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Note

The Synthesis of the Fluorescence Probe, 12-(1-Pyrenyl)dodecanoic Acid

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The synthesis of the fluorescence probe, 12-(1-pyrenyl)dodecanoic acid, was accomplished by the Wittig reaction between 1-pyrenecarboxaldehyde and 10-methoxycarbonyldecyltriphenylphosphonium bromide, followed by hydrogenation of the unsaturated product and hydrolysis of methyl ester. The Wittig reaction was carried out with sodium methoxide in dimethylformamide, at room temperature and under a N_2 atmosphere. This reacion yielded a mixture of 53% *trans* and 47% *cis* isomers of 12-(1-pyrenyl)-11-dodecenoate, as determined by pulsed Fourier transform NMR technique.

In the course of fluorescence studies with micellar systems[1,2] and biological macromolecules[3–5] which have been carried out in this Laboratory, it became necessary to develop new fluorescence probes which would enable selective positioning of a fluorophore within the investigated systems. Bearing in mind that pyrene (Py) attached to a long chain of an acid figures both as surfactant analog and as an analog of biological fatty acid, we prepared 12-(1-pyrenyl)-dodecanoic acid (**4**).

The synthesis was accomplished by the Wittig reaction[6] between 1-pyrenecarboxaldehyde and phosphonium bromide (**1**), followed by hydrogenation of the unsaturated product (**2**) and hydrolysis of methyl ester (**3**).

If unpurified phosphonium bromide (**1**) was used in the first step, as suggested by Yoshi et al.[7], complex mixtures were obtained. We succeeded to prepare pure phosphonium salt (**1**) in good yield, which enabled an easier purification of the product from the Wittig reaction.

The Wittig reaction was carried out with sodium methoxide in dimethylformamide[7], at room temperature and under a N_2 atmosphere. This reaction yielded a mixture of 53% *trans* and 47% *cis* isomers of methyl 12-(1-pyrenyl)-11-dodecenoate (**2**). This ratio was determined by analysis of the NMR spectra, where it was possible clearly to distinguish ABX_2 systems of *trans* and *cis* protons in the mixture ($—CH_A=CH_B—CH_{2X}—$). Pulsed Fourier transform NMR technique enabled better resolution and lower signal-to-noise ratio compared to conventional NMR technique.

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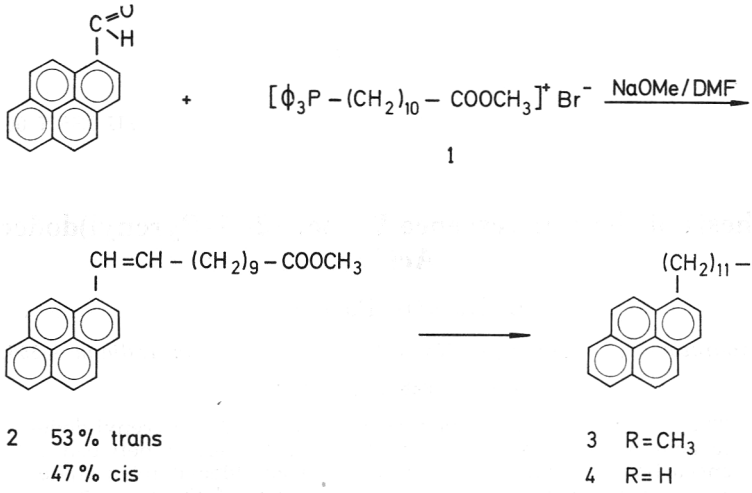

EXPERIMENTAL

Melting points were determined on a Kofler melting point apparatus and are uncorrected. The purity of the products was confirmed by TLC using silica gel plates and benzene or benzene/ether as solvents. The ^{1}H nuclear magnetic resonance spectra were recorded on a Varian XL-100 spectrometer using pulse radiofrequency power and Fourier transform analysis. Optical absorption spectra were taken with a Cary 14 spectrophotometer and infrared spectra on a Perkin-Elmer Infracord 137 spectrophotometer.

Methyl 11-bromoundecanoate was prepared according to the general esterification procedure of Kadaba[8] as applied by Schore and Turro[9].

10-Methoxycarbonyldecyltriphenylphosphonium Bromide (1)

A solution of triphenylphosphine (9.6 g; 36.5 mmol) and methyl 11-bromoundecanoate (10.2 g; 36.5 mmol) in dry benzene (60 ml) was refluxed for 4 days. After evaporation of the solvent, the residual yellow gum was recrystallized from methylene chloride/ethyl acetate and white solid was obtained; yield 12.1 g (61%); m. p. 120—122 °C.

IR (KBr): ν_{max} = 2950, 2890 (C—H); 1730 (C=O); 768, 753, 726, 695 cm^{-1} (arom.).

^{1}H-NMR ($CDCl_3$): δ = 7.45—7.85 (m, 15 H_{arom}), 3.47—3.86 (m, 5 H, PCH_2, OCH_3), 2.23 (br t, 2 H, CH_2CO, J = 6.5 Hz), 1.07—1.76 ppm (m, 16 H chain).

Anal. $C_{30}H_{38}O_2PBr$ (541.5) calc'd.: C 66.54; H 7.07; P 5.72; Br 14.76%
found: C 66.33; H 7.00; P 5.53; Br 14.93%

Methyl 12-(1-pyrenyl)-11-dodecenoate (2)

10-Methoxycarbonyldecyltriphenylphosphonium bromide (5 g; 9.2 mmol), previously dried in vacuo at 30 °C, was dissolved in dry dimethylformamide (15 ml), and the solution added dropwise to a stirred solution of sodium (0.21 g; 9.2 mmol) in anhydrous methanol (10 ml) in a N_2 atmosphere. After the addition of 1-pyrenecarboxaldehyde (2.07 g; 9 mmol) in dry dimethylformamide (15 ml), the solution was stirred 4 days at room temperature, in dark and under N_2 atmosphere. The solvent was evaporated in vacuo and the residue triturated with ether/hexane (350 ml). Insoluble material was separated by filtration, the filtrate evaporated in vacuo and the crude product was chromatographed on a silica gel column with benzene. Elution of the pale yellow zone gave a pale yellow oily product with yield of 2.44 g (65.5%). For elemental analysis the compound was purified by thin layer chromatography on silica gel with benzene.

IR (KBr): ν_{max} = 2980, 2900 (C—H); 1735 (C=O), 850, 763, 713 cm^{-1} (arom.).

UV (*n*-hexane): λ_{max} 356 sh (ε = 23500), 343 (29100), 329 sh (18900), 277 (28600), 268 sh (19100), 244 (42600), 238 sh (31400), 223 nm (18000).

^{1}H-NMR ($CDCl_3$): δ = 7.74—8.35 (m, 9 H_{arom}), 7.32 br d, 1 H, PyC*H*=CH, *trans*, J_{AB} = 15 Hz), 7.06 (br d, 1 H, PyC*H*=CH, *cis*, J_{AB} = 12 Hz), 6.35 (sex., 1 H, PyCH= =C*H*CH_2, *trans*, J_{AB} = 15 Hz, J_{BX} = 6.5 Hz), 5.96 (sex., 1 H, PyCH=C*H*CH_2, *cis* J_{AB} = 12 Hz, J_{BX} = 7.5 Hz), 3.60 (s, 3 H, OCH_3), 2.03—2.47 (m, 4 H, CH=CHCH_2, CH_2CO), 1.00—1.78 ppm (m, 14 H, chain).

Anal. $C_{29}H_{32}O_2$ (412.55) calc'd.: C 84.42; H 7.82%
found: C 84.37; H 7.78%

Methyl 12-(1-pyrenyl)dodecanoate (**3**)

Methyl 12-(1-pyrenyl)-11-dodecenoate (2.7 g; 6.55 mmol) in anhydrous ether (40 ml) was hydrogenated at 2 atm* at room temperature in the presence of 10% palladium on charcoal (0.1 g) for 0.5 h. After evaporation of the filtrate, a white solid product was obtained, which was recrystallized from petroleum ether; yield 2.32 g, (86%); m. p. 63—65 °C.

IR (KBr): ν_{max} = 2980, 2900 (C—H); 1740 (C=O), 845, 711 cm^{-1} (arom).

UV (*n*-hexane): λ_{max} = 342.5 (ε = 42800), 326 (26800), 312 (10800), 276 (54000), 264 (24400), 254 (10400), 243 (72000), 233.5 nm (39200).

^{1}H-NMR ($CDCl_3$): δ = 7.86—8.40 (m, 9 H_{arom}), 3.65 (s, 3 H, OCH_3), 3.30 (t, 2 H, $PyCH_2$, J = 7.5 Hz), 2.27 (br t, 2 H, CH_2CO, J = 7.5 Hz), 1.16—1.93 ppm (m, 18 H, chain).

Anal. $C_{29}H_{34}O_2$ (414.56) calc'd.: C 84.01; H 8.27%
found: C 84.06; H 8.45%

12-(1-Pyrenyl)dodecanoic acid (**4**)

Methyl 12-(1-pyrenyl)dodecanoate (1.67 g; 4 mmol) was suspended in methanol (5 ml) and 10% NaOH aqueous (2 ml) and refluxed for 1 hour. The solvent was evaporated in vacuo and the residue acidified with 10% HCl (~ 30 ml) to pH 2. The resulting suspension was stirred for 0.5 hour, filtered and pale tan coloured solid recrystallized from acetone; yield 1.33 g (83%); m. p. 123—125 °C.

1R (KBr): ν_{max} = 2950, 2880 (C—H), 1700 (C=O), 846, 712 cm^{-1} (arom).

UV (95% ethanol): λ_{max} = 343 (ε = 38400), 326 (24960), 312.5 (10160), 276 (48000), 265 (21600), 255 (9600), 243 (64800), 234 nm (35600).

^{1}H-NMR ($CDCl_3$): δ = 7.84—8.38 (m, 9 H_{arom}), 3.32 (t, 2 H, $PyCH_2$, J = 7.5 Hz), 2.32 (t, 2 H, CH_2CO, J = 7.5 Hz), 0.90—2.00 ppm (m, 18 H, chain).

Anal. $C_{28}H_{32}O_2$ (400.54) calc'd.: C 83.96; H 8.05%
found: C 84.08; H 7.87%

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REFERENCES

1. M. Grätzel and J. K. Thomas, *The Application of Fluorescence Techniques to the Study of Micellar Systems*, in E. L. Wehry (Ed.), *Modern Fluorescence Spectroscopy*, Vol 2, Plenum Press, New York, N. Y. 1976, p. 168.
2. J. K. Thomas, *Acc. Chem. Res.* **10** (1977) 133.
3. S. Cheng, J. K. Thomas, and C. F. Kulpa, *Biochemistry* **13** (1974) 1135.
4. M. Wong, C. F. Kulpa, and J. K. Thomas, *Biochim. Biophys. Acta* **426** (1976) 711.
5. H. E. Edwards, J. K. Thomas, G. R. Burleson, and C. F. Kulpa, *Biochim. Biophys. Acta* **448** (1976) 451.

* 1 atm = 101 325 Pa

6. U. Schöllkopf, *Carbonyl-Olefin Transformation Using Triphenylphosphinemethylenes. The Wittig Reaction,* in W. Först (Ed.), *Newer Methods of Preparative Organic Chemistry,* Vol. 3, Academic Press, New York and London, 1964, p. 111.
7. B. S. Joshi, N. Viswanathan, D. H. Gawad, and W. von Philipsborn, *Helv. Chim. Acta* **58** (1975) 1551.
8. P. K. Kadaba, *Synthesis* (1971) 316.
9. N. E. Schore and N. Y. Turro, *J. Amer. Chem. Soc.* **97** (1975) 2488.

SAŽETAK

Priprema fluorescentne probe, 12-(1-pirenil)dodekanske kiseline

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Wittigovom reakcijom pripremljena je 12-(1-pirenil)dodekanska kiselina polazeći od 1-pirenkarboksaldehida; za tim je slijedila hidrogenacija nezasićenog produkta i hidroliza metilnog estera. Wittigova reakcija provedena je s natrijevim metoksidom u dimetilformamidu na sobnoj temperaturi i u atmosferi dušika. Sadržaj od 47% *cis*- i 53% *trans*-izomera nezasićenog estera određen je pulsnom NMR-tehnikom s Fourier-ovim transformacijama.

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