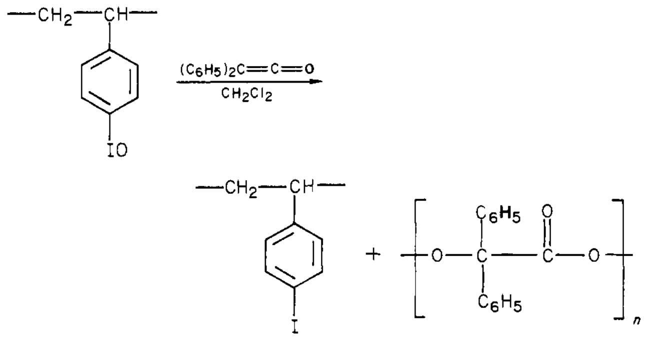
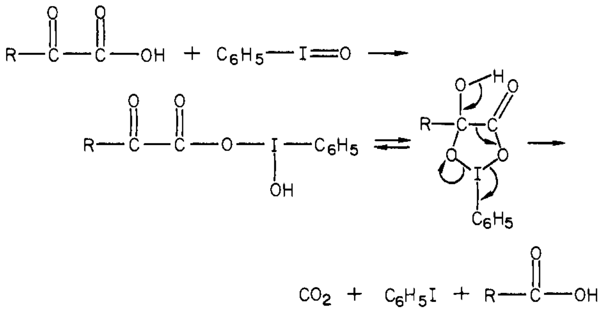


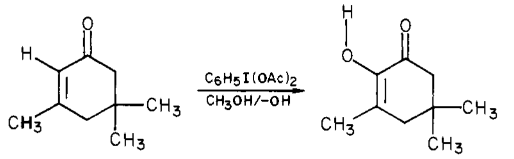
II, high-yield oxidative decarboxylation occurs, affording the lower homologous carboxylic acid, CO_2, and C_6H_5I. The mildness of these reaction conditions relative to H_2O_2 in base[17] which also effects oxidative decarboxylation is evident.

A reasonable mechanistic pathway for this reaction would involve intervention of the cyclic intermediate A formed either from a precursor mixed anhydride or from direct nucleophilic attack of $C_6H_5I{=}O$ upon the ketonic carbonyl group. We favor initial mixed-anhydride formation because $C_6H_5I{=}O$ is an effective catalyst for anhydride formation[18] (eq 4).

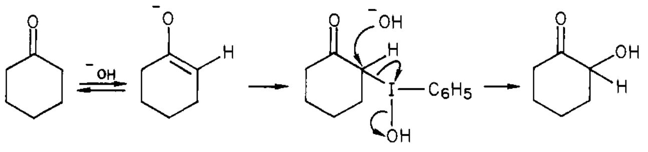

(4)

The cleavage reaction of mandelic acid to benzaldehyde and CO_2 with $C_6H_5I(OAc)_2$ is known[19] and a cyclic intermediate has been proposed in this case.[20]

Our next objective was to learn whether $C_6H_5I{=}O$ might serve as the synthetic equivalent of the hydroperoxide anion in the epoxidation of α,β-unsaturated ketones.[21] Reaction of isophorone (**1**) with $C_6H_5I(OAc)_2/{-}OH$[22] yielded the enolic 3,5,5-trimethyl-1,2-cyclohexanedione (**2**).[23]


1 **2**

This reaction does not involve the epoxy ketone as an intermediate since this compound is stable under the reaction conditions. α-Hydroxylation with $C_6H_5I(OAc)_2$ is not restricted to α,β-unsaturated ketones since cyclohexanone yields α-hydroxycyclohexanone (80%)[24] under the above conditions.[25] Although the overall stoichiometry conforms to eq 1, the source of the oxygen atom is possibly from the attachment of -OH upon the α-iodoso ester.



One may conclude that $C_6H_5I{=}O$ may function as an effective reagent for the transfer of an oxygen atom. Other known examples of this type of reaction are the conversion of a metal-carbenoid complex into a carbonyl product, $(EtO)(C_6H_5)W(CO)_5 \rightarrow C_6H_5COOEt$ (36%),[26] and the conversion of benzyl chloride into benzaldehyde.[18]

Acknowledgment. We thank the National Science Foundation for support of this work under Grant CHE-77-06617. A gift of bis(trifluoromethyl)ketene supplied by D. C. England of Central Research Experimental Research Department, E. I. du Pont de Nemours and Co., is gratefully acknowledged.

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[17] A. F. Holleman, *Recl. Trav. Chim. Pays-Bas*, **23**, 169 (1904); J. Boeseken, *ibid.*, **30**, 142 (1911); E. Weitz and A. Scheffer, *Ber. Dtsch. Chem. Ges. B*, **54**, 2327 (1921); H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Menlo Park, CA, 1972.

[18] T. Takaya, H. Enyo, and E. Imoto, *Bull. Chem. Soc. Jpn.*, **41**, 1032 (1968).

[19] (a) R. Criegee and H. Beuker, *Ann. Chem.*, **541**, 218 (1939); (b) K. Criegee, *Angew. Chem.*, **70**, 173 (1958); (c) C. A. Bunton, "Oxidation in Organic Chemistry", K. B. Wiberg, Ed., Academic Press, New York, 1965, p 402.

[20] H. Singh, *Curr. Sci.*, **10**, 233 (1970).

[21] E. P. Kohler, N. K. Richtmyer, and W. F. Hester, *J. Am. Chem. Soc.*, **53**, 205 (1931).

[22] Phenyliodoso diacetate is rapidly hydrolyzed to iodosobenzene in excess base.

[23] (a) R. L. Wasson and H. O. House, *J. Am. Chem. Soc.*, **79**, 1488 (1957); (b) P. S. Wharton and D. H. Bohlen, *J. Org. Chem.*, **26**, 3615 (1961).

[24] L. Bouveault and F. Chereau, *C. R. Hebd. Seances Acad. Sci.*, **142**, 1086 (1906).

[25] A series of substituted acetophenones undergo oxidation with $C_6H_5I{=}O/CH_3OH/OH$ to yield the corresponding acyloin; these results will be published in the future.

[26] C. M. Lukehart and J. V. Zeile, *J. Organomet. Chem.*, **97**, 421 (1975).

Synthetic Studies on Arene-Olefin Cycloadditions: Total Synthesis of (±)-α-Cedrene

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The meta- or 1,3-photoaddition of olefins to arenes[1] (eq 1) is unique among cycloaddition reactions. It proceeds from readily available materials under mild conditions with the development of three new rings and up to six stereocenters[2] and provides a cycloadduct which could serve as a precursor to a variety of synthetically important ring systems.[3] Since its discovery in 1966 by Wilzbach and Kaplan[4a] and Bryce-Smith, Gilbert, and Orger,[4b] the intermolecular version of this reaction has understandably attracted considerable interest[1] while the intramolecular variant, uncovered by Morrison[5] in his elegant studies on bichromophoric molecules,[1b,c] has received little attention.[6] In connection with


(1)

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† Fellow of the Alfred P. Sloan Foundation.

[1] For reviews pertinent to this and related arene photochemistry, see: (a) Wagner-Jauregg, T. *Synthesis* **1980**, 165. (b) Morrison, H. *Acc. Chem. Res.* **1979**, *12*, 383. (c) Morrison, H. *Org. Photochem.* **1979**, *4*, 143. (d) Bryce-Smith, D.; Gilbert, A. *Tetrahedron* **1976**, *32*, 1309. (e) *Ibid.* **1977**, *33*, 2459. (f) Noyes, W. A.; Al-Ani, K. E. *Chem. Rev.* **1974**, *74*, 29. (g) Bryce-Smith, D. *Pure Appl. Chem.* **1973**, *34*, 213. (h) *Ibid.* **1968**, *16*, 47. (i) Gilbert, A. *Photochemistry* **1970-1979**, *1-10*.

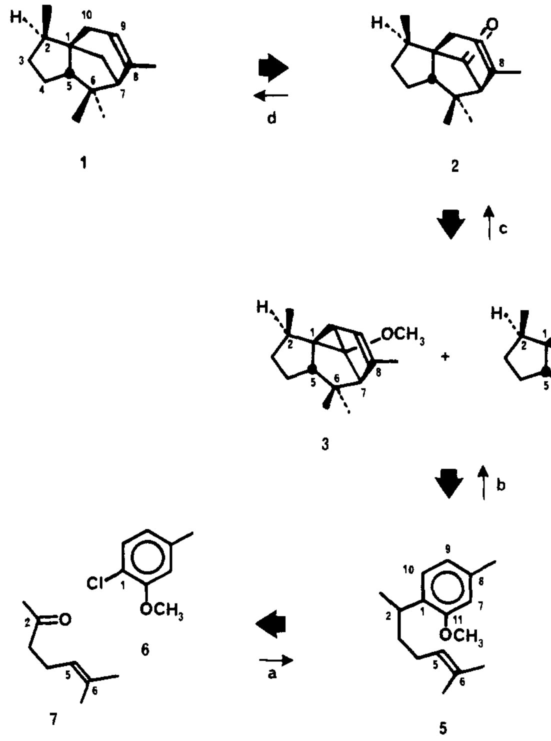
[2] These criteria, which define in part the inherent value of a method(ology), i.e., its capability to efficiently translate simple systems into the more complex, allow one to more fully appreciate the potential of this cycloaddition and its relationship to other more thoroughly explored and exploited cycloadditions such as the Diels-Alder reaction.

[3] The translation of the tricyclo[3.3.0.$0^{2,8}$]oct-3-ene cycloadduct into three-, five-, and seven-membered carbocycles, bicyclo[3.3.0]octanes, and bicyclo[3.2.1]octanes is possible (cf. ref 1).

[4] (a) Wilzbach, K. E.; Kaplan, L. *J. Am. Chem. Soc.* **1966**, *88*, 2066. (b) Bryce-Smith, D.; Gilbert, A.; Orger, B. H. *Chem. Commun.* **1966**, 512.

[5] (a) Morrison, H.; Ferree, W. *J. Chem. Soc., Chem. Commun.* **1969**, 268. (b) Ferree, W.; Grutzner, J.; Morrison, H. *J. Am. Chem. Soc.* **1971**, *93*, 5502.

Scheme I

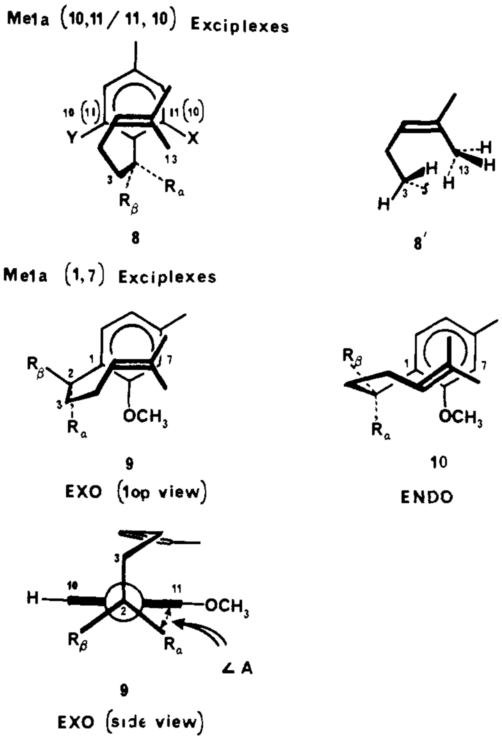


^{a} (a) **6** + Li/Et$_2$O; **7**; Li/NH$_3$; NH$_4$Cl; (b) *hν* (450-W Hanovia source; Vycor filter); (c) Br$_2$/CH$_2$Cl$_2$; *n*-Bu$_3$SnH; (d) NH$_2$NH$_2$, KOH/(HOCH$_2$CH$_2$)$_2$O, ca. 200 °C.

our studies on this process, we describe herein a total synthesis of (±)-α-cedrene (**1**)[7] which serves to define those features of the intramolecular cycloaddition which bear on its general use in synthesis.

The questions which necessarily arise in the implementation of this cycloaddition methodology center around standard issues: mode selectivity,[8] regioselectivity, endo/exo selectivity, and degree of stereoinduction. In the absence of such selectivity the magnitude of the synthetic problem becomes apparent: 168 cycloadducts could be formed in the *intermolecular* reaction involving an unsymmetrically trisubstituted arene and a similarly substituted alkene with one stereocenter, a common synthetic situation. The constraints imposed on the corresponding *intramolecular* reaction, as seen in the cedrene synthesis design (Scheme I: **5** → **3** + **4**),[9] considerably improve the potential outcome; only 36 cycloadducts are possible.[10] Our expectation that this situation could be further improved was based on the following analysis of the fate of arenealkene **5**[11] which serves, more generally, as an evaluation protocol for other synthetic applications. Mode selectivity is determined largely by olefin and arene substitution and may generally be predicted on the basis of the difference in ionization potential between the arene and olefin (ΔIP);[1e,13a,14] a small value for ΔIP, as expected in the case of arenealkene **5**, generally correlates with a preference for meta cycloaddition over ortho and para modes. Of the 24 meta cycloadducts which would be designated as allowed on the basis of this correlation, only those arising from addition of the olefin across alkyl or alkoxyl groups of the arene (i.e., involving centers C10, C11 and C1, C7 in the specific case of **5**)[9] were expected to be obtained due to the directing effect of these substituents as suggested by Srinivasan's pioneering studies[15] in this area. His finding that the closely related *intermolecular* addition of olefins to 2-methylanisole is "too slow to be detected"[15c] was not expected to offset the concentration advantage for the corresponding *intramolecular* addition[16] involving **5**. Of the remaining meta possibilities, addition to centers C1, C7 was considered to be more favorable than C10, C11 addition due to the unfavorable steric interactions (cf. **8** and **8′**: C3, C13 interaction, Scheme II) which would develop in the exciplex for the latter reaction. For the remaining C1, C7 meta addition, the endo/exo selectivity issue was expected to be resolved in favor of the exo orientation (cf. **9** and **10**) due, in part, to the better alignment of the exo exciplex (**9**) which is an understandable

Scheme II



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(6) Work in this area consists of Morrison's original study (cf. ref 5), its recent extension to polycyclics (Morrison, H.; Pallmer, M. *J. Chem. Soc., Chem. Commun.* **1978**, 558, *J. Org. Chem.* **1980**, *45*, 798), and studies by A. Gilbert and G. Taylor (*J. Chem. Soc., Chem. Commun.* **1978**, 129; **1979**, 229).

(7) For previous cedrene syntheses, see: Stork, G.; Clark, F. H. *J. Am. Chem. Soc.* **1955**, *77*, 1072; **1961**, *83*, 3114. Corey, E. J.; Girotra, N. N.; Matthew, C. T. *Ibid.* **1969**, *91*, 1557. Crandall, T. G.; Lawton, R. G. *Ibid.* **1969**, *91*, 2127. Demole, E.; Enggist, P.; Borer, C. *Helv. Chim. Acta* **1971**, *54*, 1845. Andersen, N. H.; Syrdal, D. D. *Tetrahedron Lett.* **1972**, 2455. Ohta, Y.; Hirose, Y. *Chem. Lett.* **1972**, 263. Corey, E. J.; Balanson, R. D. *Tetrahedron Lett.* *1973*, 3153. Lansbury, P. T.; Haddon, V. R.; Stewart, R. C. *J. Am. Chem. Soc.* **1974**, *96*, 896. Breitholle, E. G.; Fallis, A. G. *J. Org. Chem.* **1978**, *43*, 1964. Cedrene has also been prepared in connection with work on the synthesis of khusimone (Büchi, G.; Hauser, A.; Limacher, J. *Ibid.* **1977**, *42*, 3323).

(8) Arene–olefin cycloadditions may involve addition of the olefin to adjacent carbons of the aromatic ring (ortho or 1,2 mode), addition to positions 1 and 3 (meta or 1,3 mode), and addition to positions 1 and 4 (para or 1,4 mode).

(9) The site numbering which appears in structures **2**–**10** corresponds to that assigned to the positions in cedrene.

(10) While many more adducts may form, those deemed "possible" are only the relatively less-strained cycloadducts which arise from olefin addition to positions 1,11 and 1,10 (8 ortho adducts); 1,9, 10,11, and 1,7 (24 meta adducts); and 1,8 (4 para adducts).

(11) The use of an exciplex mechanistic model[1b,c,4,12] for this analysis is not intended to exclude the viability of other reaction paths.[1,13]

(12) Hirayama, F. *J. Chem. Phys.* **1965**, *42*, 3163. Birks, J. B. *Nature (London)* **1967**, *214*, 1187. Yang, N. C.; Yates, R. L.; Masnovi, J.; Shold, D. M.; Chiang, W. *Pure Appl. Chem.* **1979**, *51*, 173.

(13) For recent studies which extend the discussion of mechanism(s) presented in ref 1, see: (a) Bryce-Smith, D.; Foulger, B.; Forrester, J.; Gilbert, A.; Orger, B. H.; Tyrrell, H. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 55. (b) Dadson, M.; Gilbert, A.; Heath, P. *Ibid.* **1980**, 1314. (c) Gilbert, A.; Taylor, G. N.; Wahid bin Samsudin, M. *Ibid.* **1980**, 869.

(14) Bryce-Smith, D.; Gilbert, A.; Orger, B. H.; Tyrrell, H. M. *J. Chem. Soc., Chem. Commun.* **1974**, 334.

(15) (a) Srinivasan, R. *J. Am. Chem. Soc.* **1971**, *93*, 3555. (b) Cornelisse, J.; Merritt, V. Y.; Srinivasan, R. *Ibid.* **1973**, *95*, 6197. (c) Ors, J. A.; Srinivasan, R. *J. Org. Chem.* **1977**, *42*, 1321 (cf. ref 13b).

(16) In support of this concentration effect, irradiation of 6-(2-methoxyphenyl)-2-methylhex-2-ene, conducted as a prelude to the cedrene synthesis, proceeded with the facile formation of cycloadducts tentatively identified as the vinylcyclopropane isomers resulting from addition across the methoxy group.

consequence of its cis-fused bicyclo[3.3.0]octane-like character.[5,17] Finally, while the stereoinductive effect of the C-2 methyl could not be confidently predicted, it could be correlated with the angle A assumed in the formation and/or further reaction of the exciplex. For angles between 0 and 30°, a clear preference for a β-methyl orientation would be expected on the basis of this model.

The arenealkene **5** required for the cedrene study and, in general, a wide range of aryl-substituted alkenes are readily prepared in an exceptionally straightforward and preparatively useful manner by using the procedure of Hall and co-workers.[18] Thus, *in one operation*, 2-chloro-5-methylanisole was converted to its lithio derivative which was treated with 6-methylhept-5-en-2-one; condensation of ammonia into the resulting mixture and addition of excess lithium provided the starting material for the photolysis, **5**, in 74% yield (distilled).[19] Irradiation of **5** in pentane (~0.13 M; milligram to multigram quantities) at room temperature using Vycor-filtered light from a 450-W Hanovia source proceeded with the gradual disappearance of **5** [NMR ($CDCl_3$) δ 3.80 (OCH_3)] and concomitant appearance of largely, if not exclusively, two cycloadducts [NMR ($CDCl_3$) δ 3.36 and 3.32 (OCH_3)]. After complete disappearance of starting material (ca. 12 h), these compounds (**3**:**4** = 1:1)[20] were isolated in a combined yield of 65%. Subsequent treatment of this mixture with 4 N HCl/acetone (1:4)[15c] provided cedren-11-one (**2**) along with its Δ^9 isomer. A more effective method for effecting the conversion of both cycloadducts to a single product (**2**) involved treatment of a mixture of **3** and **4** with bromine (1 equiv in CH_2Cl_2) which by electrophilic attack on the double bond induced cleavage of the cyclopropane ring and resulted in the formation of only 10α- and 10β-bromocedren-11-one. The absence of the corresponding tertiary allylic bromides in this reaction is an expected consequence of the facile rearrangement of such intermediates to the more stable secondary allylic bromide isomers. After removal of solvent in vacuo, the bromides were treated without isolation with neat tri-*n*-butyltin hydride (2 equiv) to give **2** in 59% overall yield.[21] Wolff–Kishner reduction of this product provided (±)-α-cedrene (**1**), free of any isomeric product, as established by its comparison with commercially available cedrene.[22] This structural assignment was further afforced by spectroscopic comparison of the crystalline alcohols obtained from the hydroboration of racemic and natural α-cedrene.[23]

The facility and effectiveness of this chemistry (cedrene in four steps), the increasing predictability of such arene–olefin cycloadditions, and the number and variety of potential applications of this methodology beyond this initial exercise in total synthesis clearly suggest a significant role for this cycloaddition in organic synthesis. Further studies are in progress.

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[17] The interactions between centers 5 and 1 and 6 and 7 in the exciplex or transition state may be considered as part of a five-membered ring. The resulting cis-fused bicyclo[3.3.0]octane-like subunit would be expected to be more stable than the trans isomer by analogy with the parent ring system (cf. Barret, J. W.; Linstead, R. P. *J. Chem. Soc.* **1936**, 611).

[18] Hall, S. S.; McEnroe, F. J. *J. Org. Chem.* **1975**, *40*, 271 and references cited therein.

[19] All new compounds reported were homogeneous by TLC and gave satisfactory IR and NMR spectra and exact mass and combustion analyses. Analytical data for selected intermediates are as follows. Photoadduct **3**: partial NMR ($CDCl_3$) δ 5.37 (m, 1 H), 3.31 (s, 3 H), 2.53 (br s, 1 H), 1.77 (d, J = 1.5 Hz, 3 H), 1.00 (s, 3 H), 0.89 (s, 3 H), 0.88 (d, J = 6.8 Hz, 3 H); mass spectrum (70 eV), *m/e* (% base peak) 232 (M^+, 18), 149 (B), 110 (21); high-resolution mass spectrum *m/e* 232.18274 (calcd 232.18271). Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.61; H, 10.56. Photoadduct **4**: partial NMR ($CDCl_3$) δ 5.55 (br s, 2 H), 3.35 (s, 3 H), 1.32 (s, 3 H), 1.02 (d, J = 6.9 Hz, 3 H), 1.00 (s, 6 H); mass spectrum (70 eV) 232 (M^+, 16), 149 (B), 110 (19); high-resolution mass spectrum, *m/e* 232.18272 (calcd 232.18271). Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.69; H, 10.49. Ketone **2**: partial NMR ($CDCl_3$) δ 5.36 (m, 1 H), 2.08 (s, 1 H), 1.73 (q, J = 1.9 Hz, 3 H), 1.16 (s, 3 H), 0.87 (s, 3 H), 0.85 (d, J = 7.1 Hz, 3 H); IR (film) 1735 cm^{-1}; mass spectrum (70 eV) *m/e* 218 (M^+, 84), 163 (69), 135 (B); high-resolution mass spectrum, *m/e* 218.16709 (calcd 218.16706). Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.46; H, 10.20.

[20] That these compounds are related as vinylcyclopropane isomers was demonstrated by the thermal (GC: T_{inj} = 250 °C; T_{col} = 190 °C or pyrolysis at 205–230 °C) conversion of **4** to **3** (cf.: Simpson, J. M.; Rickey, H. G. *Tetrahedron Lett.* **1973**, 2545 and ref 1).

[21] This product was accompanied by what is tentatively assigned as cedradienone (13%).

[22] Aldrich, puriss.

[23] Brown, H. C.; Acharya, S. P. *J. Org. Chem.* **1970**, *35*, 196. Racemic cedranol: mp 114.5–116 °C; natural cedranol: mp 141–145 °C (lit. 145–147 °C).

A Type I Aqueous Cholesteric Lyomesophase

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Cholesteric thermotropic liquid crystals[1] have a twist or helical axis, and using opposed optical enantiomers, they exist with the helices of opposite sign.[1-3] The relationship to nematic states is important, and it was shown that equimolar mixtures of opposite enantiomers of cholesteric mesophases became nematic.[1,4] Nematic phases align spontaneously in magnetic fields, and thermotropic nematics align almost exclusively with the director along the magnetic field direction.[5] This has been called type I behavior, i.e., $\Delta\chi > 0$ for the mesophase.[6] Very recently a new class of nematic thermotropic mesophases was discovered with type II properties[7] (with $\Delta\chi < 0$); they align with the director perpendicular to the magnetic field. It is clear that these magnetic susceptibility properties, besides providing a classification for nematic materials, imply that there are two corresponding types of cholesteric mesophases.[3] Balanced enantiomeric mixtures can yield type I or type II nematics, depending on the type of cholesteric phases from which they are derived.[8] While type II nematics of the thermotropic variety were only recently discovered,[7] as far as the authors are aware, there is only one report of true aqueous lyotropic type II cholesteric.[8] While Radley and Saupe[9] and Diehl and Tracey[10] added small amounts of optically active compounds to nematic lyotropic systems to induce a twist, these workers did not prepare a racemic amphiphile mixture to regenerate the balanced nematic system, and the majority of the amphiphiles in the micelle were not chiral compounds.

Some years ago it was shown that two cholesteric forms must exist,[3] the distinction being that the helical axis, although always

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[†] Visiting Professor, Universidade de Sao Paulo, Brazil, from 1967 to present.

[1] Frank, F. C. *Discuss. Faraday Soc.* **1958**, *25*, 19.

[2] Friedel, M. G. *Ann. Phys.* **1922**, *18*, 273.

[3] Sackmann, E.; Meiboom, S.; Snyder, L. C.; Meixner, A. E.; Dietz, R. E. *J. Am. Chem. Soc.* **1968**, *90*, 3567.

[4] Sackmann, E.; Meiboom, S.; Snyder, L. C. *J. Am. Chem. Soc.* **1968**, *90*, 2183.

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[6] Radley, K.; Reeves, L. W.; Tracey, A. S. *J. Phys. Chem.* **1976**, *80*, 174.

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[8] Acimis, M.; Reeves, L. W. *Can. J. Chem.* **1980**, *58*, 1533.

[9] Radley, K.; Saupe, A. *Mol. Phys.* **1978**, *35*, 1405.

[10] Diehl, P.; Tracey, A. S. *FEBS Lett.* **1975**, *59*, 131.

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