*o*-Tol)$_3$ (8 mol%), DMF, 120 °C, 18 h

Trifluoromethylamino-Substituted Heterobiaryls as a Dopant for Ferroelectric LCs. Ferroelectric LCs having an (*S*)-2-octylamino group show chiral smectic C (Sc^*) phase in a range of temperatures wider than those with an (*S*)-2-octyloxy group.[10] Chiral *N*-alkyl-*N*-methylamino-substituted LCs are reported to possess relatively low viscosity values and an Sc^* phase over a wide temperature range.[11] Although these properties are favorable as a switching element for surface stabilizing ferroelectric LC displays, the basicity and low oxidation potential of an amino group hampered their applications. In contrast, the low basicity and high oxidation potential of trifluoromethylamines apparently allow such applications. We thus prepared a host LC mixture containing trifluoromethylamine component **5d** (phase transition temperature of this mixture: rt Sc 44 S_A 68.5 N 69.5 Iso, see Fig. 1) and then mixed in 2 wt% chiral dopant **9** (Chart 1)[12] as illustrated in Fig. 2. The resulting mixture showed a phase transition of rt Sc^* 48 S_A 67 N 69 Iso. Response time (τ_{0-90}) of the mixture in a LC cell (2 μm thin) was 78 μs at 25 °C, whereas τ_{0-90} of a mixture lacking **5d** was 83 μs, indicating that **5d** improved both the range of the Sc^* phase and the response speed.

To estimate the thermal and chemical stability of trifluoromethylamino-substituted LC **5c**, we prepared an LC mixture consisting of **5c** (5 wt%) and 8 other LC compounds. The phase transition temperatures and color of the mixture did not



m = 7, n = 9: 28.5 wt%; m = 8, n = 10: 28.5 wt%
m = 8, n = 8: 19.0 wt%; m = 9, n = 9: 19.0 wt%



5d 5.0 wt%

host mixture: Sc 44 S_A 68.5 N 69.5 Iso

Fig. 1. A host LC mixture containing **5d**.

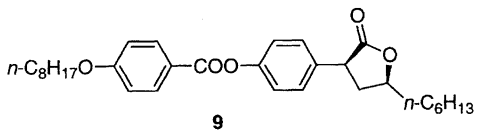


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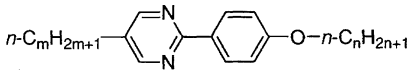
Chart 1.

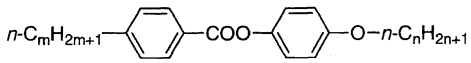
Table 1. Synthesis of Trifluoromethylamino-Substituted Heterobiaryls.[a,b]

Entry	R′	X	R	Heterobiaryl	Yield/%[c]	Phase transition temperature/°C[d]
1	CH_3O	CH	CF_3	**5a**	20	Cr 69 Iso (Iso 53 Cr)
2	n-C_3H_7O	CH	CF_3	**5b**	58 (29)[e]	Cr 66 S_A 93 Iso (Iso 92 S_A 62 Cr)
3	n-$C_6H_{13}O$	CH	CF_3	**5c**	67	Cr 53 S_A 70 Iso (Iso 69 S_A 42 Cr)
4	n-$C_8H_{17}O$	CH	CF_3	**5d**	20[e]	Cr 51 S_A 62 Iso (Iso 60 S_A 36 Cr)
5	n-C_3H_7O	CH	CH_3	**7b**	39	Cr 128 Iso (Iso 116 Cr)
6	n-$C_6H_{13}O$	CH	CH_3	**7c**	35	Cr 104 Iso (Iso 96 Cr)
7	n-C_3H_7	CH	CF_3	**5e**	62	Cr 54 S_A 65 Iso[f]
8	CH_3O	N	CF_3	**6a**	71	Cr 101 Iso (Iso 52 Cr)
9	n-C_3H_7O	N	CF_3	**6b**	45	Cr 94 Iso (Iso 83 Cr)
10	n-$C_6H_{13}O$	N	CF_3	**6c**	38	Cr 84 Iso (Iso 60 Cr)
11	n-$C_8H_{17}O$	N	CF_3	**6d**	88	Cr 84 Iso (Iso 62 Cr)
12	n-C_3H_7O	N	CH_3	**8b**	48	Cr 106 Iso (Iso 95 Cr)
13	n-$C_6H_{13}O$	N	CH_3	**8c**	37	Cr 96 Iso (Iso 93 Cr)

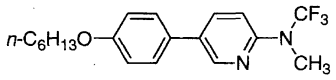
a) All the reaction was performed with an organozinc reagent (1.0 mol) and an amine (1.2 mol) in the presence of $[Pd(PPh_3)_4]$ (1.8 mol%) in THF at a reflux temperature. b) Respective organozinc reagent was prepared from 1-alkyloxy-4-halobenzene by lithiation with n-BuLi and transmetallation with $ZnCl_2$·TMEDA. c) Isolated yields are given. d) Measured by DSC on second heating. Values in parentheses were measured by DSC on first cooling. Cr: Crystal. Iso: Isotropic liquid. S_A: Smectic A phase. e) $ZnCl_2$·Et_2O was used. f) Determined by optical polarization microscopy.



m = 7, n = 9: 2.9 wt%; m = 8, n = 9: 25.6 wt%
m = 8, n = 6: 5.7 wt%; m = 8, n = 10: 22.8 wt%



m = 8, n = 8: 9.5 wt%; m = 9, n = 6: 9.5 wt%
m = 8, n = 10: 9.5 wt%; m = 10, n = 8: 9.5 wt%



5c: 5.0 wt%

LC mixture: Sc 46 S_A 61 N 69.5 Iso

Fig. 2. An LC mixture containing **5c** for stability test.

change at all after heating at 100 °C for 50 h. Thus the trifluoromethylamino-substituted LC compounds are demonstrated to be thermally stable. When the mixture shown in Fig. 2 was kept at −20 °C for a week, no crystallization nor phase separation was detected. Thus, the miscibility of trifluoromethylamino-substituted LCs seems satisfactory.

Trifluoromethylamino-Substituted LCs with a 4-Cyclohexylcyclohexenylarene Core. We next planned the synthesis of 1-trifluoromethylamino-4-[4-(*trans*-4-substituted cyclohexyl)cyclohexen-1-yl]arenes, starting with 4-bromo-*N*-trifluoromethylaniline **10**, **11**, or **1**. Lithiation of **10**, **11**, or **1** with n-BuLi, followed by treatment with 4-(*trans*-4-propylcyclohexyl)cyclohexanone, gave tertiary cyclohexanols, which were converted into cyclohexene derivatives **12**, **13**, or **14** in hot benzene in the presence of an acid catalyst. Total yields and phase transition temperatures are summarized in Table 2. The yields turned out to be relatively low, probably because hydrolysis of a trifluoromethylamino group took place under the dehydration conditions. Indeed, a product tentatively assigned as fluoroformamide **15** (Chart 2) was detected in the synthesis of **12a** (Table 2, Entry 1, see Experimental). Compounds **12**, **13**, and **14** exhibited a smectic phase. In particular, cyclohexenylbenzene derivative **12** and its fluoro derivative **13** exhibited a smectic B (S_B), and cyclohexenylpyridine **14** showed an S_A phase over a wide range of temperatures. As readily seen in Table 2, either the fluorine

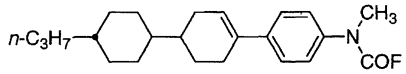


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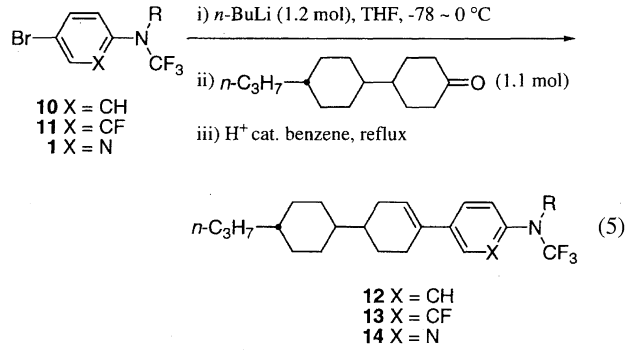
Chart 2.

Table 2. The Yield and Phase Transition Temperatures of Compounds **12**, **13**, or **14**

Entry	X	R	H^+	Product	Yield/%	Phase transition temperature/°C	
						DSC (heating)	DSC (cooling)
1	CH	Me	PPTS	**12a**	10	Cr 24 S_B 158 Iso	Cr -23 S_B 155 Iso
2	CH	Et	MS 4A	**12b**	15	Cr 25 S_B 110 Iso	Cr -47 S_B 110 Iso
3	CF	Me	p-TsOH	**13a**	28	<23 S_B 70 Iso[a]	
4	CF	Et	p-TsOH/MS 4A	**13b**	9	<23 S_B 37 Iso[a]	
5	N	Me	p-TsOH	**14a**	49	Cr 82 S_A 139 Iso	Cr 64 S_A 138 Iso
6	N	Et	p-TsOH/MS 4A	**14b**	25	Cr 78 S_A 98 Iso	Cr 61 S_A 98 Iso

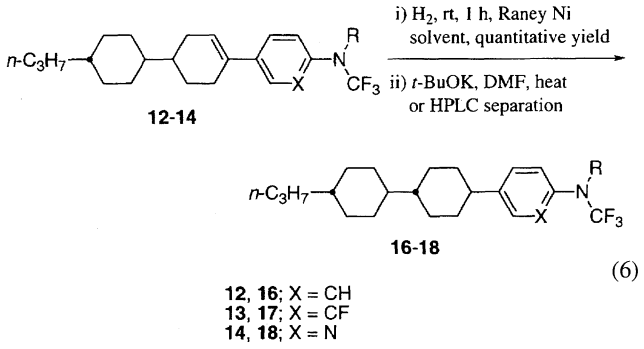
a) Examined by optical polarization microscopy. S_B: Smectic B phase.

atom on a phenyl ring or an ethyl group on nitrogen tends to make the temperature range of a smectic phase narrower and to lower the transition temperature from a smectic phase to an isotropic phase.



(5)

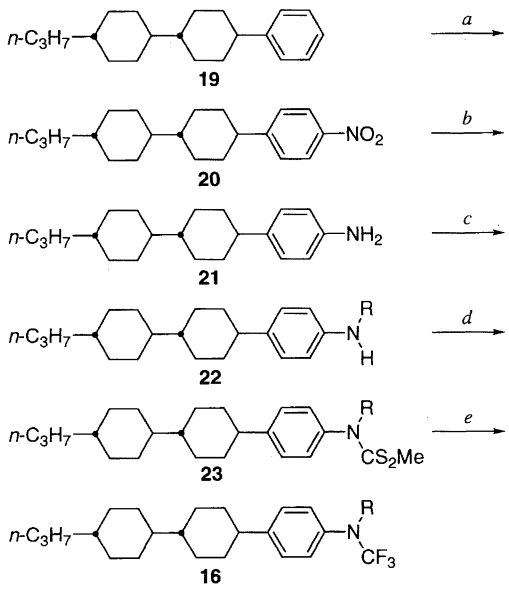
Trifluoromethylamino-Substituted LCs with a 4-Cyclohexylcyclohexylarene Core. Hydrogenation of trifluoromethylamino- substituted cyclohexyl(cyclohexenyl)-benzenes **12**, **13**, or -pyridines **14** using a Raney Ni (W2) catalyst gave quantitatively 1 : 1 to 1 : 2 mixtures of *cis*- and *trans*-isomers of **16**, **17**, or **18**, respectively. The *trans*-isomers were separated by preparative HPLC. Alternatively, isomerization of the *cis*-isomers of **16**, **17**, or **18** to the *trans*-isomers was effected by treatment with excess *t*-BuOK in hot DMF.



(6)

In order to facilitate the synthesis of **16** in a large amount, a sequence of reactions were carried out as shown in Scheme 1. Nitration of commercially available 1-phenyl-*trans*-4-(4-propyl)cyclohexylcyclohexane (**19**) and catalytic reduction of resulting nitrobenzene derivative **20** gave aniline derivative **21**. *N*-Alkylation of **21** by treatment with *n*-BuLi and an alkyl iodide gave **22**. To avoid dialkylation, **22a** was better prepared by the reaction of **21** with formaldehyde and $NaBH_4$ in the presence of sodium methoxide.[13] Treatment of **22** with *n*-BuLi, CS_2, and MeI gave dithiocarbamate **23** in high yields. Trifluoromethylation of **23** was quantitatively performed using tetrabutylammonium dihydrogentrifluoride ($TBAH_2F_3$) and 1,3-dibromo-5,5-dimethylhydantoin (DBH).[6d]

Phase transition behaviors of these compounds are summarized in Table 3. All of trifluoromethylamino-substituted compounds **16**, **17**, and **18** exhibited an S_B phase[14] over a wide range of temperatures. In addition, compound **18a** consisting of a (trifluoromethylamino)pyridine mesogen exhibited a nematic phase.



R = Me:	**22a**, 28%;	**23a**, 71%;	**16a**, quant.
R = Et:	**22b**, 79%;	**23b**, 94%;	**16b**, quant.
R = *n*-C_3H_7:	**22c**, 80%;	**23c**, 81%;	**16c**, 94%.

a: H_2SO_4/HNO_3, CH_2Cl_2, 0 °C to r.t., 2 h, 81% yield.
b: Pd/C, H_2, EtOH, r.t., 3.5 h, 90% yield.
c: i) *n*-BuLi (1.0 mol), -78 to 0 °C, ii) RI (1.0 mol).
d: *n*-BuLi (1.0 mol), CS_2 (2.0 mol), MeI (2.0 mol).
e: $TBAH_2F_3$ (5.0 mol), DBH (4.0 mol), CH_2Cl_2, 0 °C, 1 h.

Scheme 1.

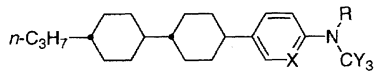
Worthy of note is that, with the carbon number of R increasing from 1 to 3 (or 2), the temperature ranges of LC phase of **16**, **17**, and **18** became narrower, and the phase transition took place at lower temperatures. Therefore, a long alkyl side-chain of R appears to destabilize the mesophase (see also Table 2). In contrast, the corresponding methylamine derivatives **24b** and **24c**[15] did not show any LC phase; these exhibited high melting points only. Therefore, the trifluoromethylamino substituent tends to induce liquid crystallinity.

Electro-Optical Properties of Trifluoromethylamino-Substituted LCs with a 4-Cyclohexylcyclohexylarene Core. Trifluoromethylamines **16a**, **16b**, or **24b** were added (20 wt%) to the host nematic LC mixture[16] listed in Table 4. The physical and electro-optical properties of the resulting mixtures were measured and are summarized in Table 4.

When we compare **16a** with **16b**, a substitutent effect is obvious. For example, the nematic-isotropic phase transition temperature (T_{NI}) of a **16a**-host mixture was higher than that of the host, whereas T_{NI} of a **16b**-host mixture became lower. Thus, **16a** apparently stabilizes the nematic phase of the host.

We extrapolated the dielectric anisotropy ($\Delta\varepsilon$) value of the **16b**-host mixture to 100% purity and estimated $\Delta\varepsilon'$ of **16b** to be 0.10, much smaller than $\Delta\varepsilon'$ of **16a** or **24b**. When we compare $\Delta\varepsilon'$ of **16a** with that of **26**, it is obvious that a $-N(CF_3)Me$ group induces $\Delta\varepsilon$ in a degree comparable with a fluoro substituent.

When **16a** was added to the host LC mixture, T_{NI} of the resulting mixture became slightly higher than that of the host



X = CH, Y = F; **16** X = N, Y = F; **18**
X = CF, Y = F; **17** X = CH, Y = H; **24**

Table 3. Phase Transition Temperatures of Compounds **16**, **17**, **18**, and the Corresponding *N*-Methyl Counterpart **24**

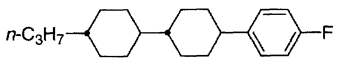
Entry	X	Y	R	Compound	Phase transition temp/°C[a]
1	CH	F	Me	**16a**	<20 S_B 173 Iso[b]
2	CH	F	Et	**16b**	Cr 35 S_B 141 Iso (Iso 141 S_B −50)
3	CH	F	Pr	**156c**	Cr 57 S_B 109 Iso (Iso 108 S_B −18 Cr)
4	CH	F	Me	**17a**	Cr 62 S_B 101 Iso[b]
5	CH	F	Et	**17b**	Cr 38 S_B 73 Iso[b]
6	N	F	Me	**18a**	Cr 62 S_X 73 S_B 120 N 121 Iso (Iso 121 N 119 S_B 70 S_X 37 Cr)
7	N	F	Et	**18b**	Cr 50 S_B 100 Iso (Iso 98 S_B 48 Cr)
8	CH	H	Me	**24a**	Cr 59 S_X 189 Iso[b]
9	CH	H	Et	**24b**	Cr 181 Iso[b]
10	CH	H	Pr	**24c**	Cr 168 Iso[b]

a) Measured by DSC on second heating. Values in parentheses were measured by DSC on first cooling. b) Examined by an optical polarizing microscope. S_X: higher order smectic.

Table 4. Physical and Electro-Optical Properties of Mixtures[a] of Nematic LC

	T_{NI}/°C	V_{th}/V[b]	$\Delta\varepsilon$	$\Delta\varepsilon'$ [c]	Δn[d]	$\eta_{20°C}$/cP[e]	$\eta_{0°C}$/cP[e]	τ/ms[b,f]	Applied voltage/V
Host	55	1.60	6.7	—	0.092	21.0	62.0	39.2	3.2
16a	59	1.62	5.92	2.8	0.091	—	—	46.4	3.6
16b	49	1.46	5.38	0.10	0.104	28.6	90.2	65.3	3.2
24b	68	1.84	6.59	6.1	0.100	—	—	53.9	4.0
26	73	1.91	6.31	4.75	0.096	—	—	—	—

a) A mixture containing 80% of a host mixture[16] and 20% of **16a**, **16b**, **24b**, or **26**. b) A 6 μm thick cell was used. c) Extrapolated from $\Delta\varepsilon$. d) Anisotropy of refractive index. e) Viscosity at 0 °C and 20 °C, respectively. f) Response time.



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without any change of threshold voltage (V_{th}) (compare **host** and **16a** in V_{th}). Since the phase transition temperatures remained unchanged after 50 h at 100 °C, trifluoromethylamines **16** can be used as a thermally stable nematic LC component. In particular, because the **16**–host mixture did not cause precipitation or phase separation when kept at −20 °C for 7 d, trifluoromethylamines **16a**—**16c** have excellent solubility in nematic LCs.

Conclusion

We have described the syntheses, phase transition behaviors, and electro-optical properties of CF_3N-substituted LCs. These compounds are easily accessible by the reaction of *p*-bromo-substituted (hetero)aryl(trifluoromethyl)amines or by the oxidative desulfurization–fluorination of the dithiocarbamates with all the carbon frameworks fully set up. They show mostly a smectic phase over a wide range of temperatures. The liquid crystallinity and electro-optical properties of these compounds are better than those of the corresponding methylamines, and thus the CF_3N-substituted LCs should find wide applications as a stable component of a chiral smectic C or nematic LCs mixture.

Experimental

General. All of the temperatures are uncorrected. Unless otherwise noted, reagents and solvents were purchased from Aldrich Chemical Co., Kanto Chemicals, Tokyo Kasei, or Wako Chemicals, Inc. and used as received. All the reaction was carried out under an argon atmosphere in a dry, freshly distilled solvent unless otherwise noted. Tetrahydrofuran (THF) was distilled from sodium/benzophenone, and *N*,*N*-dimethylformamide (DMF) from calcium hydride. Dichloromethane was pre-dried with P_2O_5 and distilled from calcium hydride. Unless otherwise stated, yields refer to materials purified by column chromatography or distillation under reduced pressure. Reactions were monitored by thin layer

chromatography using 0.25 mm E. Merck silica-gel plates (Silica Gel F_{254}) with UV light as a visualizing device and/or by dipping the plates in an ethanolic phosphomolybdic acid or *p*-anisaldehyde solution and heating the plates. Silica gel of E. Merck (Kieselgel 60, 230—400 mesh) or Nacalai Tesque (Silica Gel 60, 150—325 mesh) was used for flash column chromatography. Silica gel of E. Merck (Kieselgel 60, 70—230 mesh) or Wako (Wakogel C-200) was used for column chromatography under atmospheric or slightly positive pressure. Unless otherwise noted, NMR spectra were measured in $CDCl_3$ solutions. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a JEOL FX-100 spectrometer operating at 100 (^{1}H), 93.6 (^{19}F) MHz, on a Bruker AC-200 spectrometer at 200 (^{1}H), 50.3 (^{13}C), or 188 (^{19}F) MHz, or on a Varian Mercury-300 spectrometer at 300 (^{1}H), 75.5 (^{13}C), or 282 (^{19}F) MHz, respectively. Chemical shifts of ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR signals are quoted relative to internal standard Me_4Si ($\delta = 0.00$), $CDCl_3$ ($\delta = 77.00$), or $CFCl_3$ ($\delta = 0.00$), respectively. IR spectra were recorded on a Shimadzu FTIR-8100A spectrometer in neat liquid unless otherwise noted. Mass spectra were recorded on a Shimadzu GC/MS QP-5000 spectrometer or on a Hitachi H-80 double-focusing tandem GC-MS (70 eV) spectrometer. Measurement of melting points and phase transition temperatures and determination of liquid crystalline phases were carried out with an Olympus BH-2 optical polarizing microscope equipped with a Mettler FP-900 hot-stage. The thermal characterization was conducted with a SII DSC-200C (scanning rate 1 °C min^{-1}) differential scanning calorimeter (DSC) system. Recycling preparative HPLC was carried out using a Japan Analytical Industry LC-908 chromatograph.

Elemental analyses were carried out by Elemental Analysis Center, Tokyo Institute of Technology, using a Yanako MT2 CHN Corder. High-resolution mass spectra were obtained using a JEOL MStation spectrometer. $TBAH_2F_3$ was prepared according to the literature procedure[17] and dried in vacuo at room temperature overnight right before use.

General Procedure for the Preparation of Heterobiaryl-Type LCs. Method A: A hexane solution of *n*-BuLi (1.60 M, 1.1 mmol, 1 M = 1 mol dm^{-3}) was slowly added dropwise to a stirred solution of 5-bromo-2-[methyl(trifluoromethylmethylamino)]pyridine[6e] (**1a**, 1.00 mmol) in THF (or DME) (2.0 mL) at −78 °C. The resulting mixture was stirred for 10 min at −78 °C before addition of $ZnCl_2$·TMEDA complex (1.10 mmol). The reaction mixture was warmed slowly up to room temperature and stirred for 1 h at room temperature before a solution of 1-alkyloxy-4-halobenzene (1.10 mmol) and [$Pd(PPh_3)_4$] (1.9 mol%) in THF (or DME) (1.0 mL) was added. The resulting mixture was heated to reflux until all the substrate was consumed and then poured into sat. $NaHCO_3$ aq solution. The organic layer was separated; the aq layer was made alkaline (pH 10) with KOH and extracted three times with Et_2O. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography followed by HPLC to give the desired heterobiaryl.

Method B: A 1.6 M solution of *n*-BuLi in hexane (1.2 mmol) was slowly added dropwise to a stirred solution of 1-alkyloxy-4-bromobenzene (1.00 mmol) in THF (2.0 mL) at −78 °C. The resulting mixture was stirred for 30 min at −78 °C before addition of a solution of $ZnCl_2$·TMEDA (1.00 M, 1.20 mmol). The reaction mixture was warmed slowly up to room temperature, stirred for 1 h at the same temperature, and then treated with a solution of **1a** (1.20 mmol) and [$Pd(PPh_3)_4$] (21 mg, 0.018 mmol, 1.8 mol%) in THF (4.0 mL). The resulting reaction mixture was heated to reflux, stirred until all the substrate was consumed, and poured into sat. $NaHCO_3$ aq solution. Workup and purification by column chromatography followed by HPLC purification, gave the desired heterobiaryl.

5-(4-Methoxyphenyl)-2-[methyl(trifluoromethyl)amino]pyridine (5a). Yield: 20% (Method A, from 1-iodo-4-methoxybenzene, in THF), 9% (Method A, from 1-bromo-4-methoxybenzene, in THF), 25% (Method A, from 4-methoxy-1-iodobenzene, in DME), 12% (Method A, from 1-bromo-4-methoxybenzene, in DME). Colorless needles, mp 69 °C (DSC on heating); $R_f = 0.42$ (CH_2Cl_2). IR (KBr) 2967, 2944, 2917, 2843, 1608, 1559, 1521, 1459, 1429, 1438, 1423, 1362, 1344, 1255, 1243, 1188, 1125, 1068, 1043, 1027, 916, 822, 702, 619 cm^{-1}; ^{1}H NMR (200 MHz) $\delta = 3.29$ (q, $J = 2$ Hz, 3 H), 3.85 (s, 3 H), 6.95—7.03 (m, 3 H), 7.43—7.52 (m, 2 H), 7.78 (dd, $J = 3$, 9 Hz, 1 H), 8.55 (d, $J = 3$ Hz, 1 H); ^{19}F NMR (188 MHz) $\delta = -57.9$ (s); ^{13}C NMR (50.3 MHz) $\delta = 32.3$ (s), 55.3 (s), 113.6 (s), 114.5 (s), 122.9 (q, $J = 256$ Hz), 127.8 (s), 129.8 (s), 131.3 (s), 135.8 (s), 145.7 (s), 152.4 (s), 159.5 (s); MS *m/z* (rel intensity) 283 (M^++1; 16), 282 (M^+; 100), 213 (55), 198 (10), 186 (68), 185 (28), 170 (16), 143 (11), 142 (6), 141 (9), 140 (11). Found: *m/z* 282.0971. Calcd for $C_{14}H_{13}F_3N_2O$: M, 282.0980.

2-[Methyl(trifluoromethyl)amino]-5-(4-propoxyphenyl)pyridine (5b). Yield: 16% (Method A, from 1-iodo-4-propoxybenzene, in DME), 58% (Method B), 29% (Method B, $ZnCl_2$·Et_2O was used). Colorless needles, phase transition temp/°C: Cr 66 S_A 93 Iso (on heating), Iso 92 S_A 62 Cr (on cooling); $R_f = 0.50$ (CH_2Cl_2). IR (KBr) 2975, 2945, 1607, 1558, 1491, 1362, 1340, 1285, 1243, 1125, 1069, 976, 822 cm^{-1}; ^{1}H NMR (200 MHz) $\delta = 1.05$ (t, $J = 7$ Hz, 3 H), 1.60—2.00 (m, 2 H), 3.29 (q, $J = 2$ Hz, 3 H), 3.96 (t, $J = 6$ Hz, 2 H), 6.94—7.19 (m, 3 H), 7.39—7.53 (m, 2 H), 7.78 (dd, $J = 3$, 9 Hz, 1 H), 8.54 (d, $J = 3$ Hz, 1 H); ^{19}F NMR (188 MHz) $\delta = -57.9$ (dq, $J = 2$, 2 Hz); ^{13}C NMR (50.3 MHz) $\delta = 10.5$ (s), 22.6 (s), 32.3 (s), 69.8 (s), 113.7 (s), 115.1 (s), 122.9 (q, $J = 257$ Hz), 127.8 (s), 129.6 (s), 131.4 (s), 135.7 (s), 145.7 (s), 152.4 (s), 159.1 (s); MS *m/z* (rel intensity) 311 (M^++1; 14), 310 (M^+; 73), 268 (12), 267 (14), 248 (10), 199 (56), 172 (100), 170 (22), 143 (13), 141 (6). Found: *m/z* 310.1292. Calcd for $C_{16}H_{17}F_3N_2O$: M, 310.1293.

5-(4-Hexyloxyphenyl)-2-[methyl(trifluoromethyl)amino]pyridine (5c). Yield: 11% (Method A, from 1-hexyloxy-4-iodobenzene, in DME), 67% (Method B). Colorless needles, phase transition temp/°C: Cr 53 S_A 70 Iso (on heating), Iso 69 S_A 42 Cr (on cooling); $R_f = 0.65$ (CH_2Cl_2). IR (KBr) 2965, 2941, 2868, 1605, 1492, 1438, 1421, 1359, 1286, 1252, 1246, 1189, 1096, 1076, 1026, 822 cm^{-1}; ^{1}H NMR (200 MHz) $\delta = 0.91$ (t, $J = 6$ Hz, 3 H), 1.25—1.87 (m, 8 H), 3.29 (q, $J = 2$ Hz, 3 H), 4.00 (t, $J = 6$ Hz, 2 H), 6.93—7.17 (m, 3 H), 7.39—7.51 (m, 2 H), 7.78 (dd, $J = 2$, 9 Hz, 1 H), 8.54 (d, $J = 2$ Hz, 1 H); ^{19}F NMR (188 MHz) $\delta = -57.9$ (s); ^{13}C NMR (50.3 MHz) $\delta = 14.0$ (s), 22.6 (s), 25.7 (s), 29.2 (s), 31.6 (s), 32.3 (s), 68.1 (s), 113.6 (s), 115.1 (s), 122.9 (q, $J = 256$ Hz), 127.8 (s), 129.6 (s), 131.4 (s), 135.7 (s), 145.6 (s), 152.4 (s), 159.1 (s); MS *m/z* (rel intensity) 353 (M^++1; 14), 352 (M^+; 58), 268 (30), 248 (12), 199 (51), 172 (100), 171 (42), 170 (19), 115 (11). Found: *m/z* 352.1761. Calcd for $C_{19}H_{23}F_3N_2O$: M, 352.1762.

2-[Methyl(trifluoromethyl)amino]-5-(4-octyloxyphenyl)pyridine (5d). Yield: 15% (Method A, from 1-iodo-4-octyloxybenzene, in DME), 20% (Method B, $ZnCl_2$·Et_2O was used). Colorless needles, phase transition temp/°C: Cr 51 S_A 62 Iso (on heating), Iso 60 S_A 36 Cr (on cooling); $R_f = 0.67$ (CH_2Cl_2). IR (KBr) 2961, 2935, 2919, 2853, 1607, 1559, 1522, 1493, 1474, 1437, 1423, 1385, 1363, 1341, 1290, 1250, 1185, 1131, 1099, 1021, 918, 844, 825, 711 cm^{-1}; ^{1}H NMR (200 MHz) $\delta = 0.89$ (t, $J = 6$ Hz, 3 H), 1.29—1.88 (m, 12 H), 3.29 (q, $J = 2$ Hz, 3 H), 3.99 (t, $J = 6$ Hz, 2 H),

6.93—7.19 (m, 3 H), 7.42—7.51 (m, 2 H), 7.77 (dd, J = 3, 9 Hz, 1 H), 8.54 (d, J = 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = −57.9 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.1 (s), 22.6 (s), 26.1 (s), 29.3 (s), 29.4 (s), 31.8 (s), 32.3 (s), 68.1 (s), 113.6 (s), 115.1 (s), 122.9 (q, J = 256 Hz), 127.8 (s), 129.6 (s), 131.4 (s), 135.7 (s), 145.6 (s), 152.4 (s), 159.1 (s); MS m/z (rel intensity) 381 (M^++1; 24), 380 (M^+; 100), 268 (35), 248 (11), 199 (36), 172 (75), 171 (29), 170 (14), 143 (8). Found: m/z 380.2065. Calcd for $C_{21}H_{27}F_3N_2O$: M, 380.2075.

5-(4-Methoxyphenyl)-2-[methyl(trifluoromethyl)amino]pyrimidine (6a). Yield: 9% (Method A, from 1-iodo-4-methoxybenzene, in THF), 71% (Method B). Colorless needles, mp 101 °C (DSC on heating); R_f = 0.57 (CH_2Cl_2). IR (KBr) 2966, 2943, 2919, 2845, 1604, 1548, 1470, 1416, 1318, 1289, 1251, 1207, 1182, 1132, 1113, 1089, 1030, 926, 835, 823, 797, 713, 619 cm^{-1}; ^{1}H NMR (200 MHz) δ = 3.40 (q, J = 2 Hz, 3 H), 3.86 (s, 3 H), 6.97—7.05 (m, 2 H), 7.40—7.49 (m, 2 H), 8.70 (s, 2 H); ^{19}F NMR (188 MHz) δ = −57.0 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 31.7 (s), 55.4 (s), 114.8 (s), 122.0 (q, J = 258 Hz), 126.8 (s), 127.6 (s), 155.3 (s), 158.0 (s), 159.9 (s); MS m/z (rel intensity) 284 (M^++1; 15), 283 (M^+; 100), 214 (54), 187 (69), 185 (23), 171 (24), 160 (23), 155 (15), 89 (42). Found: m/z 283.0941. Calcd for $C_{13}H_{12}F_3N_3O$: M, 283.0932.

2-[Methyl(trifluoromethyl)amino]-5-(4-propoxyphenyl)pyrimidine (6b). Yield: 24% (Method A, from 1-iodo-4-propoxybenzene, in THF), 45% (Method B). Colorless needles, mp 94 °C (DSC on heating); R_f = 0.65 (CH_2Cl_2). IR (KBr) 2968, 2945, 2914, 2884, 1602, 1544, 1489, 1472, 1420, 1386, 1335, 1289, 1252, 1209, 1181, 1133, 1120, 1092, 1021, 1011, 926, 839, 822, 799, 718, 629, 614 cm^{-1}; ^{1}H NMR (200 MHz) δ = 1.05 (t, J = 7 Hz, 3 H), 1.70—2.00 (m, 2 H), 3.40 (q, J = 2 Hz, 3 H), 3.96 (t, J = 7 Hz, 2 H), 6.95—7.07 (m, 2 H), 7.36—7.47 (m, 2 H), 8.70 (s, 2 H); ^{19}F NMR (188 MHz) δ = −57.0 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 10.4 (s), 22.5 (s), 31.7 (s), 69.7 (s), 115.4 (s), 122.1 (q, J = 258 Hz), 126.5 (s), 127.6 (s), 155.2 (s), 158.0 (s), 159.5 (s); MS m/z (rel intensity) 312 (M^++1; 14), 311 (M^+; 81), 269 (29), 268 (12), 200 (57), 173 (100), 172 (33), 171 (3), 146 (18). Found: m/z 311.1238. Calcd for $C_{15}H_{16}F_3N_3O$: M, 311.1245.

5-(4-Hexyloxyphenyl)-2-[methyl(trifluoromethyl)amino]pyrimidine (6c). Yield: 9% (Method A, from 1-hexyloxy-4-iodobenzene, in THF), 38% (Method B). Colorless needles, mp 84 °C (DSC on heating); R_f = 0.74 (CH_2Cl_2). IR (KBr) 2963, 2937, 2920, 2877, 2856, 1602, 1545, 1485, 1469, 1419, 1382, 1333, 1285, 1208, 1183, 1126, 1086, 1028, 842, 822, 632, 614 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.91 (t, J = 6 Hz, 3 H), 1.10—2.00 (m, 8 H), 3.40 (q, J = 2 Hz, 3 H), 4.00 (t, J = 6 Hz, 2 H), 6.99 (d, J = 9 Hz, 2 H), 7.43 (d, J = 9 Hz, 2 H), 8.69 (s, 2 H); ^{19}F NMR (188 MHz) δ = −57.0 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.2 (s), 31.5 (s), 31.8 (s), 68.2 (s), 115.4 (s), 122.1 (q, J = 258 Hz), 126.5 (s), 127.7 (s), 155.3 (s), 158.0 (s), 159.5 (s); MS m/z (rel intensity) 354 (M^++1; 13), 353 (M^+; 64), 269 (57), 200 (48), 173 (100), 146 (12). Found: m/z 353.1709. Calcd for $C_{18}H_{22}F_3N_3O$: M, 353.1715.

2-[Methyl(trifluoromethyl)amino]-5-(4-octyloxyphenyl)pyrimidine (6d). Yield: 10% (Method A, from 1-iodo-4-octyloxybenzene, in THF), 88% (Method B). Colorless needles, mp 84 °C (DSC on heating); R_f = 0.76 (CH_2Cl_2). IR (KBr) 2964, 2937, 2922, 2876, 2855, 1603, 1544, 1491, 1470, 1421, 1390, 1334, 1287, 1250, 1210, 1183, 1134, 1089, 1029, 993, 842, 829, 799, 721, 614 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.89 (t, J = 6 Hz, 3 H), 1.22—1.53 (m, 10 H), 1.73—1.87 (m, 2 H), 3.40 (q, J = 2 Hz, 3 H), 3.99 (t, J = 7 Hz, 2 H), 6.99 (d, J = 9 Hz, 2 H), 7.42 (d, J = 9 Hz, 2 H), 8.69 (s, 2 H); ^{19}F NMR (188 MHz) δ = −57.0 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 26.0 (s), 29.2 (s), 29.3 (s), 31.8 (s), 68.2 (s), 115.4 (s), 122.1 (q, J = 258 Hz), 126.5 (s), 127.6 (s), 155.2 (s), 158.0 (s), 159.5 (s); MS m/z (rel intensity) 382 (M^++1; 14), 381 (M^+; 61), 269 (77), 268 (17), 249 (10), 200 (49), 173 (100), 172 (30), 171 (24). Found: m/z 381.2035. Calcd for $C_{20}H_{26}F_3N_3O$: M, 381.2028.

2-[Methyl(trifluoromethyl)amino]-5-(4-propylphenyl)pyridine (5e). Yield: 62% (Method B). Colorless needles, phase transition temp/°C: Cr 54 S_A 65 Iso; R_f = 0.78 (CH_2Cl_2). IR (KBr) 2965, 2935, 1606, 1558, 1490, 1362, 1342, 1280, 1245, 1127, 1071, 810, 677 cm^{-1}; ^{1}H NMR (200 MHz) δ = 0.97 (t, J = 7 Hz, 3 H), 1.68 (qt, J = 7, 7 Hz, 2 H), 2.63 (t, J = 7 Hz, 2 H), 3.29 (q, J = 2 Hz, 3 H), 7.15 (dm, J = 9 Hz, 1 H), 7.23—7.29 (m, 2 H), 7.46 (td, J = 2, 8 Hz, 2 H), 7.80 (dd, J = 3, 9 Hz, 1 H), 8.57 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = −57.9 (q, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 24.5 (s), 32.3 (s), 37.7 (s), 113.6 (s), 122.9 (q, J = 257 Hz), 126.6 (s), 129.2 (s), 131.5 (s), 134.7 (s), 136.0 (s), 142.4 (s), 145.9 (s), 152.7 (s); MS m/z (rel intensity) 295 (M^++1; 18), 294 (M^+; 100), 265 (95), 225 (48), 198 (58), 197 (23), 169 (37), 168 (13). Found: m/z 294.1340. Calcd for $C_{16}H_{17}F_3N_2$: M, 294.1344.

Synthesis of Dimethylamino-substituted Heterobiaryls. 5-Bromo-2-(dimethylamino)pyridine (3). 2-Dimethylaminopyridine (0.25 mL, 2.0 mmol) was added dropwise to a stirred suspension of 1,3-dibromo-5,5-dimethylhydantoin (DBH, 0.69 g, 2.4 mmol) in dichloromethane (4.0 mL) at −78 °C. The reaction mixture was stirred for 50 min at −78 °C and poured into sat. $NaHCO_3$ aq solution. Workup and silica-gel column chromatography (hexane–Et_2O = 5 : 1, R_f = 0.35) gave **3** (0.22 g, 54% yield) as colorless needles (mp 40.5—42.0 °C). IR (KBr) 2925, 2855, 1597, 1509, 1392, 1319, 1214, 1154, 983, 807, 764, 632 cm^{-1}; ^{1}H NMR (200 MHz) δ = 3.05 (s, 6 H), 6.38 (d, J = 9 Hz, 1 H), 7.47 (dd, J = 3, 9 Hz, 1 H), 8.15 (d, J = 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 38.1 (s), 105.9 (s), 107.2 (s), 139.3 (s), 148.3 (s), 157.8 (s); MS m/z (rel intensity) 203 (M^++3; 4), 202 (M^++2; 46), 201 (M^++1; 10), 200 (M^+; 48), 187 (54), 185 (56), 173 (71), 171 (71), 158 (34), 156 (26), 78 (50), 44 (100). Found: m/z 199.9957. Calcd for $C_7H_9^{79}BrN_2$: M, 199.9950.

5-Bromo-2-(dimethylamino)pyrimidine (4). Produced in 86% yield (1.74 g, 8.6 mmol) as colorless needles (mp 79.7—80.4 °C) from 2-dimethylaminopyrimidine (1.23 g, 10.0 mmol) by a procedure similar to that for the preparation of **3**. R_f = 0.58 (hexane–Et_2O = 1 : 1). IR (KBr) 3025, 3012, 2934, 2862, 2780, 1588, 1525, 1410, 1401, 1378, 1310, 1296, 1200, 1168, 1118, 1052, 968, 939, 785, 774, 643 cm^{-1}; ^{1}H NMR (200 MHz) δ = 3.15 (s, 6 H), 8.28 (s, 2 H); ^{13}C NMR (50.3 MHz) δ = 37.2 (s), 105.1 (s), 157.6 (s), 160.4 (s); MS m/z (rel intensity) 204 (M^++3; 7), 203 (M^++2; 99), 202 (M^++1; 30), 201 (M^+; 100), 188 (69), 186 (72), 174 (79), 172 (77), 160 (18), 158 (18). Found: m/z 200.9889. Calcd for $C_6H_8^{79}BrN_3$: M, 200.9902.

2-(Dimethylamino)-5-(4-propoxyphenyl)pyridine (7b). Yield: 39% (Method B). Colorless needles, mp 128 °C (DSC on heating); R_f = 0.24 (hexane–Et_2O = 3 : 1). IR (KBr) 2965, 2928, 1605, 1557, 1507, 1421, 1387, 1338, 1274, 1248, 1189, 1068, 988, 973, 960, 834, 822, 806, 668 cm^{-1}; ^{1}H NMR (200 MHz) δ = 1.04 (t, J = 6 Hz, 3 H), 1.72—1.92 (m, 2 H), 3.12 (s, 6 H), 3.94 (t, J = 6 Hz, 3 H), 6.57 (dd, J = 1, 9 Hz, 1 H), 6.94 (d, J = 9 Hz, 2 H), 7.42 (d, J = 9 Hz, 2 H), 7.64 (dd, J = 3, 9 Hz, 1 H), 8.38 (dd, J = 1, 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 10.5 (s), 22.6 (s), 38.2 (s), 69.6 (s), 105.7 (s), 115.7 (s), 124.4 (s), 127.1 (s), 131.1 (s), 135.5 (s), 145.7 (s), 158.2 (s), 158.3 (s); MS m/z (rel intensity) 257 (M^++1; 18), 256

(M^+; 100), 241 (21), 227 (48), 213 (44), 199 (15), 185 (31), 184 (14), 171 (18), 170 (17), 115 (12). Found: *m/z* 256.1579. Calcd for $C_{16}H_{20}N_2O$: M, 256.1576.

2-(Dimethylamino)-5-(4-hexyloxyphenyl)pyridine (7c). Yield: 35% (Method B). Colorless needles, mp 104 °C (DSC on heating); R_f = 0.24 (hexane–Et_2O = 3 : 1). IR (KBr) 2954, 2934, 2870, 2864, 1612, 1557, 1508, 1389, 1338, 1282, 1251, 1219, 1191, 1026, 961, 838, 806, 690, 669 cm^{-1}; ^1H NMR (200 MHz) δ = 0.90 (t, *J* = 6 Hz, 3 H), 1.25—1.83 (m, 8 H), 3.11 (s, 6 H), 3.98 (t, *J* = 6 Hz, 3 H), 6.56 (dd, *J* = 1, 9 Hz, 1 H), 6.94 (d, *J* = 9 Hz, 2 H), 7.42 (d, *J* = 9 Hz, 2 H), 7.64 (dd, *J* = 3, 9 Hz, 1 H), 8.38 (dd, *J* = 1, 3 Hz, 1 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.3 (s), 31.6 (s), 38.2 (s), 68.1 (s), 105.7 (s), 115.0 (s), 124.4 (s), 127.1 (s), 131.1 (s), 135.5 (s), 145.6 (s), 158.2 (s), 158.3 (s); MS *m/z* (rel intensity) 300 (M^++2; 4), 299 (M^++1; 41), 298 (M^+; 100), 283 (17), 269 (48), 213 (59), 199 (34), 185 (78), 184 (17), 171 (27), 170 (21), 115 (12). Found: *m/z* 298.2044. Calcd for $C_{19}H_{26}N_2O$: M, 298.2045.

2-(Dimethylamino)-5-(4-propoxyphenyl)pyrimidine (8b). Yield: 48% (Method B). Colorless needles, mp 106 °C (DSC on heating); R_f = 0.38 (hexane–Et_2O = 1 : 1). IR (KBr) 2964, 2934, 2876, 2859, 1606, 1534, 1510, 1409, 1394, 1328, 1284, 1277, 1253, 1242, 1178, 1117, 1069, 993, 971, 838, 827, 795 cm^{-1}; ^1H NMR (200 MHz) δ = 1.04 (t, *J* = 6 Hz, 3 H), 1.60—2.00 (m, 2 H), 3.22 (s, 6 H), 3.95 (t, *J* = 6 Hz, 2 H), 6.96 (d, *J* = 9 Hz, 1 H), 7.38 (d, *J* = 9 Hz, 2 H), 8.51 (s, 2 H); ^{13}C NMR (50.3 MHz) δ = 10.5 (s), 22.6 (s), 37.2 (s), 69.6 (s), 115.2 (s), 121.9 (s), 126.9 (s), 128.2 (s), 155.4 (s), 158.6 (s), 161.3 (s); MS *m/z* (rel intensity) 258 (M^++1; 17), 257 (M^+; 100), 228 (16), 214 (6), 186 (60), 185 (7), 171 (16). Found: *m/z* 257.1525. Calcd for $C_{15}H_{19}N_3O$: M, 257.1528.

2-(Dimethylamino)-5-(4-hexyloxyphenyl)pyrimidine (8c). Yield: 37% (Method B). Colorless needles, mp 96 °C (DSC on heating); R_f = 0.22 (hexane–Et_2O = 3 : 1). IR (KBr) 2950, 2940, 2869, 2785, 1604, 1534, 1511, 1467, 1409, 1374, 1324, 1307, 1282, 1251, 1203, 1177, 1115, 1058, 1028, 972, 837, 822, 657 cm^{-1}; ^1H NMR (200 MHz) δ = 0.91 (t, *J* = 6 Hz, 3 H), 1.20—1.90 (m, 8 H), 3.23 (s, 6 H), 3.98 (t, *J* = 6 Hz, 2 H), 6.96 (d, *J* = 9 Hz, 2 H), 7.38 (d, *J* = 9 Hz, 2 H), 8.51 (s, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.0 (s), 22.6 (s), 25.7 (s), 29.2 (s), 31.6 (s), 37.2 (s), 68.1 (s), 115.2 (s), 121.9 (s), 126.8 (s), 128.1 (s), 155.4 (s), 158.1 (s), 161.3 (s); MS *m/z* (rel intensity) 300 (M^++1; 20), 299 (M^+; 100), 215 (49), 214 (49), 200 (33), 186 (89), 171 (16). Found: *m/z* 299.2003. Calcd for $C_{18}H_{25}N_3O$: M, 299.1998.

Reaction of Dichloro(ethyl)-4-methoxyphenylsilane with 5-Bromo-2-[methyl(trifluoromethyl)amino)]pyrimidine (2a). To a suspension of potassium fluoride (174 mg, 3.0 mmol) in DMF (1.0 mL) were added dichloro(ethyl)-4-methoxyphenylsilane (138 mg, 0.58 mmol) and **2a** (89 mg, 0.34 mmol); the resulting mixture was stirred for 3 h at 60 °C. The reaction mixture was allowed to cool to room temperature; a solution of palladium(II) acetate (6.0 mg, 0.026 mmol) and tri(*o*-tolyl)phosphine (8.0 mg, 0.026 mmol) in DMF (1.0 mL) was added dropwise to the mixture. The whole mixture was stirred at 120 °C for 18 h, then cooled to room temperature, poured into saturated aq sodium chloride solution, and extracted three times with ethyl acetate. The combined organic extracts were then dried over anhydrous magnesium sulfate and filtered. Removal of the solvent under reduced pressure afforded a crude material, which was purified by thin-layer silica-gel chromatography (CH_2Cl_2) to give **6a** (64 mg, 66%) as colorless needles.

1-{4-[Methyl(trifluoromethyl)amino]phenyl}-(*trans*-4-propylcyclohexyl)cyclohexene (12a). A hexane solution of *n*-BuLi (1.6 M, 1.35 mL, 2.20 mmol) was added dropwise to a stirred solution of 4-bromo-*N*-methyl-*N*-trifluoromethylaniline (**10a**, 0.50 g, 1.97 mmol) in THF (2.0 mL) at −78 °C under an argon atmosphere. The solution was allowed to warm to −30 °C over 1 h before a THF (2.0 mL) solution of 4-(*trans*-4-propylcyclohexyl)cyclohexanone (0.50 g, 2.2 mmol) was added dropwise at the same temperature. After being stirried for 3 h at room temperature, the resulting mixture was treated with aq $NaHCO_3$ solution, the aq phase was extracted three times with Et_2O. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated. A stirred solution of the residual oil in benzene (15 mL) and pyridinium *p*-toluenesulfonate (PPTS, 20 mg) was heated to reflux for 20 min. The reaction mixture was poured into a $NaHCO_3$ solution; the aqueous phase was extracted with Et_2O three times. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (hexane) to give **12a** (73 mg, 10% yield) as colorless needles and carbamic acid fluoride derivative **15** (0.48 g, 68% yield).

Compound **12a** showed phase transition temperature/°C: Cr 24 S_B 158 Iso (on heating), Iso 155 S_B −23 Cr (on cooling) (recryst. from EtOH); R_f = 0.79 (hexane–Et_2O = 10 : 1). IR (KBr) 2915, 2849, 1613, 1518, 1445, 1345, 1283, 1260, 1208, 1148, 1094, 1061, 924, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 0.76—1.54 (m, 12 H), 1.64—2.05 (m, 6 H), 2.15—2.54 (m, 3 H), 3.02 (q, *J* = 1 Hz, 3 H), 6.06—6.16 (m, 1 H), 7.17 (d, *J* = 9 Hz, 2 H), 7.35 (d, *J* = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = −61.04 (s); MS *m/z* (rel intensity) 380 (M^++1; 19), 379 (M^+; 75), 357 (21), 254 (25), 240 (36), 227 (100), 215 (65), 205 (22), 201 (47), 188 (50), 129 (68), 109 (26), 83 (42), 81 (34), 69 (97). Found: *m/z* 379.2485. Calcd for $C_{23}H_{32}F_3N$: M, 379.2487.

***N*-Methyl-*N*-[4-(*trans*-4-propylcyclohexyl)cyclohexen-1-yl-phenyl]carbamic Fluoride (15)** showed phase transition temperature/°C: Cr 85 S_X 107 Sc 117 N 137 Iso; R_f = 0.54 (hexane–Et_2O = 10 : 1). ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 0.84—1.45 (m, 12 H), 1.72—2.06 (m, 6 H), 2.19—2.50 (m, 3 H), 3.34 (s, 3 H), 6.02—6.13 (m, 1 H), 7.14 (d, *J* = 9 Hz, 2 H), 7.39 (d, *J* = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = −16.6 (s); MS *m/z* (rel intensity) 359 (M^++2; 4), 358 (M^++1; 24), 357 (M^+; 100), 233 (23), 232 (37), 218 (66), 205 (91), 193 (42), 180 (14), 179 (84), 166 (37), 164 (20), 157 (15), 129 (26), 123 (13), 115 (16), 109 (35), 83 (26), 81 (22), 69 (57).

1-{4-[Ethyl(trifluoromethyl)amino]phenyl}-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexene (12b). In a manner similar to the synthesis of **12a**, compound **12b** (48 mg, 15% yield) was prepared from **10b** (0.22 g, 0.81 mmol) as colorless needles using PPTS (3 mg) and MS 4A. Phase transition temperature/°C: Cr 25 S_B 110 Iso (on heating), Iso 110 S_B −47 Cr (on cooling) (recryst. from EtOH); R_f = 0.82 (hexane–EtOAc = 20 : 1). IR (KBr) 2915, 2849, 1800, 1518, 1449, 1379, 1269, 1191, 1146, 1098, 1057, 912, 804 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, *J* = 7 Hz, 3 H), 1.07 (t, *J* = 7 Hz, 3 H), 0.78—1.43 (m, 11 H), 1.72—2.03 (m, 7 H), 2.20—2.51 (m, 3 H), 3.35—3.45 (m, 2 H), 6.08—6.14 (m, 1 H), 7.17 (d, *J* = 9 Hz, 2 H), 7.36 (d, *J* = 9 Hz, 2 H); ^{19}F NMR (188 MHz) δ = −58.18 (s); MS *m/z* (rel intensity) 394 (M^++1; 18), 393 (M^+; 72), 371 (38), 268 (21), 254 (30), 241 (78), 232 (22), 229 (54), 215 (33), 202 (28), 193 (31), 129 (58), 128 (41), 109 (29), 83 (40), 69 (100). Found: *m/z* 393.2635. Calcd for $C_{24}H_{34}F_3N$: M, 393.2643.

1-{3-Fluoro-4-[methyl(trifluoromethyl)amino]phenyl}-4-(*trans*-4-propylcyclohexyl)cyclohexene (13a). Cyclohexene derivative **13a** (49 mg, 28% yield) was prepared from **11a** (117 mg, 0.43 mmol) using *p*-toluenesulfonic acid monohydrate (11 mg) as a catalyst. Colorless needles, phase transition temperature/°C:

Cr 62 S_B 101 Iso (recryst. from EtOH); R_f = 0.46 (hexane). IR (KBr) 2921, 2851, 1570, 1516, 1437, 1345, 1296, 1210, 1152, 1084, 1067, 814, 741 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.78—1.49 (m 12 H), 1.68—2.08 (m, 6 H), 2.18—2.43 (m, 3H), 3.00 (q, J = 1 Hz, 3 H), 6.11—6.14 (m, 1 H), 7.05—7.21 (m, 3 H); ^{19}F NMR (188 MHz) δ = −61.46 (d, J = 5 Hz, 3 F), −121.52——121.71 (m, 1 F); MS *m/z* (rel intensity) 398 (M^++1; 7), 397 (M^+; 28), 273 (8), 272 (12), 271 (8), 258 (23), 233 (21), 219 (30), 206 (29), 164 (17), 148 (17), 147 (100), 146 (18), 127 (17), 123 (19), 109 (19), 83 (32), 69 (88), 67 (41). Found: *m/z* 397.2391. Calcd for $C_{23}H_{32}F_3N$: M, 397.2392.

1-{4-[Ethyl(trifluoromethyl)amino]-3-fluorophenyl}-4-(*trans*-4-propylcyclohexyl)cyclohexene (13b). Similarly, this compound **13b** (73 mg, 9% yield) was prepared from **12b** (0.52 g, 2.0 mmol) as colorless needles. Phase transition temperature/°C: Cr 38 S_B 73 Iso (recryst. from EtOH); R_f = 0.55 (hexane). IR (KBr) 2957, 2917, 2849, 1619, 1570, 1516, 1387, 1356, 1275, 1244, 1202, 1146, 1100, 1065, 957, 916 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.06 (t, J = 7 Hz, 3 H), 0.78—1.46 (m, 12 H), 1.48—2.08 (m, 6 H), 2.15—2.52 (m, 3 H), 3.30—3.46 (m, 2 H), 6.12—6.22 (m, 1 H), 7.06—7.22 (m, 3 H); ^{19}F NMR (188 MHz) δ = −58.16 (d, J = 5 Hz, 3 F), −121.11——121.18 (m, 1 F); MS *m/z* (rel intensity) 412 (M^++1; 7), 411 (M^+; 23), 392 (6), 260 (12), 259 (11), 250 (11), 244 (13), 233 (30), 192 (18), 161 (14), 147 (44), 146 (14), 134 (14), 109 (14), 83 (29), 81(10), 79 (11), 77 (10), 69 (100), 67 (71). Found: *m/z* 411.2545. Calcd for $C_{24}H_{33}F_4N$: M, 411.2549.

1-{2-[Methyl(trifluoromethyl)amino]pyridin-5-yl})-4-(*trans*-4-propylcyclohexyl)cyclohexene (14a). Similarly, trifluoromethylamine **14a** (0.19 g, 49% yield) was obtained from **1a** (0.26 g, 1.00 mmol) as colorless needles. Phase transition temperature/°C: Cr 82 S_A 139 Iso (on heating), Iso 139 S_A 64 Cr (on cooling) (recryst. from EtOH); R_f = 0.64 (hexane–Et_2O = 3 : 1). IR (KBr) 2959, 2851, 1601, 1559, 1435, 1352, 1339, 1281, 1117, 1073, 1022, 916, 820, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.92—1.51 (m, 11 H), 1.62—2.10 (m, 7 H), 2.14—2.53 (m, 3 H), 3.24 (q, J = 2 Hz, 3 H), 6.07—6.10 (m, 1 H), 7.02 (ddd, J = 1, 2, 9 Hz, 1 H), 7.59 (dd, J = 3, 9 Hz, 1 H), 8.37 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = −58.09 (m); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 26.4 (s), 27.8 (s), 29.8 (s), 30.0 (s), 30.2 (s), 32.3 (q, J = 2 Hz), 33.5 (s), 37.7 (s), 38.8 (s), 39.8 (s), 42.5 (s), 113.4 (q, J = 4 Hz), 123.0 (q, J = 257 Hz), 125.2 (s), 132.7 (s), 133.0 (s), 134.0 (s), 144.3 (s), 152.2 (s); MS *m/z* (rel intensity) 381 (M^++1; 23), 380 (M^+; 58), 255 (23), 241 (29), 228 (30), 227 (12), 207 (31), 197 (21), 189 (38), 159 (54), 154 (20), 132 (70), 131 (37), 130 (36), 117 (25), 116 (26), 83 (22), 79 (37), 77 (34), 69 (100), 67 (76), 65 (33). Found: *m/z* 380.2432. Calcd for $C_{22}H_{31}F_3N_2$: M, 380.2439.

1-{2-[Ethyl(trifluoromethyl)amino]pyridin-5-yl}-4-(*trans*-4-propylcyclohexyl)cyclohexene (14b). This compound (154 mg, 20% yield) was prepared from **1b** (542 mg, 2.0 mmol) in a manner similar to the procedure for **11a**. Colorless needles, phase transition temperature/°C: Cr 78 S_A 98 Iso (on heating), Iso 98 S_A 61 Cr (on cooling) (recryst. from EtOH); R_f = 0.72 (hexane–Et_2O = 5 : 1). IR (KBr) 2924, 1800, 1603, 1559, 1499, 1389, 1260, 1220, 1022, 943, 811, 802 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.21 (t, J = 7 Hz, 3 H), 0.75—1.43 (m, 11 H), 1.62—2.10 (m, 7 H), 2.43—2.20 (m, 3 H), 3.78—3.96 (m, 2 H), 6.05—6.15 (m, 1 H), 6.97—7.02 (m, 1 H), 7.60 (dd, J = 3, 9 Hz, 1 H), 8.37 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = −55.95 (m); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 14.4 (s), 20.0 (s), 26.4 (s), 27.7 (s), 29.8 (s), 30.0 (s), 30.2 (s), 33.5 (s), 37.6 (s), 38.8 (s), 39.8 (s), 40.5 (m), 42.5 (s), 113.3 (q, J = 4 Hz), 123.1 (q, J = 261 Hz), 125.2 (s), 132.4 (s), 133.1 (s), 134.0 (s), 144.5 (s), 151.3 (s); MS *m/z* (rel intensity) 394 (M^+; 10), 379 (16), 227 (19), 207 (29), 173 (8), 156 (10), 155 (22), 147 (14), 121 (14), 117 (15), 105 (27), 97 (14), 95 (17), 91 (21), 85 (26), 83 (31), 71 (30), 69 (100), 67 (39). Found: *m/z* 394.2602. Calcd for $C_{23}H_{33}F_3N_2$: M, 394.2596.

1-Nitro-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]benzene (20). To a stirred mixture of *trans*-4-(*trans*-4-propylcyclohexyl)cyclohexylbenzene (**19**, 22.8 g, 0.080 mol), conc. sulfuric acid (26 mL), and dichloromethane (15 mL) was added dropwise nitric acid (61 wt%, 28 mL) at 0 °C over 1 h. The resulting mixture was allowed to warm to room temperature in 1 h under vigorous stirring and then poured to ice. The resulting pale yellow precipitates were filtered by suction. The filtrate was neutralized with NaOH and extracted three times with Et_2O. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue and the precipitates were combined and purified by recrystallization from EtOH to give **20** (18.4 g, 81% yield) as a yellow powder. Phase transition temperature/°C: Cr 101 N 207 Iso (hexane–EtOH); R_f = 0.30 (hexane). IR (KBr) 2930, 2851, 1598, 1514, 1450, 1345, 1110, 980, 849, 860, 750 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.78—1.55 (m, 15 H), 1.63—2.00 (m, 8 H), 2.56 (tt, J = 3, 12 Hz, 1 H), 7.34 (d, J = 9 Hz, 2 H), 8.13 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.3 (s), 20.0 (s), 30.0 (s), 30.0 (s), 33.5 (s), 34.2 (s), 37.6 (s), 39.8 (s), 42.7 (s), 43.3 (s), 44.7 (s), 123.5 (s), 127.6 (s), 146.2 (s), 155.2 (s); MS *m/z* (rel intensity) 329 (M^+; 7), 312 (3), 299 (19), 133 (12), 132 (86), 126 (12), 119 (61), 109 (11), 107 (20), 106 (37), 95 (12), 93 (14), 83 (42), 81 (35), 69 (100), 67 (37), 65 (15). Found: C, 76.33; H, 9.62; N, 4.33%. Calcd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48; N, 4.25%.

4-[*trans*-4-(*trans*-4-Propylcyclohexyl)cyclohexyl]aniline (21). A mixture of **20** (17.6 g, 53 mmol) and palladium on activated carbon (10 wt%, 0.59 g) in EtOH (50 mL) was vigorously stirred for 3.5 h at room temperature under a hydrogen atmosphere with a slightly positive pressure. The mixture was filtered through a Cellite pad, which was washed with Et_2O; the combined filtrates were concentrated under reduced pressure. The residue was purified by recrystallization from EtOH to give **21** (14.4 g, 90% yield) as a colorless powder (mp 174 °C). R_f = 0.12 (hexane–Et_2O = 5 : 1). IR (KBr) 3393, 3308, 3210, 2953, 2849, 1615, 1518, 1441, 1267, 1183, 826, 776, 708, 642 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.78—1.48 (m, 15 H), 1.64—1.96 (m, 8 H), 2.33 (tt, J = 3, 12 Hz, 1 H), 3.51 (br, 2 H), 6.62 (d, J = 8 Hz, 2 H), 6.99 (d, J = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.4 (s), 33.6 (s), 34.8 (s), 37.6 (s), 39.8 (s), 42.9 (s), 43.4 (s), 43.7 (s), 115.1 (s), 127.4 (s), 138.1 (s), 144.1 (s); MS *m/z* (rel intensity) 300 (M^++1; 5), 299 (M^+; 31), 212 (2), 191 (2), 158 (5), 135 (7), 133 (22), 132 (100), 121 (5), 120 (5), 119 (51), 106 (30), 81 (12), 65 (9). Found: *m/z* 299.2614. Calcd for $C_{21}H_{33}N$: M, 299.2613.

***N*-Methy-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]-aniline (22a): Method A.**[13] A suspension of sodium methoxide (1.54 g, 29 mmol), paraformaldehyde (0.26 g, 7.7 mmol) and **21** (1.53 g, 5.1 mmol) in methanol (80 mL) was stirred for 17 h at 40 °C before sodium borohydride (0.44 g, 12 mmol) was added at room temperature. The resulting mixture was heated at 50 °C for 9 h; the methanol was removed under reduced pressure. The solid residue was partitioned between aq $NaHCO_3$ solution and diethyl ether; the organic phase was separated; the aq phase was extracted three times with diethyl ether. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (CH_2Cl_2) to give **22a** (0.95 g, 59% yield) as a colorless powder.

Method B. A hexane solution of *n*-BuLi (1.6 M, 10.5 mmol) was slowly added to a stirred solution of **21** (3.0 g, 10 mmol) in THF (50 mL) at −78 °C. After the solution was allowed to warm to 0 °C over 1 h, methyl iodide (1.25 mL, 20 mmol) was added dropwise to the mixture at 0 °C. The resulting mixture was stirred at room temperature for 3 h and then treated with aq $NaHCO_3$ solution. The organic phase was separated; the aq phase was extracted with diethyl ether three times. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (hexane–Et_2O = 10 : 1) to give **22a** (0.88 g, 28% yield) and *N*,*N*-dimethyl derivative **24a** (0.23 g, 7% yield).

22a: A colorless powder, phase transition temperature/°C: Cr 62 S_B 132 Iso (hexane–CH_2Cl_2); R_f = 0.41 (hexane–Et_2O = 10 : 1). IR (KBr) 3297, 2955, 2936, 2849, 1615, 1520, 1443, 1265, 1186, 1148, 1057, 974, 816 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.80—1.52 (m, 15 H), 1.71—1.96 (m, 8 H), 2.34 (tt, J = 3, 12 Hz, 1 H), 2.81 (s, 3 H), 3.57 (br, 1 H), 6.56 (d, J = 9 Hz, 2 H), 7.04 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.5 (s), 30.9 (s), 33.6 (s), 34.9 (s), 37.6 (s), 39.8 (s), 43.0 (s), 43.4 (s), 43.7 (s), 112.4 (s), 127.4 (s), 136.6 (s), 147.4 (s); MS *m/z* (rel intensity) 315 (M^++2; 1), 314 (M^++1; 10), 313 (M^+; 45), 147 (14), 146 (100), 133 (36), 132 (14), 120 (41), 107 (7), 106 (5), 81 (6), 69 (10). Found: *m/z* 313.2765. Calcd for $C_{22}H_{35}N$: M, 313.2769.

***N*,*N*-Dimethyl-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (24a).** A colorless powder, phase transition temperature/°C: Cr 59 S_B 189 Iso (hexane–CH_2Cl_2); R_f = 0.63 (hexane–Et_2O = 10 : 1). IR (KBr) 2951, 2849, 1617, 1524, 1447, 1350, 1229, 1165, 1063, 949, 808 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.76—1.51 (m, 16 H), 1.67—1.98 (m, 7 H), 2.34 (tt, J = 3, 12 Hz, 1 H), 2.92 (s, 6 H), 6.66 (d, J = 9 Hz, 2 H), 7.06 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.1 (s), 30.1 (s), 30.5 (s), 33.7 (s), 34.9 (s), 37.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 43.6 (s), 112.9 (s), 127.3 (s), 136.3 (s), 149.0 (s); MS *m/z* (rel intensity) 329 (M^++2; 1), 328 (M^++1; 17), 327 (M^+; 65), 161 (15), 160 (100), 147 (33), 146 (22), 134 (55), 121 (7), 81 (8), 69 (8). Found: C, 83.95; H, 11.38; N, 4.26%. Calcd for $C_{23}H_{37}N$: C, 84.34; H, 11.39; N, 4.28%. Found: *m/z* 327.2930. Calcd for $C_{23}H_{37}N$: M, 327.2926.

***N*-Ethyl-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (22b).** Aniline derivative **22b** (1.43 g, 79% yield) was obtained from **21** (1.65 g, 5.5 mmol) in a manner similar to the procedure of **22a** (Method B) except for the purification by recrystallization from EtOH–hexane and column chromatography (hexane–Et_2O = 5 : 1). A colorless powder, phase transition temperature/°C: Cr 94 N 225 Iso, R_f = 0.65 (hexane–Et_2O = 5 : 1). IR (KBr) 3450, 2920, 2840, 1869, 1616, 1522, 1446, 1350, 1229, 1165, 949, 803 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.23 (t, J = 7 Hz, 3 H), 0.80—1.50 (m, 15 H), 1.71—1.96 (m, 8 H), 2.34 (tt, J = 3, 12 Hz, 1 H), 3.13 (q, J = 7 Hz, 2 H), 3.40 (br, 1 H), 6.55 (d, J = 8 Hz, 2 H), 7.01 (d, J = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 15.0 (s), 20.0 (s), 30.1 (s), 30.5 (s), 33.7 (s), 34.9 (s), 37.7 (s), 38.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 43.7 (s), 112.8 (s), 127.4 (s), 136.9 (s), 148.5 (s); MS *m/z* (rel intensity) 328 (M^++1; 8), 327 (M^+; 44), 312 (11), 254 (8), 207 (16), 161 (16), 160 (100), 148 (26), 134 (37), 132 (50), 128 (11), 121 (20), 118 (18), 117 (14), 115 (12), 91 (14), 83 (26), 81 (25), 71 (20), 69 (40). Found: C, 84.75; H, 11.70; N, 4.37%. Calcd for $C_{23}H_{37}N$: C, 84.34; H, 11.39; N, 4.28%. Found: *m/z* 327.2919. Calcd for $C_{23}H_{37}N$: M, 327.2926.

***N*-Propyl-4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]aniline (22c).** In a manner similar to the procedure for **22a**, this compound (0.27 g, 0.80 mmol) was prepared from **21** (0.30 g, 80% yield) as a colorless powder. Phase transition temperature/°C: Cr 99 S_X 107 N 201 Iso (hexane–CH_2Cl_2); R_f = 0.52 (hexane–Et_2O = 5 : 1). IR (KBr) 3399, 2917, 2849, 1619, 1522, 1478, 1449, 1412, 1316, 1254, 1183, 978, 814 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.98 (t, J = 7 Hz, 3 H), 0.79—1.20 (m, 15 H), 1.47—1.95 (m, 10 H), 2.32 (tt, J = 3, 12 Hz, 1 H), 3.06 (t, J = 7 Hz, 2 H), 3.51 (br, 1 H), 6.54 (d, J = 9 Hz, 2 H), 7.01 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.7 (s), 14.5 (s), 20.1 (s), 22.9 (s), 30.2 (s), 30.6 (s), 33.7 (s), 35.0 (s), 37.8 (s), 38.9 (s), 43.1 (s), 43.6 (s), 43.8 (s), 46.2 (s), 112.8 (s), 127.5 (s), 136.8 (s), 146.7 (s); MS *m/z* (rel intensity) 342 (M^++1; 22), 341 (M^+; 85), 313 (18), 312 (100), 175 (15), 174 (99), 161 (25), 148 (24), 146 (13), 144 (12), 132 (50), 130 (10), 121 (10), 120 (12), 119 (12), 118 (11), 106 (17), 83 (14), 81 (19), 69 (35), 67 (22). Found: C, 84.19; H, 11.31; N, 4.05%. Calcd for $C_{24}H_{39}N$: C, 84.39; H, 11.51; N, 4.10%.

***N*-Ethyl-*N*-methyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}amine (24b).** In a manner similar to the procedure for **22a**, compound **24b** was prepared from **22b** (90 mg, 0.27 mmol) in 91% yield as a colorless powder, mp 181 °C. R_f = 0.65 (hexane–Et_2O = 5 : 1). IR (KBr) 2930, 2850, 1867, 1614, 1530, 1466, 1370, 1269, 1211, 1157, 1082, 978, 812 cm^{-1}. ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.10 (t, J = 7 Hz, 3 H), 0.76—1.51 (m, 16 H), 1.67—1.98 (m, 7 H), 2.34 (tt, J = 3, 12 Hz, 1 H), 2.87 (s, 3 H), 3.35 (q, J = 7 Hz, 2 H), 6.66 (d, J = 9 Hz, 2 H), 7.06 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.3 (s), 14.1 (s), 20.1 (s), 22.7 (s), 30.2 (s), 30.5 (s), 33.7 (s), 34.9 (s), 37.5 (s), 37.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 47.0 (s), 112.6 (s), 127.3 (s), 135.6 (s), 147.4 (s); MS *m/z* (rel intensity) 343 (M^++2; 4), 342 (M^++1; 25), 341 (M^+; 100), 327 (26), 326 (95), 175 (13), 174 (91), 161 (16), 160 (11), 148 (46), 146 (48), 131 (10), 120 (12), 81 (16), 69 (25), 67 (17). Found: *m/z* 341.3080. Calcd for $C_{24}H_{39}N$: M, 341.3082.

***N*-Methyl-*N*-propyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}amine (24c).** This compound **24c** (0.33 g, 93% yield) was prepared from **22c** (0.34 g, 1.00 mmol) as a colorless powder, mp 168 °C. R_f = 0.50 (hexane–EtOAc = 10 : 1). IR (KBr) 2851, 1617, 1520, 1447, 1372, 1294, 1244, 1209, 1156, 1082, 968, 810 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 8 Hz, 3 H), 0.91 (t, J = 8 Hz, 3 H), 0.76—1.51 (m, 16 H), 1.58 (q, J = 8 Hz, 2 H), 1.63—1.98 (m, 7 H), 2.34 (tt, J = 3, 12 Hz, 1 H), 2.88 (s, 3 H), 3.21 (t, J = 7 Hz, 2 H), 6.66 (d, J = 9 Hz, 2 H), 7.06 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.5 (s), 14.4 (s), 20.1 (s), 30.1 (s), 30.5 (s), 33.6 (s), 34.6 (s), 37.7 (s), 38.3 (s), 39.9 (s), 43.0 (s), 43.5 (s), 54.8 (s), 112.1 (s), 127.2 (s), 135.3 (s), 147.7 (s); MS *m/z* (rel intensity) 356 (M^++1; 7), 355 (M^+; 29), 327 (25), 326 (100), 200 (3), 188 (7), 146 (22), 131 (6), 120 (7), 93 (6), 81 (13), 69 (17). Found: *m/z* 355.3240. Calcd for $C_{25}H_{41}N$: M, 355.3239.

A General Procedure for the Preparation of Methyl Dithiocarbamates (23): A hexane solution (1.6 M) of *n*-BuLi (12 mmol) was slowly added dropwise to a stirred solution of secondary amine **22** (10.0 mmol) in THF (20 mL) at −10 °C. The solution was allowed to warm to 0 °C over 1 h; carbon disulfide (20 mmol) was added dropwise to this mixture at 0 °C; the mixture was stirred for 12 h at room temperature; methyl iodide (20 mmol) was added dropwise to the reaction mixture at 0 °C; the whole mixture was stirred at room temperature for 3—5 h and was poured to sat. $NaHCO_3$ aq solution. The organic phase was separated; the aq phase was extracted three times with diethyl ether. The combined organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography or by recrystallization to give **23**. Yield

and spectral properties of products were as follows.

Methyl *N*-Methyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)-cyclohexyl]phenyl}dithiocarbamate (23a). Yield: 71%, pale yellow needles, mp 167.4—169.2 °C (EtOH). R_f = 0.57 (hexane–Et_2O = 10 : 1). IR (KBr) 2951, 2849, 1507, 1447, 1368, 1266, 1100, 1021, 955, 839 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.75—1.55 (m, 15 H), 1.64—2.01 (m, 8 H), 2.41—2.54 (m, 1 H), 2.53 (s, 3 H), 3.76 (s, 3 H), 7.14 (d, J = 8 Hz, 2 H), 7.28 (d, J = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 20.8 (s), 30.1 (s), 30.2 (s), 33.6 (s), 34.5 (s), 37.6 (s), 39.8 (s), 42.8 (s), 43.4 (s), 44.3 (s), 46.8 (s), 126.5 (s), 128.0 (s), 142.5 (s), 148.9 (s), 200.5 (s); MS *m/z* (rel intensity) 404 (M^++1; 1), 403 (M^+; 4), 357 (2), 356 (6), 161 (2), 148 (2), 115 (1), 91 (5), 90 (5), 89 (5), 88 (100), 69 (5). Found: C, 71.29; H, 9.41; N, 3.39%. Calcd for $C_{24}H_{37}NS_2$: C, 71.41; H, 9.24; N, 3.47%.

Methyl *N*-Ethyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexyl]phenyl}dithiocarbamate (23b). Yield: 95%, pale yellow needles, mp 152.1—153.0 °C (EtOH). R_f = 0.53 (hexane–Et_2O = 10 : 1). IR (KBr) 2924, 2851, 1503, 1456, 1450, 1406, 1273, 1235, 1103, 1073, 994, 961, 899, 812 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.26 (t, J = 7 Hz, 3 H), 0.79—1.57 (m, 15 H), 1.68—2.06 (m, 8 H), 2.42—2.55 (m, 1 H), 2.51 (s, 3 H), 4.33 (q, J = 7 Hz, 2 H), 7.10 (d, J = 9 Hz, 2 H), 7.28 (d, J = 9 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.9 (s), 14.4 (s), 20.0 (s), 20.5 (s), 30.1 (s), 30.2 (s), 33.5 (s), 34.5 (s), 37.6 (s), 39.8 (s), 42.8 (s), 43.3 (s), 44.3 (s), 52.5 (s), 127.5 (s), 127.9 (s), 140.7 (s), 148.9 (s), 199.9 (s); MS *m/z* (rel intensity) 417 (M^+; 5), 415 (2), 413 (1), 289 (1), 287 (1), 280 (1), 276 (2), 234 (2), 228 (1), 208 (2), 182 (2), 148 (4), 121 (6), 118 (7), 115 (3), 112 (5), 110 (4), 103 (11), 102 (100), 91 (7), 85 (8), 83 (10), 81 (10), 74 (12), 69 (20). Found: C, 71.51; H, 9.61; N, 3.16%. Calcd for $C_{25}H_{39}NS_2$: C, 71.89; H, 9.41; N, 3.35%. Found: *m/z* 417.2523. Calcd for $C_{25}H_{39}NS_2$: M, 417.2524.

Methyl *N*-Propyl-*N*-{4-[*trans*-4-(*trans*-4-propylcyclohexyl)-cyclohexyl]phenyl}dithiocarbamate (23c). Yield: 81%, pale yellow needles, mp 122.2—123.1 °C (EtOH–hexane). R_f = 0.66 (hexane–Et_2O = 10 : 1). IR (KBr) 2921, 2830, 1505, 1441, 1397, 1362, 1296, 1258, 1231, 1136, 1103, 955, 835, 828 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.91 (t, J = 7 Hz, 3 H), 0.72—1.58 (m, 15 H), 1.60—2.07 (m, 10 H), 2.41—2.62 (m, 1 H), 2.51 (s, 3 H), 4.18—4.25 (m, 2 H), 7.09 (d, J = 8 Hz, 2 H), 7.27 (d, J = 8 Hz, 2 H); ^{13}C NMR (50.3 MHz) δ = 11.0 (s), 14.4 (s), 20.0 (s), 20.6 (s), 30.1 (s), 30.3 (s), 33.6 (s), 34.5 (s), 37.6 (s), 39.8 (s), 42.9 (s), 43.4 (s), 44.3 (s), 59.2 (s), 127.5 (s), 127.9 (s), 141.0 (s), 149.0 (s), 200.5 (s). Found: C, 72.18; H, 9.54; N, 3.07%. Calcd for $C_{26}H_{41}NS_2$: C, 72.33; H, 9.57; N, 3.24%.

A General Procedure for the Preparation of Trifluoromethylamino-Substituted LCs with a Cyclohexylarene Core. Method A: To a stirred suspension of $TBAH_2F_3$ (25 mmol) and DBH (20 mmol) in dichloromethane (10 mL) was added dropwise a solution of dithiocarbamate **23** (5.0 mmol) in dichloromethane (5.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C until all the substrate was consumed and was then poured into an aq buffer solution of $NaHCO_3$/NaOH/$NaHSO_3$ (pH = 10). The resultant was extracted three times with diethyl ether. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give the corresponding trifluoromethylamines **16**.

Method B: A suspension of cyclohexene derivative **12**, **13**, or **14** (0.12 mmol) and Raney Ni (W 2, 100 mg) in EtOAc (8 mL) was vigorously stirred for 1 h at room temperature under a hydrogen atmosphere with a slightly positive pressure. The mixture was filtered, and the filtrate was concentrated. The residue was purified by silica-gel column chromatography (hexane) to give **16**, **17**, or **18** and its *cis*-isomer. Separation of the stereoisomers was carried out with recycling preparative HPLC ($CHCl_3$ eluent).

1-{4-[Methyl(trifluoromethyl)amino]phenyl}-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (16a). This compound was prepared by Method A in a quantitative yield as colorless needles. Recrystallization from EtOH gave an analytical sample which showed phase transition temperature/°C: 20 S_B 173 Iso. R_f = 0.79 (hexane–Et_2O = 5 : 1). IR (KBr) 2957, 2919, 2849, 1617, 1518, 1447, 1345, 1267, 1204, 1150, 1092, 1059, 897, 833 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.78—1.55 (m, 15 H), 1.68—2.00 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 3.00 (q, J = 1 Hz, 3 H), 7.17 (s, 4 H); ^{19}F NMR (188 MHz) δ = −61.23 (s); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.3 (s), 33.6 (s), 34.6 (s), 36.4 (q, J = 2 Hz), 37.7 (s), 39.8 (s), 42.9 (s), 43.4 (s), 44.1 (s), 123.6 (q, J = 257 Hz), 125.1 (s), 127.4 (s), 140.4 (s), 146.1 (s); MS *m/z* (rel intensity) 383 (M^++2; 1), 382 (M^++1; 17), 381 (M^+; 66), 359 (13), 215 (13), 214 (48), 202 (13), 201 (91), 188 (62), 179 (18), 166 (10), 144 (5), 132 (7), 115 (10), 111 (10), 109 (15), 97 (17), 95 (11), 91 (17), 83 (57), 81(19), 77 (12), 69 (100), 67 (40). Found: C, 72.42; H, 8.91; N, 3.74%. Calcd for $C_{23}H_{34}F_3N$: C, 72.41; H, 8.98; N, 3.67%.

1-[4-{Ethyl(trifluoromethyl)amino}phenyl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (16b). Method A, quantitative yield, colorless needles. Phase transition temperature/°C: Cr 35 S_B 141 Iso (EtOH); R_f = 0.79 (hexane–Et_2O = 10 : 1). IR (KBr) 2919, 2849, 1516, 1449, 1381, 1271, 1196, 1144, 1098, 1055, 912, 813 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 1.07 (t, J = 7 Hz, 3 H), 0.80—1.56 (m 15 H), 1.68—2.01 (m, 8 H), 2.44 (tt, J = 3, 11 Hz, 1 H), 3.37 (q, J = 7 Hz, 2 H), 7.16 (s, 4 H); ^{19}F NMR (188 MHz) δ = −58.22 (s); ^{13}C NMR (50.3 MHz) δ = 13.8 (s), 14.4 (s), 20.1 (s), 30.2 (s), 30.4 (s), 33.7 (s), 34.6 (s), 37.7 (s), 39.8 (s), 43.0 (s), 43.5 (s), 43.9 (q, J = 1.3 Hz), 44.2 (s), 123.7 (q, J = 255 Hz), 126.9 (q, J = 1 Hz), 127.4 (s), 138.3 (s), 146.1 (s); MS *m/z* (rel intensity) 396 (M^++1; 8), 395 (M^+; 33), 373 (21), 228 (23), 215 (33), 202 (20), 193 (25), 180 (15), 158 (7), 132 (8), 115 (9), 109 (12), 97 (12), 91 (8), 83 (38), 81 (33), 79 (14), 69 (100), 67 (33). Found: C, 73.11; H, 9.51; N, 3.46%. Calcd for $C_{24}H_{36}F_3N$: C, 72.88; H, 9.17; N, 3.54%. Found: *m/z* 395.2792. Calcd for $C_{24}H_{36}F_3N$: M, 395.2800.

1-(*trans*-4-Propylcyclohexyl)-*trans*-4-[4-{propyl(trifluoromethyl)amino}phenyl]cyclohexane (16c). Method A, 94% yield. Colorless needles; phase transition temperature/°C: Cr 57 S_B 109 Iso (on heating), Iso 108 S_B −18 Cr (on cooling) (recryst. from EtOH); R_f = 0.62 (hexane). IR (KBr) 2923, 2851, 1514, 1451, 1381, 1358, 1293, 1258, 1240, 1190, 1148, 1057, 928, 837 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 6 H), 0.77—1.55 (m, 18 H), 1.64—2.00 (m, 7 H), 2.42 (tt, J = 3, 12 Hz, 1 H), 3.25 (dt, J = 1, 7 Hz, 2 H), 7.16 (s, 4 H); ^{19}F NMR (188 MHz) δ = −58.39 (s); ^{13}C NMR (50.3 MHz) δ = 11.0 (s), 13.8 (s), 20.1 (s), 21.5 (s), 30.2 (s), 30.4 (s), 33.7 (s), 34.6 (s), 37.7 (s), 39.9 (s), 43.0 (s), 43.5 (s), 44.2 (s), 50.9 (s), 123.7 (q, J = 254 Hz), 127.1 (q, J = 1 Hz), 127.4 (s), 138.6 (s), 146.6 (s); MS *m/z* (rel intensity) 410 (M^++1; 16), 409 (M^+; 58), 380 (13), 348 (8), 314 (7), 304 (9), 242 (29), 229 (23), 208 (15), 200 (29), 156 (12), 127 (13), 118 (16), 103 (18), 83 (23), 81 (36), 79 (20), 70 (28), 69 (100) 67 (58). Found: C, 72.77; H, 9.25; N, 3.33%. Calcd for $C_{25}H_{38}F_3N$: C, 73.31; H, 9.35; N, 3.42%. Found: *m/z* 409.2965. Calcd for $C_{25}H_{38}F_3N$: M, 409.2956.

1-[3-Fluoro-4-{methyl(trifluoromethyl)amino}phenyl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (17a). A 2 : 1 mixture of **17a** and *cis*-isomer (48 mg, quantitative) was obtained by Method B from **13a** (47 mg, 0.118 mmol). Separation of **17a** and its *cis*-iso-

mer was carried out by recycling preparative HPLC ($CHCl_3$ eluent) to give **17a** as colorless needles, phase transition temperature/°C: Cr 62 S_B 101 Iso (EtOH). R_f = 0.89 (hexane–EtOAc = 10 : 1). IR (KBr) 2924, 2851, 1580, 1518, 1449, 1409, 1348, 1296, 1196, 1148, 1084, 1061, 956, 941, 889, 826 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 0.60—1.52 (m, 15 H), 1.60—1.98 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 2.99 (q, J = 1 Hz, 3 H), 6.98—7.02 (m, 2 H), 7.16—7.35 (m, 1 H); ^{19}F NMR (188 MHz) δ = −61.47 (dm, J = 5 Hz), −120.75——121.63 (m); MS *m/z* (rel intensity) 399 (M^+; 22), 377 (8), 232 (4), 220 (3), 219 (24), 206 (26), 197 (11), 136 (8), 83 (42), 81 (25), 69 (100), 66 (35). Found: C, 68.99; H, 8.38; N, 3.55%. Calcd for $C_{23}H_{33}F_4N$: C, 69.15; H, 8.33; N, 3.51%.

1-[4-{Ethyl(trifluoromethyl)amino}-3-fluorophenyl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (17b). A 2.7 : 1 mixture of compound **17b** and its *cis*-isomer was prepared (15 mg, 20% yield) from **13b** (73 mg, 0.177 mmol) by Method B. Purification of **17b** was carried out by recycling preparative HPLC ($CHCl_3$ eluent) as colorless needles, phase transition temperature/°C: Cr 38 S_B 73 Iso (EtOH). R_f = 0.55 (hexane). IR (KBr) 2924, 2851, 1578, 1541, 1449, 1387, 1271, 1284, 1196, 1146, 1096, 1061, 954, 826 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.06 (t, J = 7 Hz, 3 H), 0.80—1.58 (m, 15 H), 1.65—1.96 (m, 8 H), 2.44 (tt, J = 3, 12 Hz, 1 H), 3.37 (q, J = 7 Hz, 2 H), 6.92—6.98 (m, 2 H), 7.16—7.20 (m, 1 H); ^{19}F NMR (188 MHz) δ = −58.48 (dm, J = 5 Hz), −121.11——121.24 (m); MS *m/z* (rel intensity) 414 (M^+; 9), 413 (M^+; 51), 391 (19), 233 (20), 220 (18), 218 (14), 211 (10), 192 (12), 109 (8), 97 (8), 95 (11), 83 (44), 81 (25), 79 (15), 69 (100). Found: *m/z* 413.2697. Calcd for $C_{24}H_{35}F_4N$: M, 413.2705.

1-[2-{Methyl(trifluoromethyl)amino}pyridin-5-yl]-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (18a). A 1 : 1 mixture of **18a** and its *cis*-isomer (92 mg, quantitative) was obtained by Method B using EtOH as a hydrogenation solvent from **14a** (92 mg, 0.24 mmol). *trans*-Isomer **18a** was separated by recycling preparative HPLC ($CHCl_3$ eluent) as colorless needles, phase transition temperature/°C: Cr 62 S_X 73 S_B 120 N 121 Iso (on heating), Iso 121 N 119 S_B 70 S_X 37 Cr (on coolong) (recryst. from EtOH). R_f = 0.67 (hexane : Et_2O = 5 : 1). IR (KBr) 2923, 2851, 1605, 1572, 1499, 1447, 1437, 1404, 1352, 1337, 1277, 1200, 1123, 1103, 1075, 1024, 830 cm^{-1}; ^1H NMR (200 MHz) δ = 0.87 (t, J = 7 Hz, 3 H), 0.75—1.53 (m, 15 H), 1.63—1.97 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 3.22 (q, J = 2 Hz, 3 H), 7.03 (ddd, J = 1, 2, 9 Hz, 1 H), 7.45 (dd, J = 3, 9 Hz, 1 H), 8.20 (dd, J = 1, 3 Hz, 1 H); ^{19}F NMR (188 MHz) δ = −58.36 (dq, J = 2, 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.4 (s), 20.0 (s), 30.1 (s), 30.2 (s), 32.5 (s), 33.6 (s), 34.4 (s), 37.6 (s), 39.8 (s), 41.3 (s), 42.8 (s), 43.4 (s), 114.1 (q, J = 4 Hz), 123.1 (q, J = 256 Hz), 136.1 (s), 137.9 (s), 146.5 (s), 152.0 (s); MS *m/z* (rel intensity) 383 (M^++1; 10), 382 (M^+; 38), 381 (5), 362 (11), 313 (36), 286 (20), 215 (10), 189 (22), 183 (10), 157 (9), 133 (25), 120 (11), 116 (14), 106 (28), 105 (14), 104 (14), 93 (14), 83 (25), 81 (16), 79 (27), 78 (18), 77 (15), 69 (100), 67 (43). Found: C, 69.17; H, 9.24; N, 7.36%. Calcd for $C_{22}H_{33}F_3N_2$: C, 69.08; H, 8.70; N, 7.32%. Found: *m/z* 382.2590. Calcd for $C_{22}H_{33}F_3N_2$: M, 382.2596.

1-[2-{Ethyl(trifluoromethyl)amino}pyridin-5-yl}-*trans*-4-(*trans*-4-propylcyclohexyl)cyclohexane (18b). A 1 : 1 mixture of **18b** and its *cis*-isomer (122 mg, 79% yield) was obtained from **14b** (155 mg, 0.39 mmol) by Method B. Separation of **18b** was carried out by recycling preparative HPLC ($CHCl_3$ eluent). Colorless needles; phase transition temperature/°C: Cr 50 S_B 100 Iso (on heating), Iso 98 S_B 48 Cr (on cooling) (recryst. from EtOH); R_f = 0.68 (hexane : Et_2O = 5 : 1). IR (KBr) 2917, 2851, 2361, 1610, 1568, 1495, 1449, 1387, 1329, 1281, 1260, 1183, 1132, 1096, 1069, 1024, 945, 926, 822, 785, 758 cm^{-1}; ^1H NMR (200 MHz) δ = 0.88 (t, J = 7 Hz, 3 H), 1.20 (t, J = 7 Hz, 3 H), 0.76—1.55 (m, 15 H), 1.63—1.96 (m, 8 H), 2.43 (tt, J = 3, 12 Hz, 1 H), 3.75—3.89 (m, 2 H), 6.99 (dm, J = 9 Hz, 1 H), 7.44 (dd, J = 2, 9 Hz, 1 H), 8.20 (dm, J = 2 Hz, 1 H); ^{19}F NMR (188 MHz) δ = −56.07 (dm, J = 2 Hz); ^{13}C NMR (50.3 MHz) δ = 14.2 (s), 14.4 (s), 20.4 (s), 30.1 (s), 30.2 (s), 33.6 (s), 34.4 (s), 37.6 (s), 39.8 (s), 40.6 (br), 41.3 (s), 42.8 (s), 43.4 (s), 114.0 (q, J = 4 Hz), 123.1 (q, J = 256 Hz), 136.0 (s), 137.5 (s), 146.6 (s), 151.1 (s); MS *m/z* (rel intensity) 396 (M^+; 5), 382 (30), 381 (100), 361 (30), 327 (36), 203 (13), 181 (12), 160 (11), 155 (28), 147 (11), 131 (10), 120 (9), 116 (9), 105 (13), 83 (15), 81 (19), 79 (13), 70 (17), 69 (72), 67 (34). Found: C, 69.33; H, 8.98; N, 6.90%. Calcd for $C_{23}H_{35}F_3N_2$: C, 69.67; H, 8.90; N, 7.06%. Found: *m/z* 396.2745. Calcd for $C_{23}H_{35}F_3N_2$: M, 396.2752.

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14 Miscibility test revealed that the texture was smectic B (hexatic) phase.

15 Compounds **23b** and **23c** were prepared by methylation of **21b** and **21c**, respectively; see Experimental Section.

16 The host nematic LCs mixture was composed of 3 compounds of a 4′-alkyl-4-cyanobiphenyl type and 6 compounds of a 4-alkyloxyphenyl *trans*-4-alkylcyclohexane-1-carboxylate type.

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