Phospholipids Chiral at Phosphorus (1982-92). Tsai then brought the chiral phosphates into the field of phospholipids and developed a unique field "phospholipids chiral at phosphorus". His lab synthesized various chirally labeled phospholipids, and used them to study the mechanism of several enzymatic reactions, as well as biophysical properties of these lipid analogs at different physical states using various physical techniques. An important finding is that Rp and Sp isomers of the phosphorothioate analog of phospholipids display different physical properties at liquid crystal phases, which suggests that stereospecific interactions involving the phosphate group of phospholipids is an important factor in determining the physical properties of membranes. This subfield is truly one developed and dominated exclusively by Tsai and his associates. It also led Tsai into two projects involving phospholipid enzymology: phospholipase A_2 and PI-specific phospholipase C. Publications: #22, 23, 24, 25, 26, 29, 30, 31, 32, 35, 38, 39, 40, 41, 42, 45, 46, 49, 50, 51, 55, 58, 59, 61, 66, 68, 69, 77. (Note: Some papers can belong to PLA2, PLC, or PLD; the last has not been mentioned as a separate category.)

1. "Phospholioids Chiral at Phosphorus. 1. Stereochemistry of Transphosphatidylation Catalyzed by Phospholipase D," K. Bruzik and M.-D. Tsai, *J. Am. Chem. Soc. 104*, 863-865 (1982).

2. "Phospholipids Chiral at Phosphorus. 2. Preparation, Property and Application of Chiral Thiophospholipids" K. Bruzik, S. M. Gupte and M.-D. Tsai, *J. Am. Chem. Soc. 104*, 4682-4684 (1982).

3. "Phospholipids Chiral at Phosphorus. 3. Preparation and Spectral Properties of Chiral Thiophospholipids," K. Bruzik, R.-T. Jiang and M.-D. Tsai, *Biochemistry 22*, 2478-2486 (1983).

4. "Phospholipids Chiral at Phosphorus. 4. Could Membranes be Chiral at Phosphorus?" M.-D. Tsai, R.-T. Jiang and K. Bruzik, *J. Am. Chem. Soc. 105*, 2478-2480 (1983)

5. "Phospholipids Chiral at Phosphorus. Synthesis, Absolute Configurations and Applications." K. Bruzik, R.-T. Jiang and M.-D. Tsai, *Phosphorus and Sulfur 18*, 369-372 (1983).

6. "Phospholipids Chiral at Phosphorus. 5. Synthesis and Configurational Analysis of Chiral [^{17}O,^{18}O]-Phosphatidylethano1amine." K. Bruzik and M.-D. Tsai, *J. Am. Chem. Soc. 106,* 747-754 (1984).

7. "Phospholipids Chiral at Phosphorus. 6. Synthesis of Chiral Phosphatidylcholine and Stereochemistry of Phospholipase D." K. Bruzik and M.-D. Tsai, *Biochemistry 23*, 1656-1661 (1984).

8. "Phospholipids Chiral at Phosphorus. 7. Absolute Configuration of Chiral Thiophospholipids and Stereochemistry of Phospholipase D." R.-T. Jiang, Y.-J. Shyy, and M.-D. Tsai, *Biochemistry 23*, 1661-1667 (1984).

9. "Phospholipids Chiral at Phosphorus. 8. Properties of Small Unilamellar Vesicles of Chiral Thiophosphatidylcholine." T.-C. Tsai, R.-T. Jiang and M.-D. Tsai, *Biochemistry 23*, 5564-5570 (1984).

10. "Phospholipids Chiral at Phosphorus. 9. Use of Chiral Thiophosphatidylcholine to Study the Metal-Binding Properties of Bee Venom Phospholipase A_2,"T.-C. Tsai, J. Hart, R.-T. Jiang, K. Bruzik and M.-D. Tsai, *Biochemistry 24*, 3180-3188 (1985).

11. "Phospholipids Chiral at Phosphorus. 10. Use of Chiral Thiophospholipids to Study the Mechanism of Phospholipase A_2," M.-D. Tsai, K. Bruzik, J. Hart, R.-T. Jiang, T. Rosario-Jansen, T.-C. Tsai and D. A. Wisner, in "*Mechanisms of Enzymatic Reactions: Stereochemistry*", P. A. Frey, ed., Elsevier, 115-126 (1986).

12. "Phospholipids Chiral at Phosphorus. 11. FT-IR Study on the Gel-Liquid Crystalline Transition of Chiral Thiophosphatidylcholine," S.-B. Chang, J. O. Alben, D. A. Wisner and M.-D. Tsai, *Biochemistry 25*, 3435-3440 (1986).

13. "Phospholipids Chiral at Phosphorus. 12. Configurational Effect on the Thermotropic Properties of Chiral Dipalmitoylthiophosphatidylcholine," D. A. Wisner, T. Rosario-Jansen and M.-D. Tsai, *J. Am. Chem. Soc., 108*, 8064-8068 (1986).

14. "Phospholipids Chiral at Phosphorus. 13. Stereochemical Comparison of Phospholipase A_2, Lecithin-Cholesterol Acyl Transferase, and Platelet-Activating Factor," T. Rosario-Jansen, H. J. Pownall, J. P. Noel and M.-D. Tsai, *Phosphorus and Sulfur 30*, 601-604 (1987).

15. Phospholipids Chiral at Phosphorus. 14. Stereochemical Effects on the Thermotropic Properties of Thiophosphatidylcholines and Thiosphingomyelins,"M.-D. Tsai, K. S. Bruzik, D. Wisner and S.-H. Liu, in"*Biophosphates and Their Analogues, Synthesis, Structure, Metabolism and Activity*", K.S. Bruzik and W.J. Stec, Eds., Elsevier, pp. 561-570 (1987).

16. "Phospholipids Chiral at Phosphorus. 15. Steric Course of Phosphatidylserine Synthases from E. coli and Yeast," C. R. H. Raetz, G. M. Carman, W. Dowhan, R.-T. Jiang, W. Waszkuc, W. Loffredo and M.-D. Tsai, *Biochemistry, 26* 4022-4027 (1987).

17. "A Calorimetric Study of the Thermotropic Behavior of Pure Sphingomyelin Diastereomers," K. S. Bruzik and M.-D. Tsai, *Biochemistry 26*, 5364-5368 (1987).

18. "Steric Course of the Reaction Catalyzes by Phosphatidylserine Decarboxylase from E. coli". Z. No, C. R. Sanders II, W. Dowhan, and M.-D. Tsai, *Bioorg. Chem., 16*, 184-188 (1988).

19. "Phospholipids Chiral at Phosphorus. 16. Synthesis and Stereospecificity of Phosphorothioate Analogues of Platelet Activating Factor." T. Rosario-Jansen, R.-T. Jiang, D. J. Hanahan, and M.-D. Tsai, *Biochemistry, 27*, 4619-4624 (1988).

20. "Phospholipids Chiral at Phosphorus. 17. Characterization of the Subgel Phase of Thiophosphatidylcholines by Use of X-Ray Diffraction, P-31 NMR, and FT-IR". H. E. Sarvis, W. Loffredo, R. A. Dluhy, L. Hernqvist, D. A. Wisner, and M.-D. Tsai, *Biochemistry, 27*, 4625-4631 (1988).

21. "Phospholipids Chiral at Phosphorus. 18. Stereochemistry of Phosphatidylinositide-specific Phospholipase C". G. Lin and M.-D. Tsai, *J. Am. Chem. Soc., 111*, 3099-3101 (1989).

22. "Phospholipids Chiral at Phosphorus. 19. Synthesis and Configurational Assignment of Phosphorothioate Analogues of Phosphatidylserine". W. M. Loffredo and M.-D. Tsai, *Bioorg. Chem. 18*, 78-84 (1990).

23. "Phospholipids Chiral at Phosphorus. 20. Stereochemical Mechanism of the Reactions Catalyzed by Phosphatidylinositide-Specific Phospholipase C From *Bacillus Cereus* and Guinea Pig Uterus". G. H. Lin, C. F. Bennett, and M.-D. Tsai, *Biochemistry 29*, 2747-2757 (1990).

24. "Phospholipids Chiral at Phosphorus. 22. Synthesis of Chiral Dioleoylthiophosphatidylcholine and Stereospecificity of Lecithin-Cholesterol Acyltransferase". T. Rosario-Jansen, H. Pownall, R.-T. Jiang, and M.-D. Tsai, *Bioorg. Chem*. *18*, 179-184 (1990).

25. "Phospholipids Chiral at Phosphorus. 23. Dramatic Effect of P-Chirality on the Deuterium NMR Properties of the Choline Head Group of Phospholipids in the Liquid Crystalline Phase". W. M. Loffredo, R.-T. Jiang, and M.-D. Tsai, *Biochemistry 29*, 10912-10918 (1990).

26. "Phospholipids Chiral at Phosphorus. 21. Phospholipase Stereospecificity at Phosphorus." K. Bruzik and M.-D. Tsai, *Methods Enzymol. 197*, 258-269 (1991).

27. "Phospholipids Chiral at Phosphorus. 24. Phosphorothioate Analogs of Phosphatidylinositol and Inositol 1,2-Cyclic Phosphate: Applications to the Mechanism of Phospholipase C." K. Bruzik, G. Lin, and M.-D. Tsai, *ACS Symp. Series 463*, 172-185 (1991).

28. "Phospholipids Chiral at Phosphorus. 25. Stereochemical Mechanism for the Formation of Inositol 1-Phosphate Catalyzed by Phosphatidylinositide-Specific Phospholipase C." K. S. Bruzik, A. M. Morocho, D.-Y. Jhon, S. G. Rhee, and M.-D. Tsai, *Biochemistry 31*, 5183-5193 (1992).