Synthesis of Novel Liquid Crystals which Possess *gem*-Difluorocyclopropane Moieties

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Synthesis of two types of novel chiral liquid crystal molecules that possess a *gem*-difluorocyclopropane moiety has been accomplished and their properties of liquid crystal were examined.

The utility of cyclopropane derivatives in the construction of a variety of cyclic and acyclic organic compounds has been amply demonstrated.[1,2] The substitution of a fluorine atom on an organic molecule can alter both its chemical reactivity and biological activity due to the strong electron-withdrawing nature of the fluorine, thus making it possible to create a new molecule that exhibits unique physical- or biological properties.[3] The synthesis of chiral mono-*gem*-diflurocyclopropane and bis-*gem*-diflurocyclopropane was accomplished using lipase technology[4–6] and we demonstrated the synthesis of oligo *gem*-difluocococyclopropanes using these cyclopropanes as building blocks.[7] Results of the CD spectroscopic analysis of 9-anthracencarboxylic acid diester of (*trans*,*trans*)-1,6-bishydroxylmethyl-2,2,5,5-tetrafluorobicyclopropane showed that tetrafluorobicyclopropane group exists with a helical shape configuration;[5] this seems to suggest that a unique helical shaped compound may be produced from *gem*-diflurocyclopropanes as building blocks. Recently, synthesis of unique ferroelectric liquid crystalline compounds which possess a 7,7-difluorospiro[2.0.2.1]heptane moiety has been reported by Miyazawa, de Meijere and co-workers.[8] Here we report the synthesis of novel liquid crystals which have *gem*-difluorocyclopropane moieties in their structures.

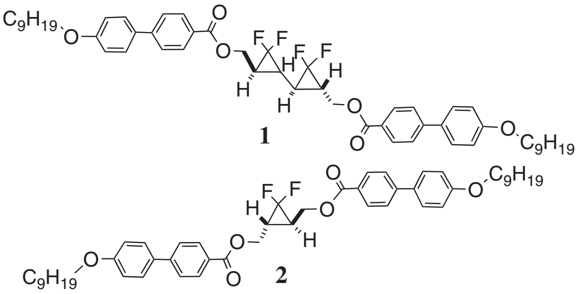
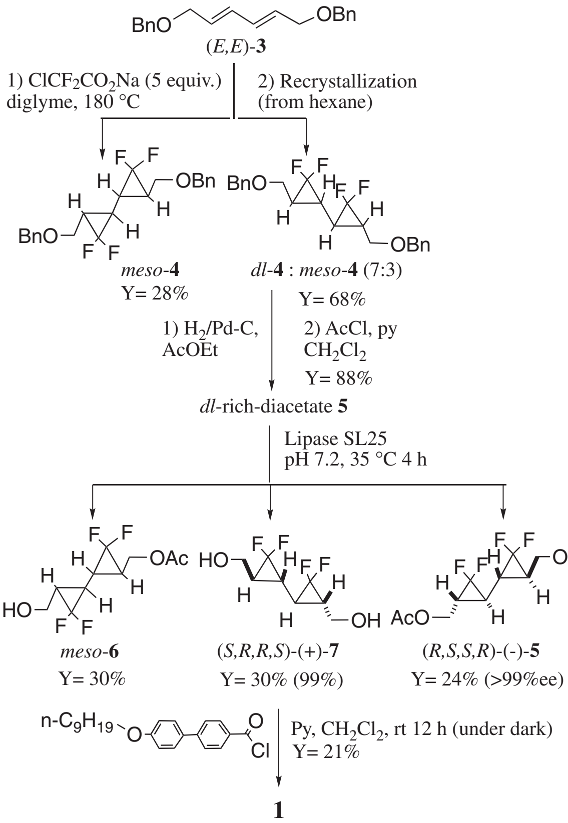


Figure 1. Liquid crystals derived from optically active *gem*-difluorocyclopropanes.

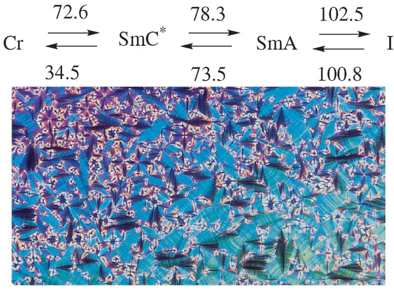


Scheme 1.

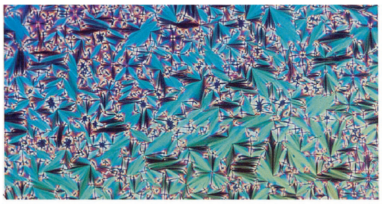
We synthesized two types of bis[4-(4-nonyloxyphenyl)-benzoate] derivatives, **1** and **2** (Figure 1), and determined their properties as liquid crystals. Synthesis of a novel liquid crystal compound **1** was accomplished following Scheme 1. (*E*,*E*)-1,6-Bisbenzyloxyhexa-2,4-diene (**3**) was treated with difluorocarbene produced from pyrolysis of sodium chlorodifluoroacetate to give the corresponding bis-*gem*-difluorocyclopropane **4** as a mixture of *meso*- and *dl*-form (1:1). We found that *meso*-**4** was crystallized preferentially from hexane; *dl*-rich bis-*gem*-difluorocyclopropane **4** (*dl*-**4**:*meso*-**4** = 6:4 up to 7:3) was thus obtained in 68% yield by removing *meso*-**4** by a single recrystallization from hexane and this was converted to the corresponding *dl*-rich-diacetate **5** in 88% yield. The lipase SL-catalyzed hydrolysis of *dl*-rich-diacetate **5** gave the diol (*S*,*R*,*R*,*S*)-**7** in 30% yield with 99% ee, and the unreacted diacetate (*R*,*S*,*S*,*R*)-**5** in 24% yield with >99% ee. The *meso*-isomer was obtained as the monoacetate **6** in 30% yield. This method is better than the previously reported one[5] because the enantiomeric excess of diol **7** reached 99% ee, while the highest % ee of the diol **7** was 92% ee when a 1:1 mixture of *dl*-**5** and *meso*-**5** was used as substrate for the lipase-catalyzed reaction.[5] To a dichloromethane (CH_2Cl_2) solution of 4-(4-nonyloxyphenyl)benzoylchloride were added a CH_2Cl_2 solution of (*S*,*R*,*R*,*S*)-**7** (99% ee) and pyridine (1.5 mL) and the mixture was stirred at 0 °C to rt for 1 day. The product was extracted into CH_2Cl_2 and the combined organic layer was washed with 1 M hydrochloric acid and dried over anhydrous sodium sulphate. The solvent was evaporated off, and the remaining material was purified by silica gel thin layer chromatography (ethyl acetate: hexane = 1:3) to give the ester **1** as a white powder; the powder was recrystallized from a mixed solvent (ethyl acetate: hexane = 1:1) to give 1-[4-(4-nonyloxyphenyl)benzoyloxylmethyl]-(1*S*,3*R*,4*R*,6*S*)-2,2,5,5-tetrafluorobicyclopropylmethyl 4-(4-nonyloxyphenyl)-benzoate (**1**) in 21% yield. Although we attempted to improve the chemical efficiency using several condensation protocols, no method was successful and we found that the esterification step had to be carried out under dark conditions because significant decomposition occurred under light conditions.[9] This is interesting because diester **1** was stable once it was purified. Optically active 1-[4-(4-nonyloxyphenyl)benzoyloxylmethyl]-(1*R*,3*R*)-2,2-difluorocyclopropylmethyl 4-(4-nonyloxyphenyl)-benzoate (**2**) was also prepared from >99% ee of (1*R*,3*R*)-1,3-bis(hydroxymethyl)-2,2-difluorocyclopropane[4] in a similar chemical yield. The phase transition temperatures of these three compounds are illustrated in Figure 2.

Compound **1** exhibited an unidentified smectic phase below the SmA phase (Figure 2, upper), while compound **2** showed only a SmA phase over a wide temperature range (Figure 2, below). The unidentified smectic phase showed a lined focal conic fan texture which was similar to that shown by a SmC* phase (Figure 2, upper), however, no spontaneous polarization was detected using a triangular-wave method under a field of ±80 $V_{p\text{-}p}$ in a 20 mm-thick cell. Although further investigation is required to determine the mesogenic properties of **1**, we tentatively assigned this form as SmC* phase. Because two *gem*-difluroocyclopropane rings have a helical shape, this configuration might be responsible for this unique physical property of compound **1**.

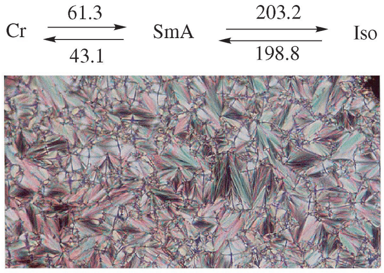
In summary, using optically active bis(hydroxymethyl)-*gem*-difluorocyclopropane compounds as building blocks, synthesis of two types of novel liquid-crystalline compounds has been accomplished. These compounds have some interesting properties, in particular, compound **1** showed a unique SmC* like phase, although no spontaneous polarization was caused by the triangular-wave method. We are hopeful that unique properties might be identified allowing further investigation of liquid crystals that have *gem*-difluorocyclopropane moieties.



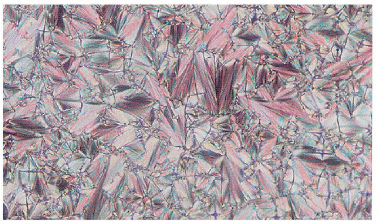
SmC* phase of **1** at 77 °C
(SmC*:Tentative characterization)



SmA pahse of **1** at 85 °C



SmA phase of **2** at 79 °C



SmA phase of **2** at 170 °C

Figure 2. Properties of liquid crystal **1** and **2**.

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References and Notes

1 For a recent review of this field see: M. J. Tozer and T. F. Herpin, *Tetrahedron*, **52**, 8619 (1996).
2 For recent examples see: a) A. G. M. Barrett and W. Tam, *J. Org. Chem.*, **62**, 7673 (1997). b) A. G. M. Barrett, D. Hamprecht, R. A. James, M. Ohkubo, A. J. P. White, and D. J. Williams, *J. Org. Chem.*, **66**, 2187 (2001) and references cited therein.
3 For reviews, see: a) J. T. Welch, *Tetrahedron*, **43**, 3123 (1987). b) G. Resnati, *Tetrahedron*, **49**, 9385 (1993).
4 T. Itoh, K. Mitsukura, and M. Furutani, *Chem. Lett.*, **1998**, 903.
5 K. Mitsukura, S. Korekiyo, and T. Itoh, *Tetrahedron Lett.*, **40**, 5739 (1999).
6 Kirihara and co-workers reported a successful synthesis of a different type of optically active *gem*-difluorocyclopropane using the lipase-technology: M. Kirihara, T. Takuwa, M. Kawasaki, H. Kakuda, S-i. Hirokami, and H. Takahata, *Chem. Lett.*, **1990**, 405.
7 a) T. Itoh, K. Mitsukura, N. Ishida, and K. Uneyama, *Org. Lett.*, **2**, 1431 (2000). b) T. Itoh, *J. Synth. Org. Chem. Jpn.*, **58**, 316 (2000). c) T. Itoh, N. Ishida, K. Mitsukura, and K. Uneyama, *J. Fluorine Chem.*, **63**, 112 (2001).
8 M. Miyazawa, D. S. Yufit, J. A. K. Howard, and A. de Meijere, *Eur. J. Org. Chem.*, **2000**, 4109.
9 Only a trace amount of desired product was obtained and an unidentified product lacking *gem*-difluorocyclopane rings was produced when the esterification was carried out under light. Direct condensation using EDC or DCC gave 1 in similar yields.

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