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Synthesis of a new troponoid liquid crystalline library on solid support

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This paper is dedicated to Emeritus Professor Soichi Misumi on the occasion of his 77th birthday

Abstract—Five types of troponoids including 40 molecules were prepared by means of palladium(0)-catalyzed carbonylation and successive acylation or benzoylation after immobilization of 2-methoxy-5-trifluoromethylsulfonyloxytropone on solid support. Four types of them showed mesophases. The final products have enough purity to detect their mesomorphic properties. © 2003 Elsevier Science Ltd. All rights reserved.

We are currently preparing new types of liquid crystals with a troponoid core.[1] One of the most characteristic points when we are using a tropone skeleton as a core of liquid crystals is the presence of the carbonyl group, which formed an intramolecular hydrogen bonding with the NH proton of an amide group at C-2[2] or an intermolecular hydrogen bonding with neighboring molecules. The typical structure of liquid crystals consists of a rigid core part and flexible side chains.[3] In order to prepare new types of liquid crystalline compounds, we usually select a core structure and introduce alkyl or alkoxy side chains into the core until liquid crystalline states appear. But it sometimes takes much time and efforts to find lead compounds.

Combinatorial chemistries[4] are widely applied in preparations of drugs, bioactive molecules,[5] and material sciences[6] such as catalysts, superconducting, magnetoresistive, ferroelectric, dielectric, and luminescent materials as well as zeolites, organic materials, and polymers. In this regard, it is thought that combinatorial chemistry is a suitable tool for searching lead compounds of new types of liquid crystals. Here, we report the first preparation of troponoid liquid crystals using solid support.

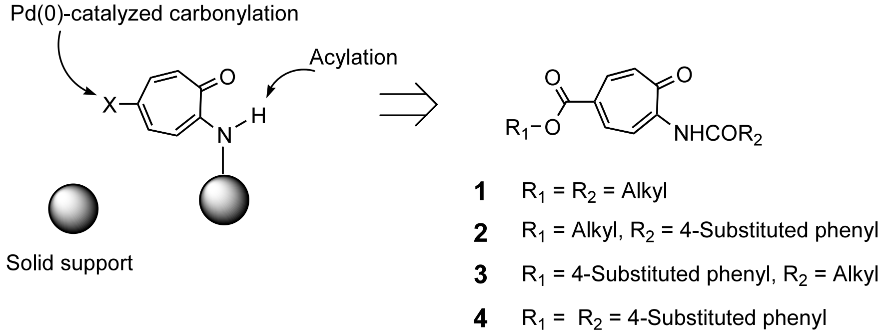

Figure 1. Synthetic strategy of troponoid liquid crystals.

Keywords: troponoid liquid crystals; solid-phase synthesis; Pd-catalyzed carbonylation.

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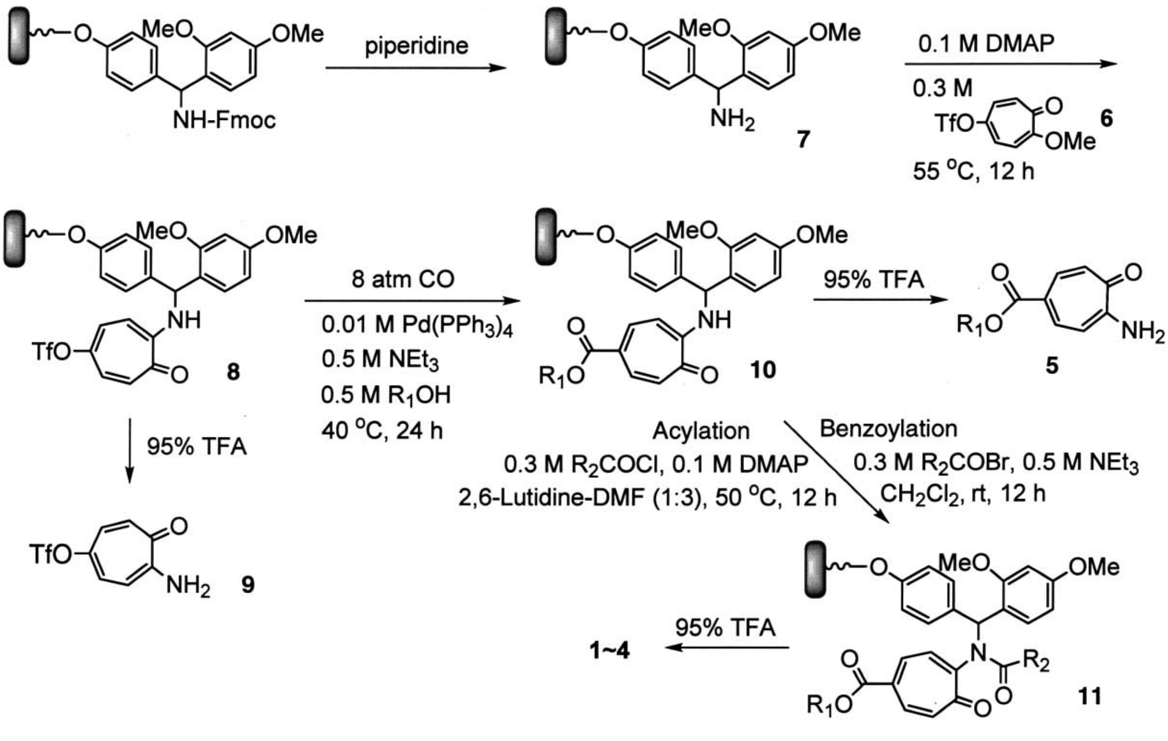
Our strategy for the synthesis of troponoid liquid crystals on solid support is shown in Figure 1. We select the route that the immobilized position on a solid support is on a trivalent nitrogen atom because an amide chromophore should be regenerated by removal from the support at the final stage. Secondly, we have already observed that the thermal stability of the mesophases of troponoid liquid crystals with an amide linking unit is higher than those of other linking units such as an ester one.[2] We adopted Pd(0)-catalyzed carbonylation at C-5 position and acylation or benzoylation on the nitrogen atom at C-2 position to lead to the target molecules. In this paper, we report preparations of five types of new troponoids (**1**–**5**) by means of palladium(0)-catalyzed carbonylation[7] of 2-methoxy-5-trifluoromethylsulfonyloxytropone (**6**)[8] and followed by acylation or benzoylation on solid support and cleavage from solid support by 95% TFA.

Reaction of amino linker **7** (Scheme 1), obtained from Fmoc-protected Rink resin by removal of the Fmoc group by means of piperidine, with triflate **6** in the



Scheme 1.

Table 1. Purity, conversion, and transition temperatures of compounds **1** and **2**

	R_1	R_2	Purity[a] (%)	Conv.[a] (%)	MS[b]	Transition temp. (°C)[c]
1a	C_4H_9	C_5H_{11}	82	98	320.2	Cr · 59 · Iso
1b		C_9H_{19}	59	75	376.2	Cr · 48 · Iso
1c		$C_{13}H_{27}$	75	88	432.3	Cr · 51 · Iso
1d	C_8H_{17}	C_5H_{11}	62	90	376.2	Cr · 58 · Iso
1e		C_9H_{19}	70	83	432.3	Cr · 63 · Iso
1f		$C_{13}H_{27}$	93	>99	488.4	Cr · 63 · Iso
1g	$C_{14}H_{29}$	C_5H_{11}	72	96	460.3	Cr · 73 · Iso
1h		C_9H_{19}	71	87	516.4	Cr · 65 · Iso
1i		$C_{13}H_{27}$	74	87	572.4	Cr · 67 · Iso
2a	C_4H_9	4-C_4H_9Ph	23	38	382.2	Cr · 63 · Iso
2b		4-C_8H_{17}Ph	42	94	438.6	Cr · 75 · Iso
2c	C_8H_{17}	4-C_4H_9Ph	58	98	438.3	Cr · 74 · Iso
2d		4-C_8H_{17}Ph	53	86	494.3	Cr · 85 · Iso
2e		4-$C_{12}H_{25}$OPh	62	78	566.4	Cr · 84 · SmC · 89 · Iso
2f	$C_{14}H_{29}$	4-C_4H_9Ph	35	77	522.4	Cr · 104 · Iso
2g		4-C_8H_{17}Ph	44	91	578.4	Cr · 117 · Iso
2h		4-$C_{12}H_{25}$OPh	48	83	650.1	Cr · 77 · SmC · 88 · Iso

[a] Purity and conversion were determined by HPLC (Inertsil C8-3, 0.1% HCOOH/H_2O and 0.1%/MeCN) with peak area (UV) at 254 nm.

[b] Electrospray-TOF MS data were recorded as $[M+H]^+$ on a Mariner TK3500 Biospectrometry.

[c] Cr, crystals; SmC, a smectic C phase; Iso, isotropic liquid. The transition temperatures were obtained during the first heating process.

Table 2. Purity, conversion, and transition temperatures of compounds **3** and **4**

	R_1	R_2	Purity (%)	Conv. (%)	MS	Transition temp. (°C)[a]
3a	4-C_4H_9OPh	C_5H_{11}	88	92	412.2	Cr · 91 · Iso
3b		C_9H_{19}	56	73	468.3	Cr · 87 · (SmC · 64 ·) Iso
3c		$C_{13}H_{27}$	72	80	524.3	Cr · 86 · (SmC · 64 ·) Iso
3d	4-C_8H_{17}OPh	C_5H_{11}	68	73	468.3	Cr · 86 · Iso
3e		C_9H_{19}	59	66	524.3	Cr · 120 · Iso
3f		$C_{13}H_{27}$	69	73	580.4	Cr · 99 · (SmC · 94 ·) Iso
3g	4-$C_{12}H_{25}$OPh	C_5H_{11}	52	67	524.3	Cr · 121 · Iso
3h		C_9H_{19}	69	73	580.4	Cr · 139 · Iso
3i		$C_{13}H_{27}$	73	88	636.5	Cr · 94 · (SmC · 78 ·) Iso
4a	4-C_4H_9OPh	4-C_4H_9Ph	68	79	474.2	Cr · 111 · SmC · 123 · N · 149 · Iso
4b		4-C_8H_{17}Ph	67	77	530.3	Cr · 124 · (SmC · 114 ·) N · 142 · Iso
4c	4-C_8H_{17}OPh	4-C_4H_9Ph	51	86	530.3	Cr · 101 · N · 142 · Iso
4d		4-C_8H_{17}Ph	57	80	586.3	Cr · 85 · SmC · 110 · N · 133 · Iso
4e		4-$C_{12}H_{25}$OPh	56	66	658.5	Cr · 108 · SmC · 162 · N · 168 · Iso
4f	4-$C_{12}H_{25}$OPh	4-C_4H_9Ph	43	91	586.4	Cr · 93 · SmC · 120 · N · 122 · Iso
4g		4-C_8H_{17}Ph	73	82	642.4	Cr · 100 · SmC · 134 · N · 151 · Iso
4h		4-$C_{12}H_{25}$OPh	66	75	714.5	Cr · 107 · SmC · 162 · N · 166 · Iso

[a] N, a nematic phase. ( ) means monotropic transition temperatures, which were obtained by cooling and subsequent fast heating processes.

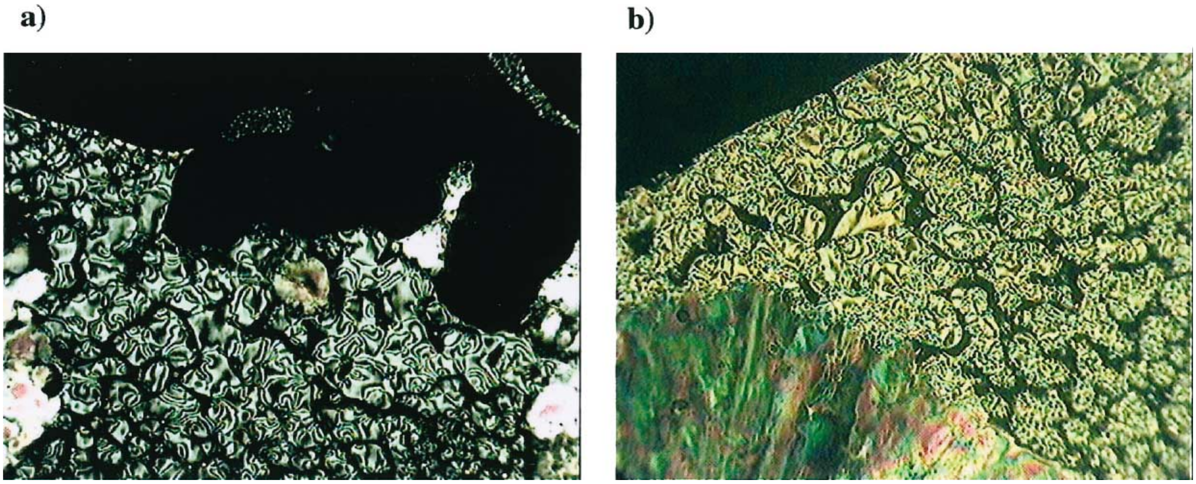


Figure 2. Textures of SmC phases of compound **3i**. (a) Texture of compound **3i** [Cr · 94 · (SmC · 78 ·) Iso] at 65°C synthesized on solid support. (b) Texture of compound **3i** [Cr · 98 · (SmC · 88 ·) Iso] at 72°C synthesized in liquid phase. Recrystallization is starting from the left corner at bottom.

presence of DMAP gave condensate **8**. The purity was determined to be >99% by transformation to 2-amino-5-trifluoromethylsulfonyloxytropone (**9**)[9] via TFA-treatment of **8**. Condensate **8** was converted to carbonylation product **10** in the presence of 0.01 M of tetrakis(triphenylphosphine)palladium under 8 atm of carbon monoxide with 0.5 M of alcohol in the presence of 0.5 M of NEt_3. The purity of **10** was determined to be 86–99% by transformation to 5-substituted 2-aminotropones (**5**) by TFA-treatment. Compounds **10** were reacted with 0.3 M of alkanoyl chlorides in the presence of 0.1 M of DMAP, 2,6-lutidine, and DMF at 50°C or 4-substituted benzoyl bromides in the presence of 0.5 M of NEt_3 to give amides **11**. Finally, cleavage of amides **11** with 95% TFA gave troponoid amides **1**–**4**. The purity of the products, checked by HPLC, is summarized in Tables 1 and 2. The structures of typical troponoid amides were determined by the direct comparison of NMR spectra with the authentic samples synthesized in liquid phase.[10]

The transition temperatures and the thermal behavior of compounds **1**–**4** were determined using a polarizing microscope equipped with a hot stage. Transition temperatures are summarized in Tables 1 and 2. Monocyclic troponoids **1** were not mesomorphic. Their transition temperatures were higher than those of 2,5-dialkanoyloxytropones[11] due to the presence of the amide group. Figure 2 shows the textures of compound **3i** synthesized in 73% purity in 88% conversion on solid support and prepared in liquid phase followed by purification using silica gel chromatography. Since photograph a) displayed schlieren textures and photograph b) schlieren and focal-conic fan textures, they are assigned to be smectic C (SmC) phases. Although the compounds obtained on solid support have lower transition temperatures than the authentic samples,[10] they showed the close thermal behaviors. This indicated that the compounds prepared by means of combinatorial synthesis have enough purity to check a primary survey. During preparation, we observed that synthetic intermediates **5** showed smectic A (SmA) phases when the alkoxy side chain on the phenyl ring is long.[12]

In conclusion, we prepared 40 molecules of two monocyclic systems (**1** and **5**), two two-ring systems (**2** and **3**), and a three-ring system (**4**). Among the products, only monocyclic **1** was not mesomorphic. Troponoids (**2**–**5**) with long alkyl chains showed mesomorphic properties. We could observe that combinatorial chemistry is a useful tool to search lead compounds in the research field of liquid crystals. The final products have enough purity to determine their mesomorphic properties although acylation and benzoylation processes reduced the purity of the products.

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9. Data for compound **9**. Found: C, 35.69; H, 2.26; N, 5.18%. Calcd for $C_8H_6F_3NO_4S$: C, 35.69; H, 2.25; N, 5.20%.
10. The transition temperatures and elemental analytic data of the authentic samples: **2h**: Found: C, 75.64; H, 9.72; N, 2.14%. Calcd for $C_{41}H_{63}NO_5$: C, 75.77; H, 9.77; N, 2.16%. Cr · 89 SmC · 90 · Iso, **3i**: Found: C, 75.42; H, 9.62; N, 2.26%. Calcd for $C_{40}H_{61}NO_5$: C, 75.55; H, 9.67; N, 2.20%. Cr · 98 · (SmC · 88 ·) Iso, and **4e**: Found: C, 74.83; H, 8.39; N, 2.11%. Calcd for $C_{41}H_{55}NO_6$: C, 74.85; H, 8.43; N, 2.13%. Cr · 116 · SmC · 186 · N · 189 · Iso.
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12. **5a** ($R_1 = C_4H_9$): Cr · 46 · Iso, **5b** ($R_1 = C_8H_{17}$): Cr · 60 · Iso, **5c** ($R_1 = C_{14}H_{29}$): Cr · 86 · Iso, **5d** ($R_1 =$ 4-C_4H_9OPh): Cr · 177 · Iso, **5e** ($R_1 =$ 4-C_8H_{17}OPh): Cr · 163 · (SmA · 154 ·) Iso, and **5f** ($R_1 =$ 4-$C_{12}H_{25}$OPh): Cr · 157 · SmA · 161 · Iso. A detailed packing model of the SmA phases will be published in a separate paper.