

## REFERENCES

- Andrawis, A. and Kanh, V. 1986. Effects of methimazole on the activity of mushroom tyrosinase. Biochem. J. 235: 91-96.
- Aviram, M. 2004. Flavonoids-rich nutrients with potent antioxidant activity prevent atherosclerosis development: the licorice example. International Congress Series. 1262: 320-327.
- Beall, H., Pranker, R. and Sloan, K. 1994. Transdermal delivery of 5-fluorouracil (5-FU) through hairless mouse skin by 1-alkyloxycarbonyl-5-FU prodrugs: physicochemical characterization of prodrugs and correlations with transdermal delivery. Int. J. Pharm. 111: 223-233.
- Belinky, P. A., Aviram, M., Fuhrman, B., Rosenblat, M. and Vaya, J. 1998. The antioxidative effects of the isoflavan glabridin on endogenous constituents of LDL during its oxidation. Atherosclerosis. 137: 49-61.
- Belinky, P. A., Aviram, M., Mahmood, S. and Vaya, J. 1998. Structural aspects of the inhibitory effect of glabridin on LDL oxidation. Free Radic. Biol. Med. 24: 1419-1429.
- Blumberg, J. B. and Halpner, A. D. 1999. Antioxidant status and function: Relationships to aging and exercise. In Papas, A. M. (ed.), Antioxidant status, diet, nutrition and health. USA: CRC Press.
- Britton, G. 1983. The biochemistry of natural pigments. London: Cambridge University Press.
- Bundgaard, H., Hansen, A. B. and Larsen, C. 1979. Pro-drugs as drug delivery systems III. Esters of malonic acids as novel pro-drug types for barbituric acids. Int. J. Pharm. 3: 341-353.
- Chen, J. S., Wei, C. I. and Marshall, M. R. 1991. Inhibition mechanism of kojic acid on polyphenol oxidase. J. Agric. Food Chem. 39: 1897-1901.
- Chen, Q. X., Ke, L. N., Song, K. K., Huang, H. and Liu, X. D. 2004. Inhibitory effects of hexylresorcinol and dodecylresorcinol on mushroom (*Agaricus bisporus*) tyrosinase. The Protein Journal. 23: 135-141.
- Chen, Q. X. and Kubo, I. 2002. Kinetics of mushroom tyrosinase inhibition by quercetin. J. Agric. Food Chem. 50: 4108-4112.

- Engelmann, F. M., Rocha, S. V. O., Toma, H. E., Araki, K. and Baptista, M. S. 2007. Determination of *n*-octanol/water partition and membrane binding of cationic porphyrins. Int. J. Pharm. 329: 12-18.
- Espin, J. C., Jolivet, S. and Wichers, H. J. 1998. Inhibition of mushroom polyphenol oxidase by agaritine. J. Agric. Food Chem. 46: 2976-2980.
- Espin, J. C. and Wichers, H. J. 1999. Slow-binding inhibition of mushroom (*Agaricus bisporus*) tyrosinase isoforms by tropolone. J. Agric. Food Chem. 47: 2638-2644.
- Espin, J. C. and Wichers, H. J. 2001. Effect of captopril on mushroom tyrosinase activity *in vitro*. Biochim. Biophys. Acta. 1544: 289-300.
- Fu, B., Li, H., Wang, X., Lee, F. S. C. and Cui, S. 2005. Isolation and identification of flavonoids in licorice and a study of their inhibitory effects on tyrosinase. J. Agric. Food Chem. 53: 7408-7414.
- Fukai, T., Marumo, A., Kaitou, K., Kanda, T., Terada, S. and Nomura, T. 2002a. Antimicrobial activity of licorice flavonoids against methicillin-resistant *Staphylococcus aureus*. Fitoterapia. 73: 536-539.
- Fukai, T., Marumo, A., Kaitou, K., Kanda, T., Terada, S. and Nomura, T. 2002b. Anti-*Helicobacter pylori* flavonoids from licorice extract. Life Sci. 71: 1449-1463.
- Fukai, T., Satoh, K., Nomura, T. and Sakagami, H. 2003. Preliminary evaluation of antinephritis and radical scavenging activities of glabridin from *Glycyrrhiza glabra*. Fitoterapia. 74: 624-629.
- Fukai, T., Sheng, C. B., Horikoshi, T and Nomura, T. 1996. Isoprenylated flavonoids from underground parts of *Glycyrrhiza glabra*. Phytochemistry. 43: 1119-1124.
- Funayama, M., Arakawa, H., Yamamoto, R., Nishino, T., Shin, T. and Murao, S. 1995. Effects of  $\alpha$ - and  $\beta$ -arbutin on activity of tyrosinases from mushroom and mouse melanoma. Biosci. Biotech. Biochem. 59: 143-144.
- van Gelder, C. W. G., Flurkey, W. H. and Wichers, H. J. 1997. Sequence and structural features of plant and fungal tyrosinases. Phytochemistry. 45: 1309-1323.
- Goetghebeur, M. and Kermasha, S. 1996. Inhibition of polyphenol oxidase by copper-melalothionein from *Aspergillus niger*. Phytochemistry. 42: 935-940.

- Haraguchi, H., Yoshida, N., Ishikawa, H., Tamura, Y., Mizutani, K. and Kinoshita, T. 2000. Protection of mitochondrial functions against oxidative stresses by isoflavans from *Glycyrrhiza glabra*. J. Pharm. Pharmacol. 52: 219-223.
- Iida, K., Hase, K., Shimomura, K., Sudo, S., Kadota, S. and Namba, T. 1995. Potent inhibitors of tyrosinase activity and melanin biosynthesis from *Rheum officinale*. Planta Med. 61: 425-428.
- Inagi, T., Muramatsu, T., Nagai, H. and Terada, H. 1981. Mechanism of indomethacin partition between *n*-octanol and water. Chem. Pharm. Bull. 29: 2330-2337.
- Jun, N., Hong, G. and Jun, K. 2007. Synthesis and evaluation of 2',4',6'-trihydroxychalcones as a new class of tyrosinase inhibitors. Bioorg. Med. Chem. 15: 2396-2402.
- Kanazawa, M., *et al.* 2003. Isoliquiritigenin inhibits the growth of prostate cancer. European Urology. 43: 580-586.
- Kent, U. M., Aviram, M., Rosenblat, M. and Hollenberg, P. F. 2002. The licorice root derived isoflavan glabridin inhibits the activities of human cytochrome P450s 3A4, 2B6, and 2C9. Drug Metab. Dispos. 30: 709-715.
- Khan, M. T. H., Khan, S. B. and Ather, A. 2006. Tyrosinase inhibitory cycloartane type triterpenoids from the methanol extract of the whole plant of *Amberboa ramosa* Jafri and their structure-activity relationship. Bioorg. Med. Chem. 14: 938-943.
- Khan, M. T. H. *et al.* 2006. Tyrosinase inhibition studies of cycloartane and cucurbitane glycosides and their structure-activity relationships. Bioorg. Med. Chem. 14: 6085-6088.
- Khatib, S., Nerya, O., Musa, R., Shmuel, M., Tamir, S. and Vaya, J. 2005. Chalcones as potent tyrosinase inhibitors: the importance of a 2,4-substituted resorcinol moiety. Bioorg. Med. Chem. 13: 433-441.
- Kim, B. Y. *et al.* 2005. Ketorolac amide prodrugs for transdermal delivery: stability and *in vitro* rat skin permeation studies. Int. J. Pharm. 293: 193-202.
- Kim, Y. J. and Uyama, H. 2005. Tyrosinase inhibitors from natural and synthetic sources: structure, inhibition mechanism and perspective for the future. Cell. Mol. Life Sci. 62: 1707-1723.

- Kinoshita, T., Kajiyama, K., Hiraga, Y., Takahashi, K., Tamura, Y. and Mizutani, K. 1996a. Isoflavan derivatives from *Glycyrrhiza glabra* (licorice). Heterocycles. 43: 581-588.
- Kinoshita, T., Kajiyama, K., Hiraga, Y., Takahashi, K., Tamura, Y. and Mizutani, K. 1996b. The isolation of new pyrano-2-arylbenzofuran derivatives from the root of *Glycyrrhiza glabra*. Chem. Pharm. Bull. 44: 1218-1221.
- Kinoshita, T., Saitoh, T. and Shibata, S. 1976. The occurrence of an isoflavene and the corresponding isoflavone in licorice root. Chem. Pharm. Bull. 24: 991-994.
- Kobayashi, Y., Kayahara, H., Tadasa, K., Nakamura, T. and Tanaka, H. 1995. Synthesis of amino acid derivatives of kojic acid and their tyrosinase inhibitory activity. Biosci. Biotech. Biochem. 59: 1745-1746.
- Kobayashi, Y., Kayahara, H., Tadasa, K., and Tanaka, H. 1996. Synthesis of *N*-kojic-amino acid and *N*-kojic-amino acid-kojiolate and their tyrosinase inhibitory activity. Bioorg. Med. Chem. Lett. 6: 1303-1308.
- Kubo, I., Chen, Q. X. and Nihei, K. 2003. Molecular design of antibrowning agents: antioxidative tyrosinase inhibitors. Food Chem. 81: 241-247.
- Kubo, I and Kinst-Hori, I. 1998a. Tyrosinase inhibitors from anise oil. J. Agric. Food Chem. 46: 1268-1271.
- Kubo, I and Kinst-Hori, I. 1998b. Tyrosinase inhibitors from cumin. J. Agric. Food Chem. 46: 5338-5341.
- Kubo, I and Kinst-Hori, I. 1999a. Flavonols from saffron flower: tyrosinase inhibitory activity and inhibition mechanism. J. Agric. Food Chem. 47: 4121-4125.
- Kubo, I and Kinst-Hori, I. 1999b. 2-Hydroxy-4-methoxybenzaldehyde: a potent tyrosinase inhibitor from African medicinal plants. Planta Med. 65: 19-22.
- Kubo, I., Kinst-Hori, I., Chaudhuri, S. K., Kubo, Y., Sánchez, Y. and Ogura, T. 2000. Flavonols from *Heterotheca inuloides*: tyrosinase inhibitory activity and structural criteria. Bioorg. Med. Chem. 8: 1749-1755.
- Kubo, I., Kinst-Hori, I., Ishiguro, K., Chaudhuri, S. K., Sánchez, Y. and Ogura, T. 1994. Tyrosinase inhibitory flavonoids from *Heterotheca inuloides* and their structure functions. Bioorg. Med. Chem. Lett. 4: 1443-1446.
- Kubo, I., Kinst-Hori, I., Kubo, Y., Yamagiwa, Y., Kamikawa, T. and Haraguchi, H. 2000. Molecular design of antibrowning agents. J. Agric. Food Chem. 48: 1393-1399.



- Kumaran, A. and Karunakaran, R. J. 2006. Antioxidant and free radical scavenging activity of an aqueous extract of *Coleus aromaticus*. Food Chem. 97: 109-114.
- Kusano, A. *et al.* 1991. Inhibition of adenosine 3',5'-cyclic monophosphate phosphodiesterase by flavonoids from licorice roots and 4-arylcoumarins. Chem. Pharm. Bull. 39: 930-933.
- Lee, H. S. 2002. Tyrosinase inhibitors of *Pulsatilla cernua* root-derived materials. J. Agric. Food Chem. 50: 1400-1403.
- Lerner, A. B. and Fitzpatrick, T. B. 1950. Biochemistry of melanin formation. Physiol. Rev. 30: 91-126.
- Li, C. Y., Lee, E. J. and Wu, T. S. 2004. Antityrosinase principles and constituents of the petals of *Crocus sativus*. J. Nat. Prod. 67: 437-440.
- Likhitwitayawuid, K., Sornsute, A., Sritularak, B. and Ploypradith, P. 2006. Chemical transformations of oxyresveratrol (*trans*-2,4,3',5'-tetrahydroxystilbene) into a potent tyrosinase inhibitor and a strong cytotoxic agent. Bioorg. Med. Chem. Lett. 16: 5650-5653.
- Likhitwitayawuid, K. and Sritularak, B. 2001. A new dimeric stilbene with tyrosinase inhibitory activity from *Artocarpus gomezianus*. J. Nat. Prod. 64: 1457-1459.
- Masamoto, Y., Ando, H., Murata, Y., Shimoishi, Y., Tada, M. and Takahata, K. 2003. Mushroom tyrosinase inhibitory activity of esculetin isolated from seeds of *Euphorbia lathyris* L. Biosci. Biotech. Biochem. 67: 631-634.
- Mitscher, L. A., Park, Y. H. and Clark, D. 1980. Antimicrobial agents from higher plants: antimicrobial isoflavanoids and related substances from *Glycyrrhiza glabra* L. var *typica*. J. Nat. Prod. 43: 259-269.
- Nerya, O., Vaya, J., Musa, R., Izrael, S., Ben-Arie, R. and Tamir, S. 2003. Glabrene and isoliquiritigenin as tyrosinase inhibitors from licorice roots. J. Agric. Food Chem. 51: 1201-1207.
- Nihei, K. I., Yamakiwa, Y., Kamikawa, T. and Kubo, I. 2004. 2-Hydroxy-4-isopropylbenzaldehyde, a potent partial tyrosinase inhibitor. Bioorg. Med. Chem. Lett. 14: 681-683.
- No, J. K. *et al.* 1999. Inhibition of tyrosinase by green tea components. Life Sci. 65: PL241-246.
- Pietta, P. G. 2000. Flavonoids as antioxidants. J. Nat. Prod. 63: 1035-1042.

- Redden, P. R., Melanson, R. L., Douglas, J.-A. E. and Dick, A. J. 1999. Acyloxymethyl acidic drug derivatives: *in vitro* hydrolytic reactivity. Int. J. Pharm. 180: 151-160.
- Rosenblat, M. *et al.* 1999. Macrophage enrichment with the isoflavan glabridin inhibits NADPH oxidase-induced cell-mediated oxidation of low density lipoprotein: a possible for protein kinase C. J. Biol. Chem. 274: 13790-13799.
- Saitoh, T., Kinoshita, T. and Shibata, S. 1976. New isoflavan and flavanone from licorice root. Chem. Pharm. Bull. 24: 752-755.
- Sanchez-Ferrer, A. , Rodriguez-Lopez, J. N. , Garcia-Canovas, F. and Garcia-Carmona, F. 1995. Tyrosinase: a comprehensive review of its mechanism. Biochim. Biophys. Acta. 1247: 1-11.
- Seo, S. Y., Sharma, V. K. and Sharma, N. 2003. Mushroom tyrosinase: recent prospects. J. Agric. Food Chem. 51: 2837-2853.
- Shi, Y., Chen, Q. X., Wang, Q, Song, K. K. and Qiu, L. 2005. Inhibitory effects of cinnamic acid and its derivatives on the diaphenolase activity of mushroom (*Agaricus bisporus*) tyrosinase. Food Chem. 92: 707-712.
- Shiino, M., Watanabe, Y. and Umezawa, K. 2001. Synthesis of *N*-substituted *N*-nitrosohydroxylamines as inhibitors of mushroom tyrosinase. Bioorg. Med. Chem. 9: 1233-1240.
- Shiino, M., Watanabe, Y. and Umezawa, K. 2003. Synthesis and tyrosinase inhibitory activity of novel of *N*-hydroxybenzyl-*N*-nitrosohydroxylamines. Bioorg. Chem. 31: 129-135.
- Shimizu, K. *et al.* 2003. Indole-3-carbaldehyde: a tyrosinase inhibitor from fungus YL185. J. Wood Sci. 49: 349-354.
- Shimizu, K., Kondo, R. and Sakai, K. 2000. Inhibition of tyrosinase by flavonoids, stilbenes and related 4-substituted resorcinols: structure-activity investigations. Planta Med. 66: 11-15.
- Shimizu, K., Kondo, R., Sakai, K., Lee, S. H. and Sato, H. 1998. The inhibitory components from *Artocarpus incisus* on melanin biosynthesis. Planta Med. 64: 408-412.
- Shin, N. H. *et al.* 1998. Oxyresveratrol as the potent inhibitor on dopa oxidase activity of mushroom tyrosinase. Biochem. Biophys. Res. Commun. 243: 801-803.

- Shirota, S., Miyazaki, K., Aiyama, R., Ichioka, M. and Yokokura, T. 1994. Tyrosinase inhibitors from crude drugs. Biol. Pharm. Bull. 17: 266-269.
- Somjen, D., Knoll, E., Vaya, J. Stern, N. and Tamir, S. 2004. Estrogen-like activity of licorice root constituents: glabridin and glabrene, in vascular tissues *in vitro* and *in vivo*. J. Steroid Biochem. Mol. Biol. 91: 147-155.
- Son, S. and Lewis, B. A. 2002. Free radical scavenging and antioxidative activity of caffeic acid amide and ester analogues: structure-activity relationship. J. Agric. Food Chem. 50: 468-472.
- Song K. K., Huang, H., Han, P., Zhang, C. L., Shi, Y. and Chen, Q. X. 2006. Inhibitory effects of *cis*- and *trans*-isomers of 3,5-dihydroxystilbene on the activity of mushroom tyrosinase. Biochem. Biophys. Res. Commun. 342: 1147-1151.
- Song, K. K., Lin, J. F. and Chen, Q. X. [2005, M D]. Inhibitory effects of 4-isopropylsalicylaldehyde on mushroom tyrosinase. Available from : <http://www.sciencedirect.com/doi:10.1016/j.foodchem.2005.08.021>.
- Song, S. *et al.* 2007. Syntheses of hydroxyl substituted 2-phenyl-naphthalenes as inhibitors of tyrosinase. Bioorg. Med. Chem. Lett. 17: 461-464.
- Tamir, S. *et al.* 2000. Estrogenic and antiproliferative properties of glabridin from licorice in human breast cancer cells. Cancer Res. 60: 5704-5709.
- Wang, b., Zhang, H., Zheng, A. and Wang, W. 1998. Coumarin-based prodrugs. part 3: structure effects on the release kinetics of esterase-sensitive prodrugs of amines. Bioorg. Med. Chem. 6: 417-426.
- Xie, L. P., Chen, Q. X., Huang, H., Liu, X. D., Chen, H. T. and Zhang, R. Q. 2003. Inhibitory effects of cupferron on the monophenolase and diaphenolase activity of mushroom tyrosinase. Int. J. Biochem. Cell Biol. 35: 1658-1666.
- Xu, C. R., He, H. T., Song, X. and Siahaan, T. J. 2003. Synthesis and comparison of physicochemical, transport, and antithrombic properties of a cyclic prodrug and the parent RGD peptidomimetic. Tetrahedron. 59: 2861-2869.
- Vaya, J., Belinky, P. A. and Aviram, M. 1997. Antioxidant constituents from licorice roots: isolation, structure elucidation and antioxidative capacity toward LDL oxidation. Free Radic. Biol. Med. 23: 302-313.
- Yagi, A., Kanbara, T. and Morinobu, N. 1987. Inhibition of mushroom tyrosinase by Aloe extract. Planta Med. 53: 515-517.

Yokota, T., Nishio, H., Kubota, Y. and Mizoguchi, M. 1998. The inhibitory effect of glabridin from licorice extracts on melanogenesis and inflammation. Pigment Cell Res. 11: 355-361.



APPENDICES

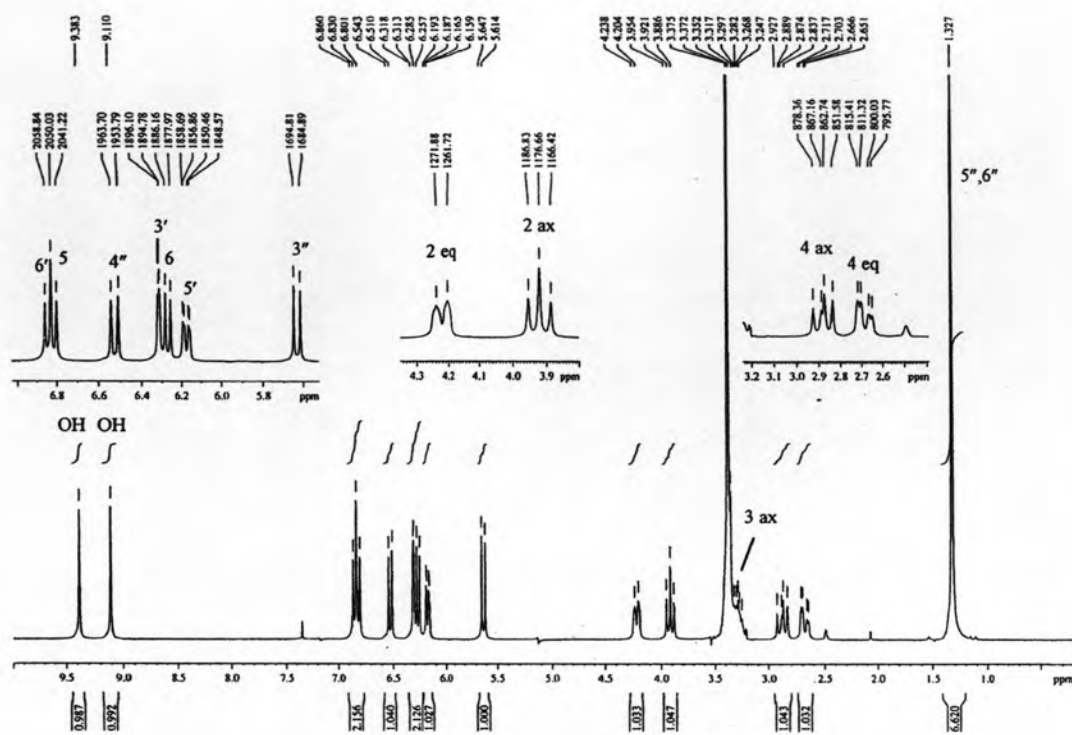


Figure 21. The 300 MHz  $^1\text{H}$ -NMR spectrum of glabridin (4) in DMSO- $d_6$ .

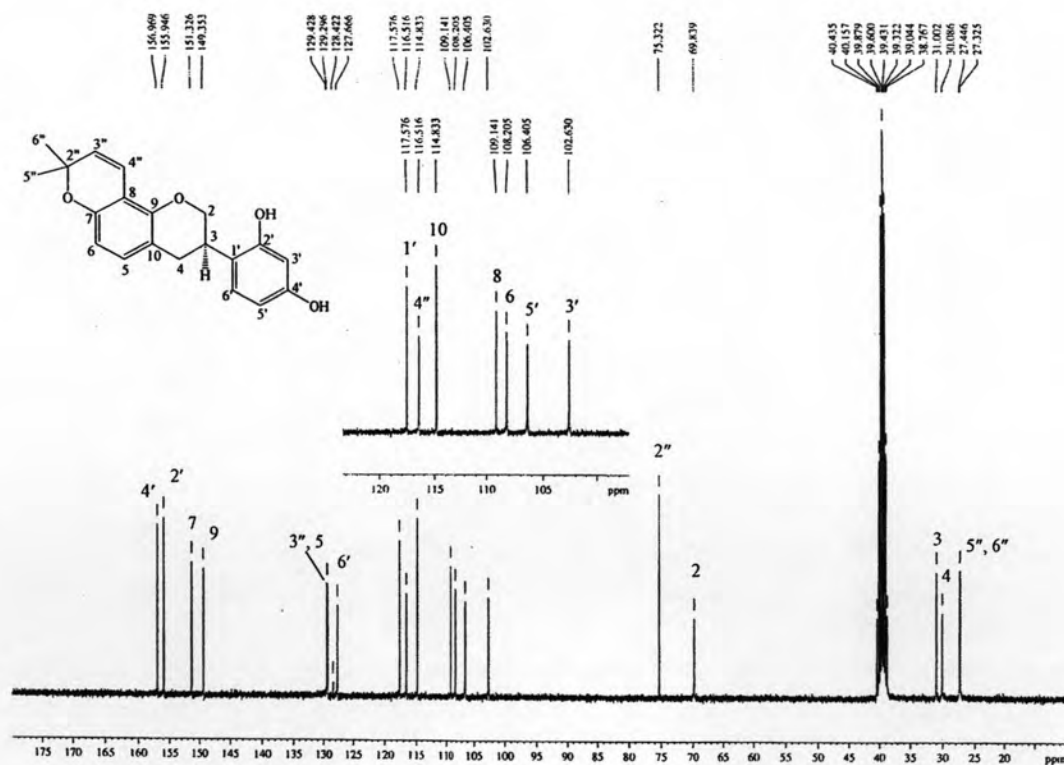
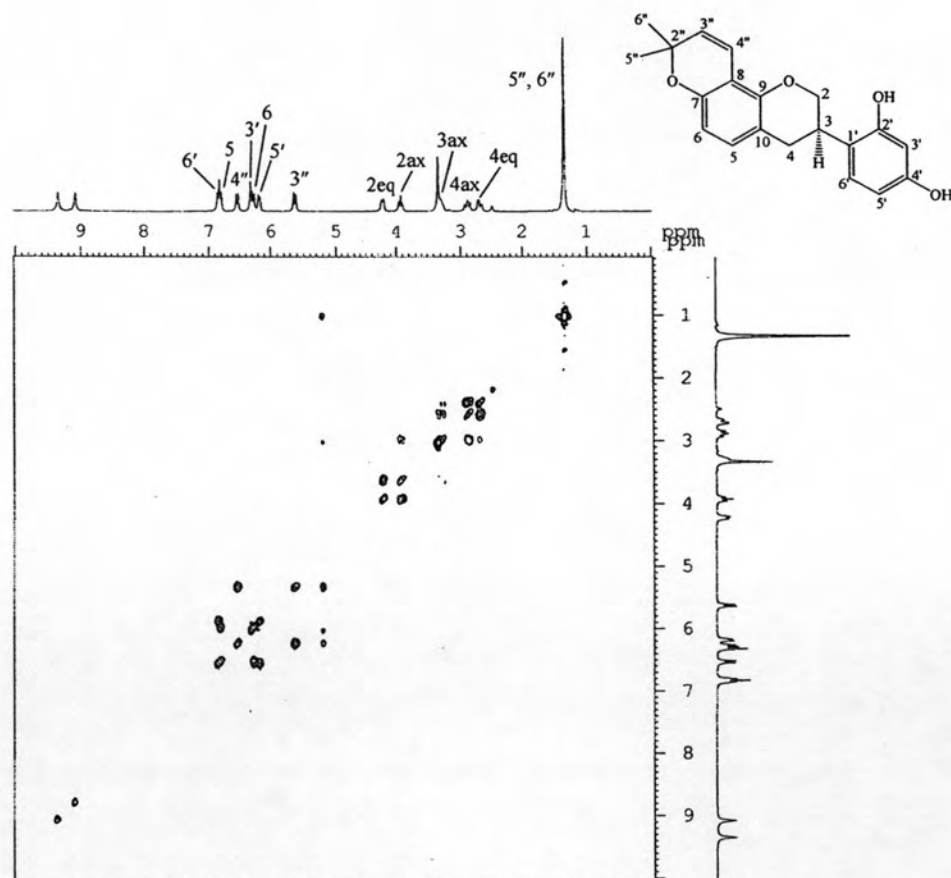
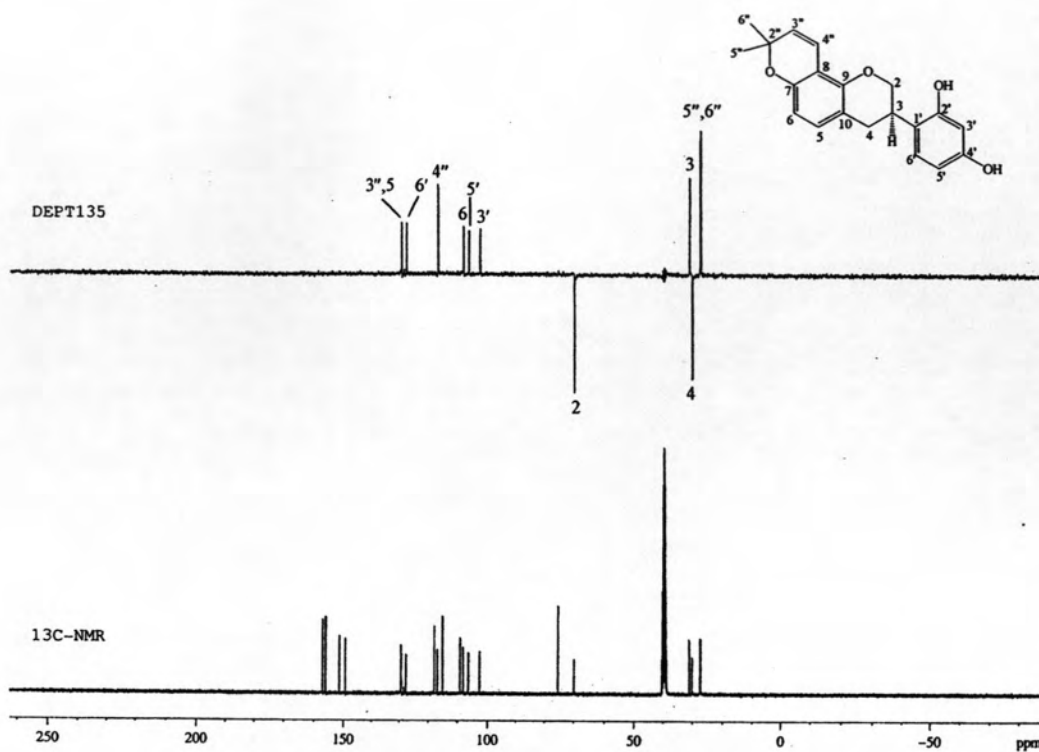


Figure 22. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin (4) in DMSO- $d_6$ .



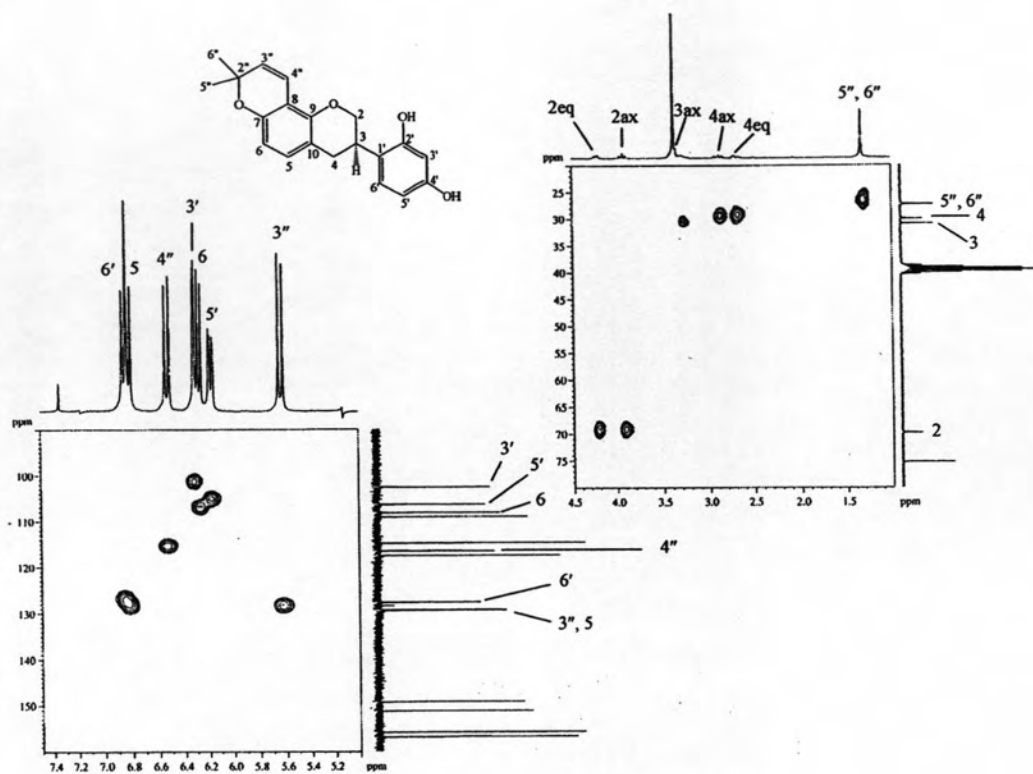


Figure 25. The HMQC spectrum of glabridin (4) in DMSO-d<sub>6</sub>.

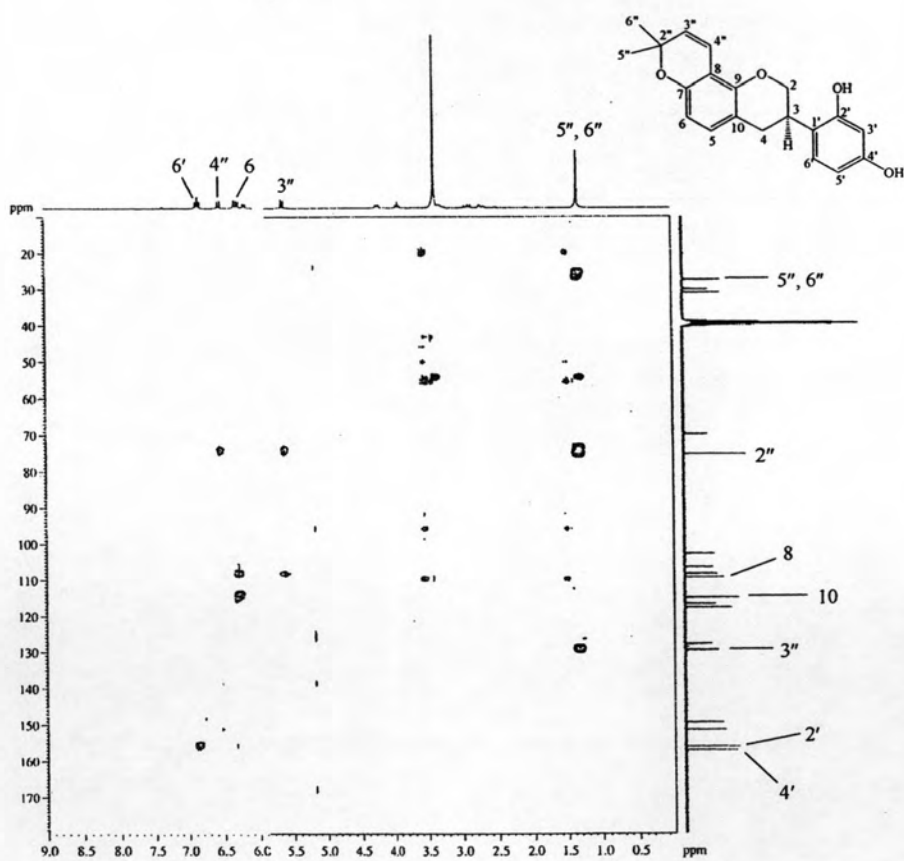


Figure 26. The HMBC spectrum of glabridin (4) in DMSO-d<sub>6</sub>.



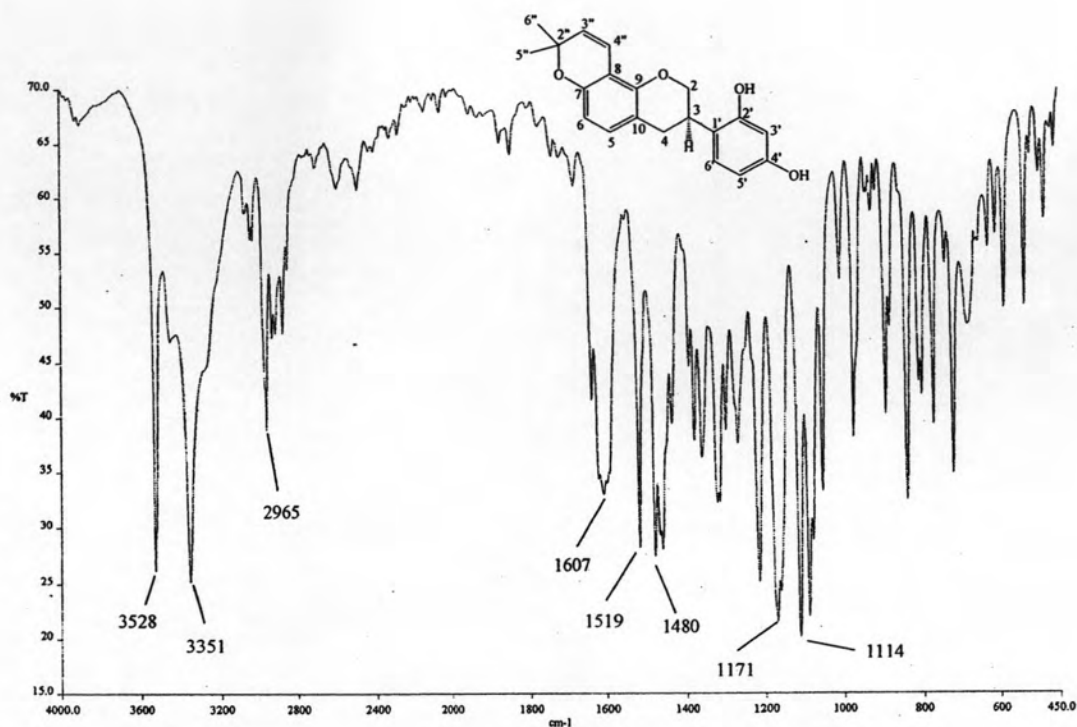


Figure 27. The infrared spectrum of glabridin (4).

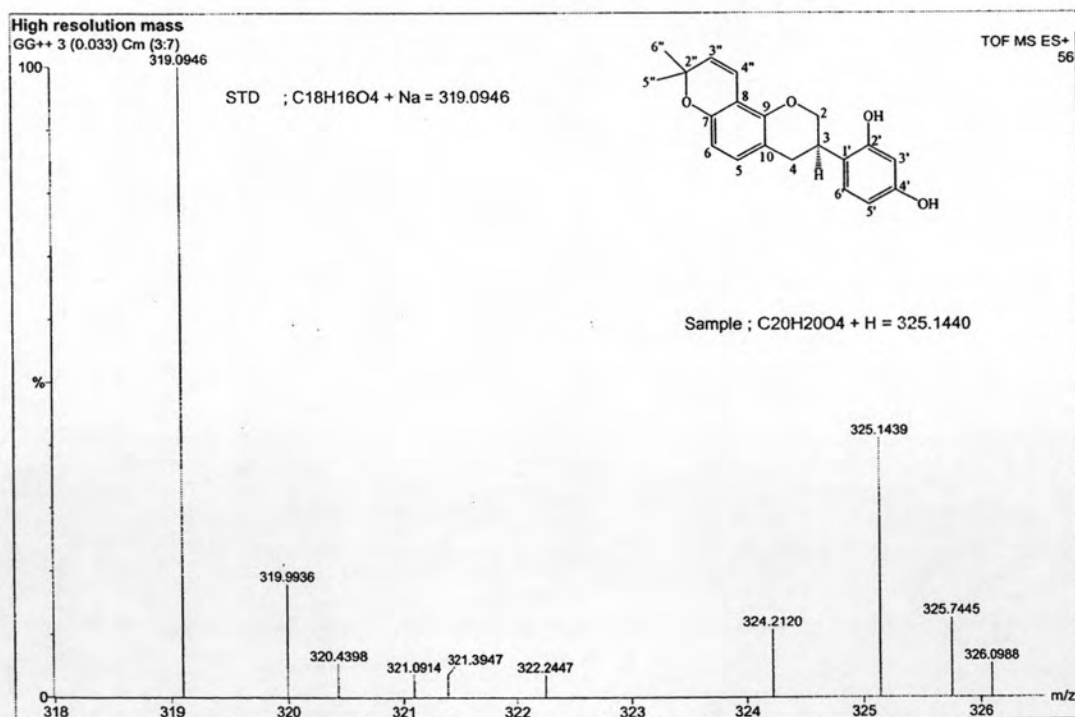


Figure 28. The TOF Mass spectrum of glabridin (4).

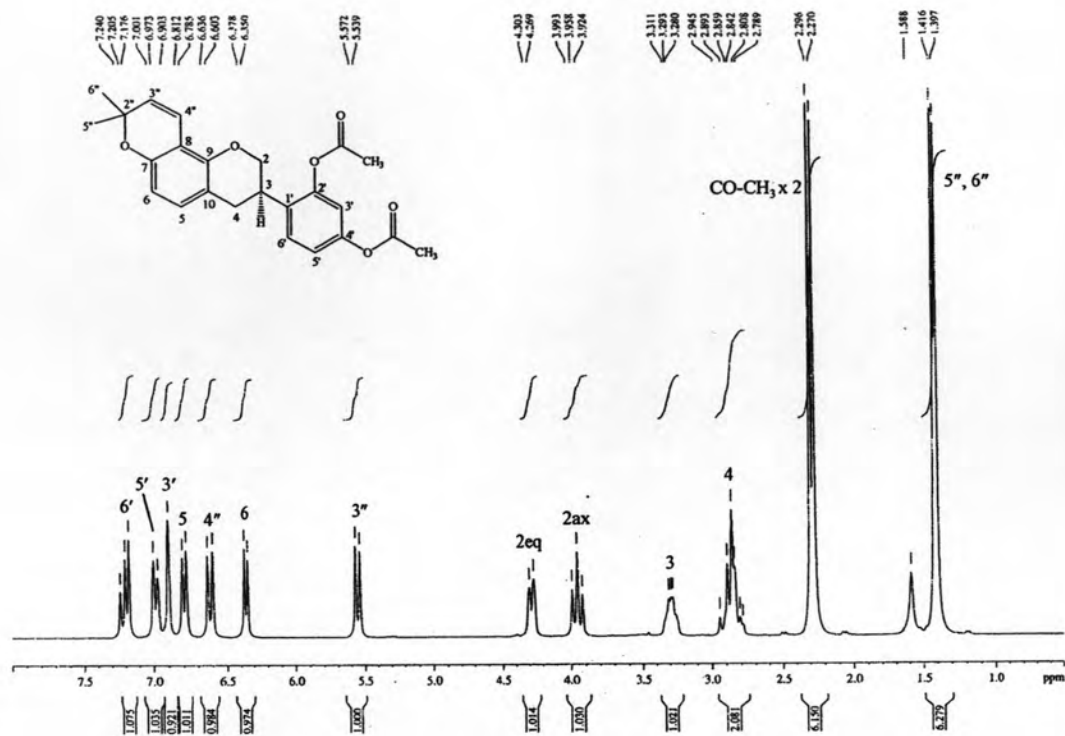


Figure 29. The 300 MHz  $^1\text{H}$ -NMR spectrum of glabridin diacetate (**16**) in  $\text{CDCl}_3$ .

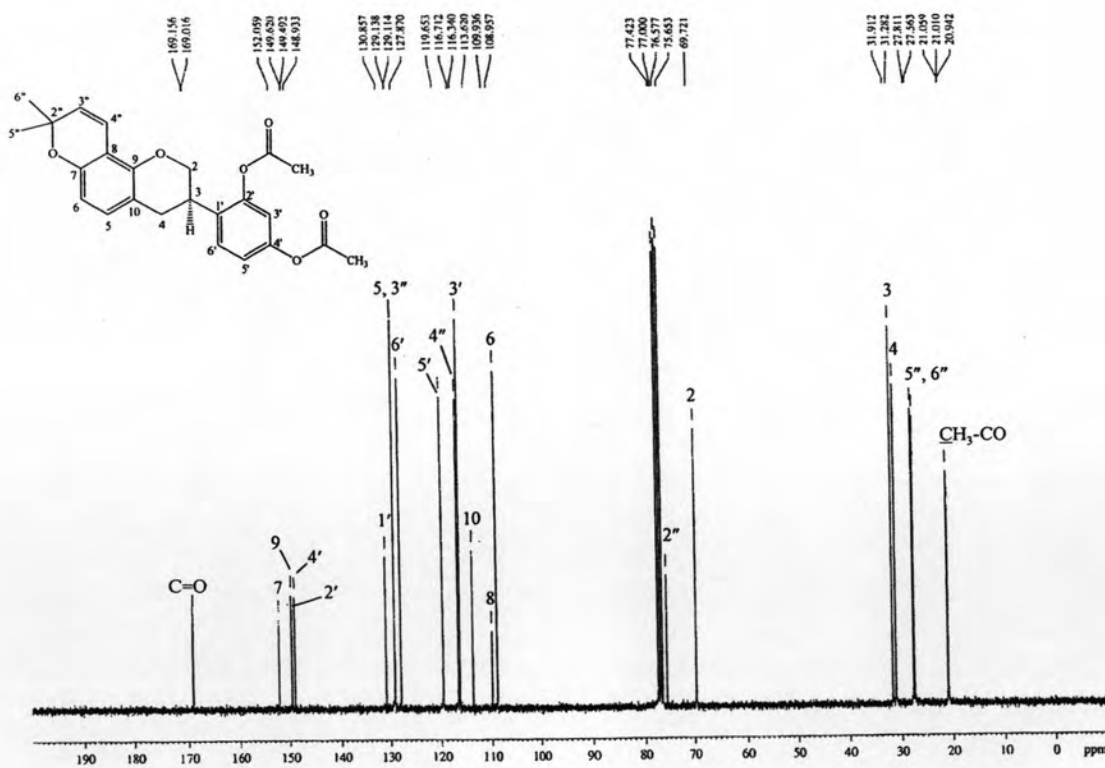


Figure 30. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin diacetate (**16**) in  $\text{CDCl}_3$ .

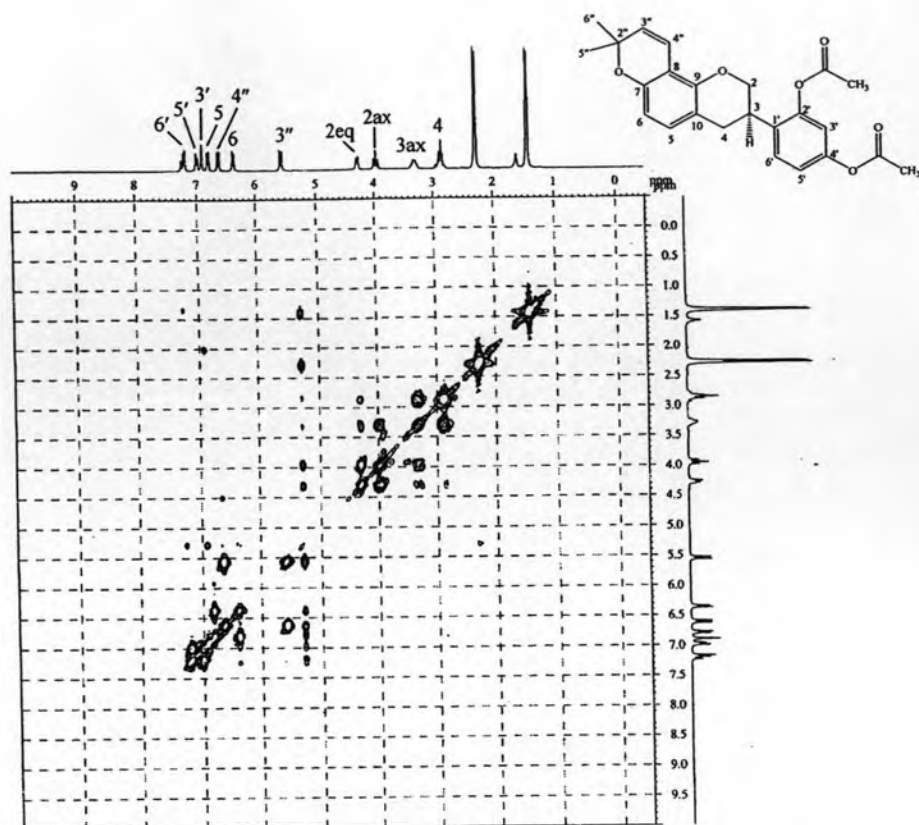


Figure 31. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin diacetate (16) in  $\text{CDCl}_3$ .

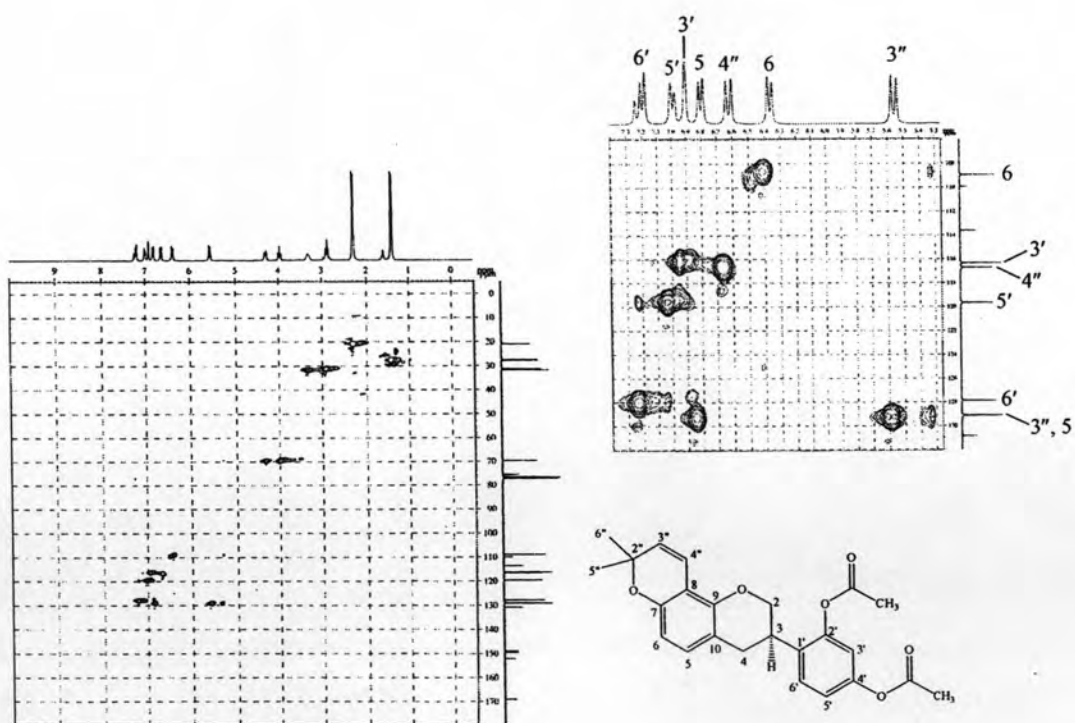


Figure 32. The HMQC spectrum of glabridin diacetate (16) in  $\text{CDCl}_3$ .

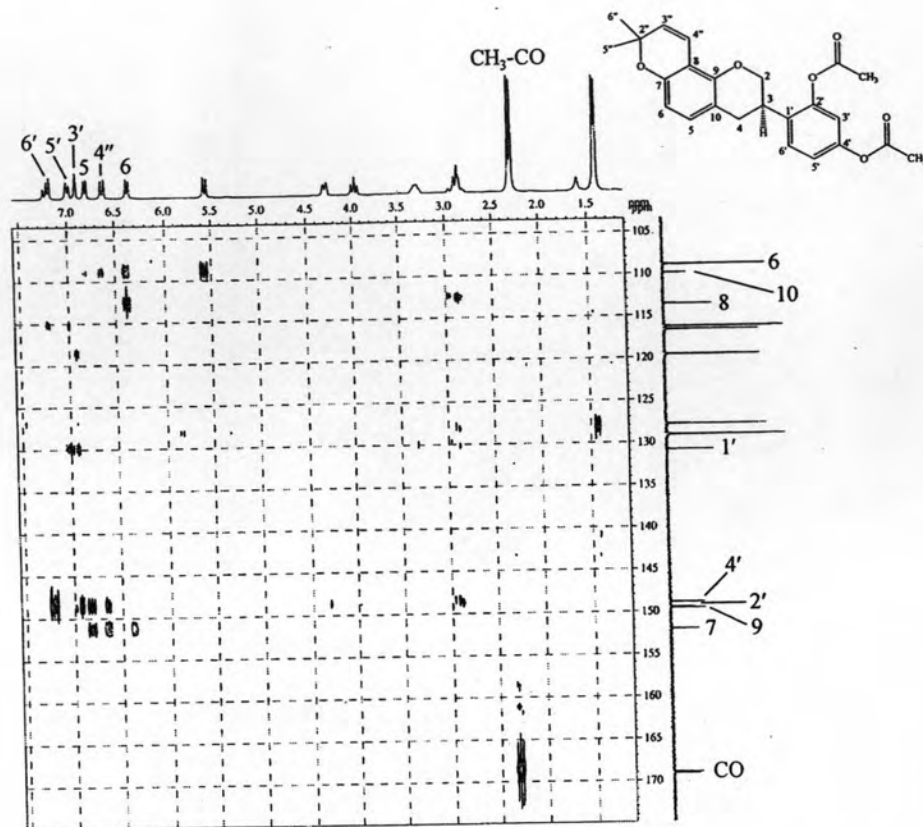


Figure 33. The HMBC spectrum of glabridin diacetate (**16**) in  $\text{CDCl}_3$ .

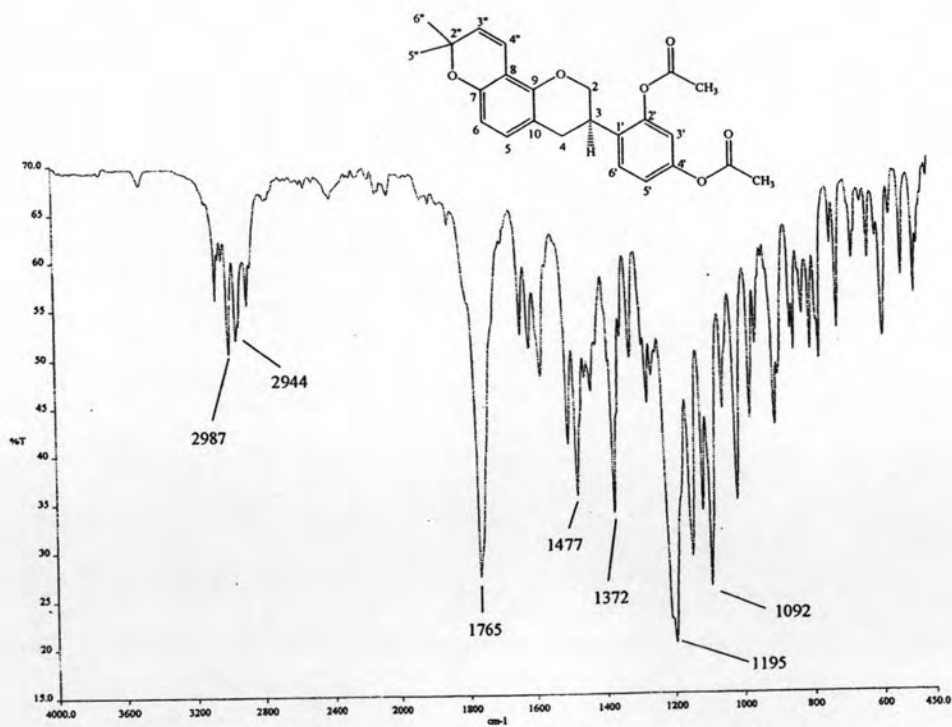


Figure 34. The infrared spectrum of glabridin diacetate (**16**).



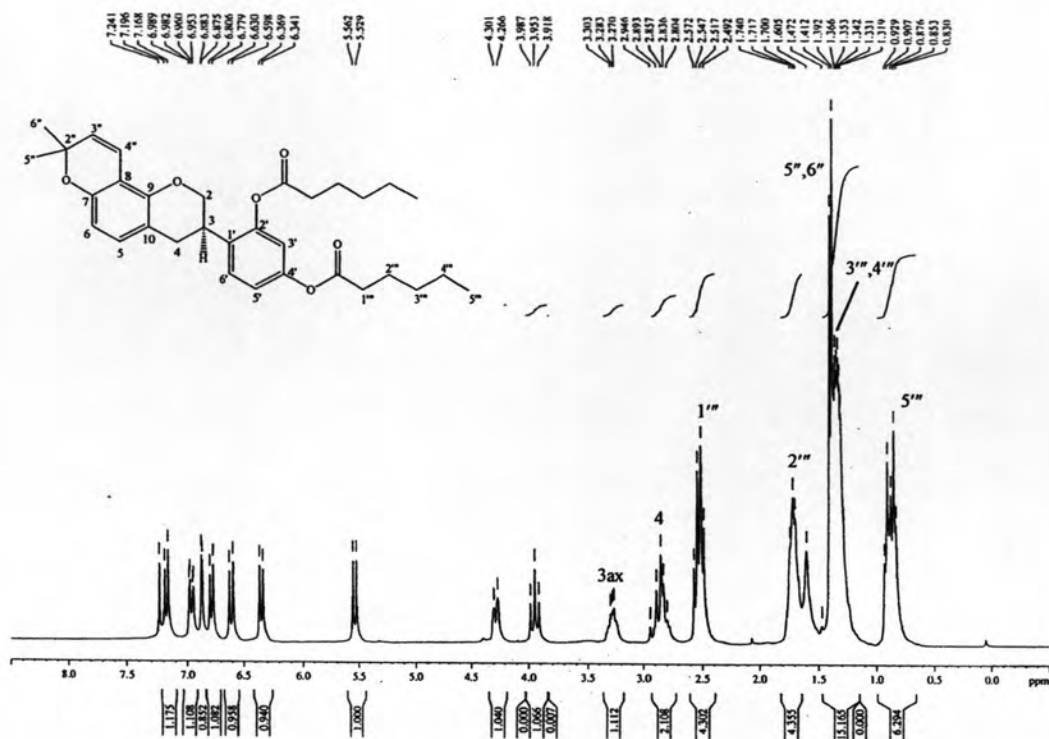


Figure 35. The 300 MHz  $^1\text{H}$ -NMR spectrum of glabridin dihexanoate (17) in  $\text{CDCl}_3$ .



Figure 36. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin dihexanoate (17) in  $\text{CDCl}_3$ .

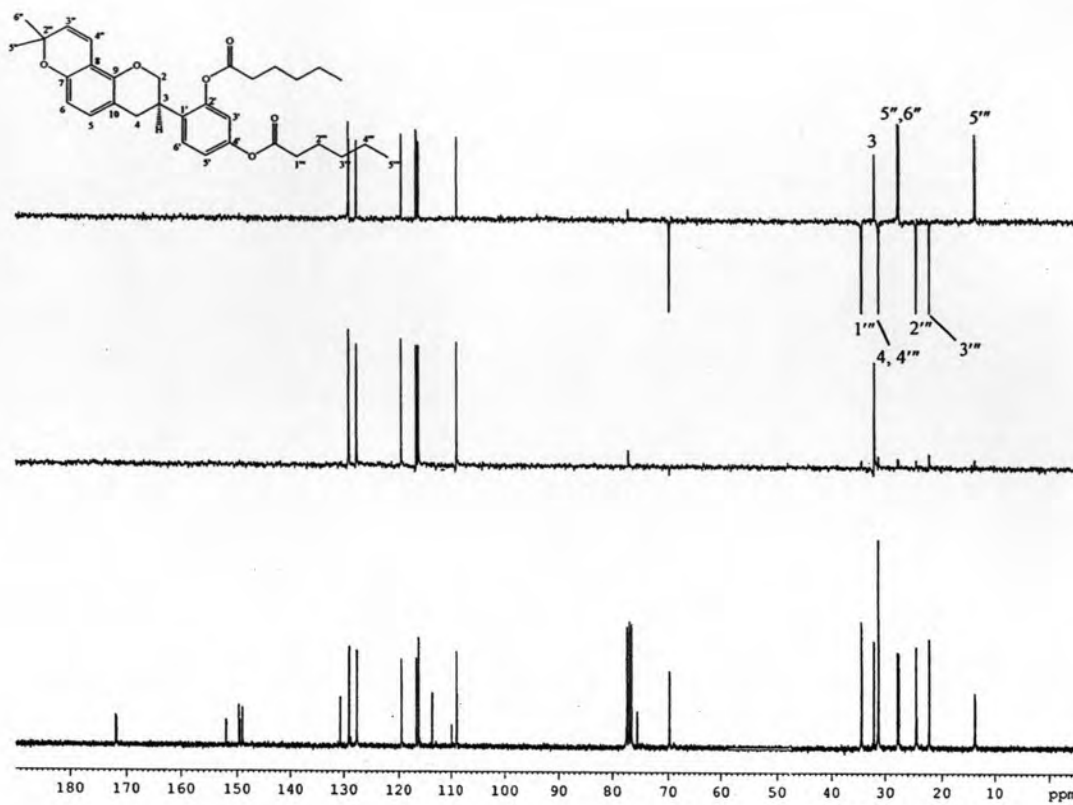


Figure 37. The DEPT 90° and 135° spectrum of glabridin dihexanoate (**17**) in CDCl<sub>3</sub>.

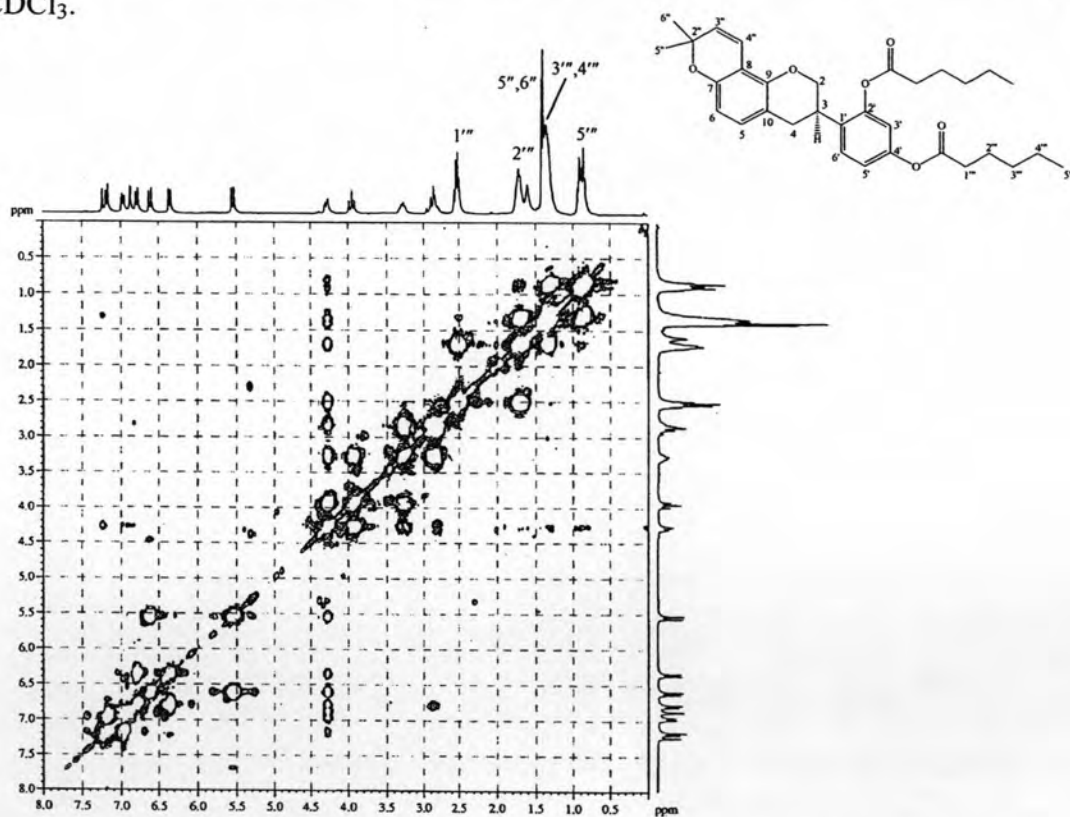


Figure 38. The <sup>1</sup>H-<sup>1</sup>H COSY spectrum of glabridin dihexanoate (**17**) in CDCl<sub>3</sub>.

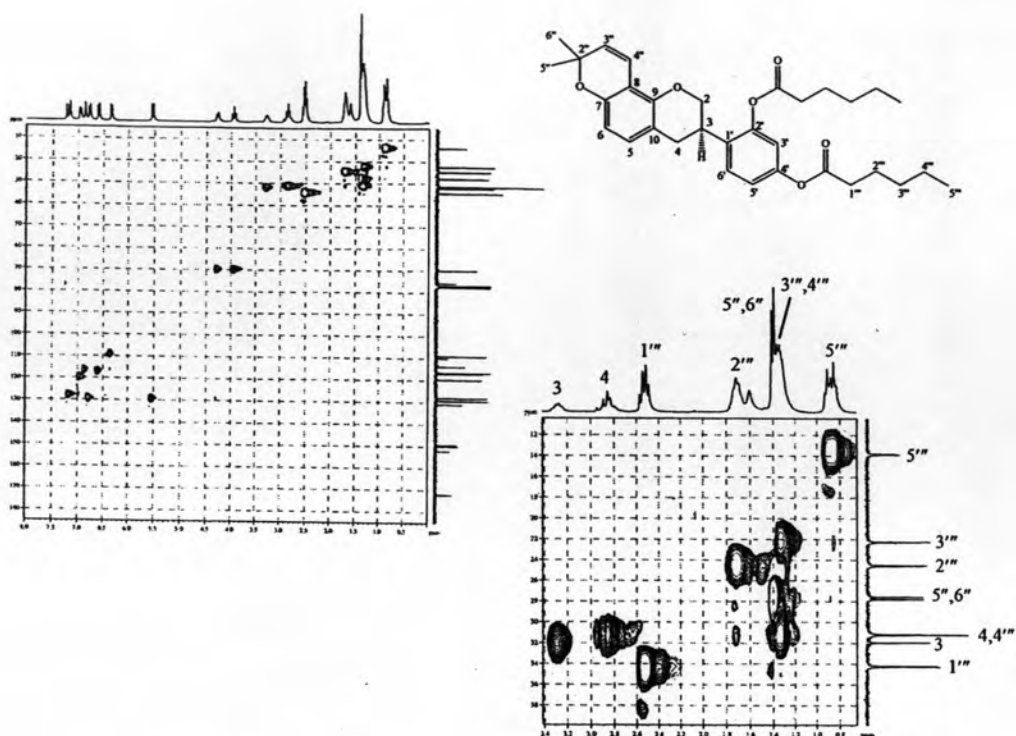


Figure 39. The HMQC spectrum of glabridin dihexanoate (17) in  $\text{CDCl}_3$ .

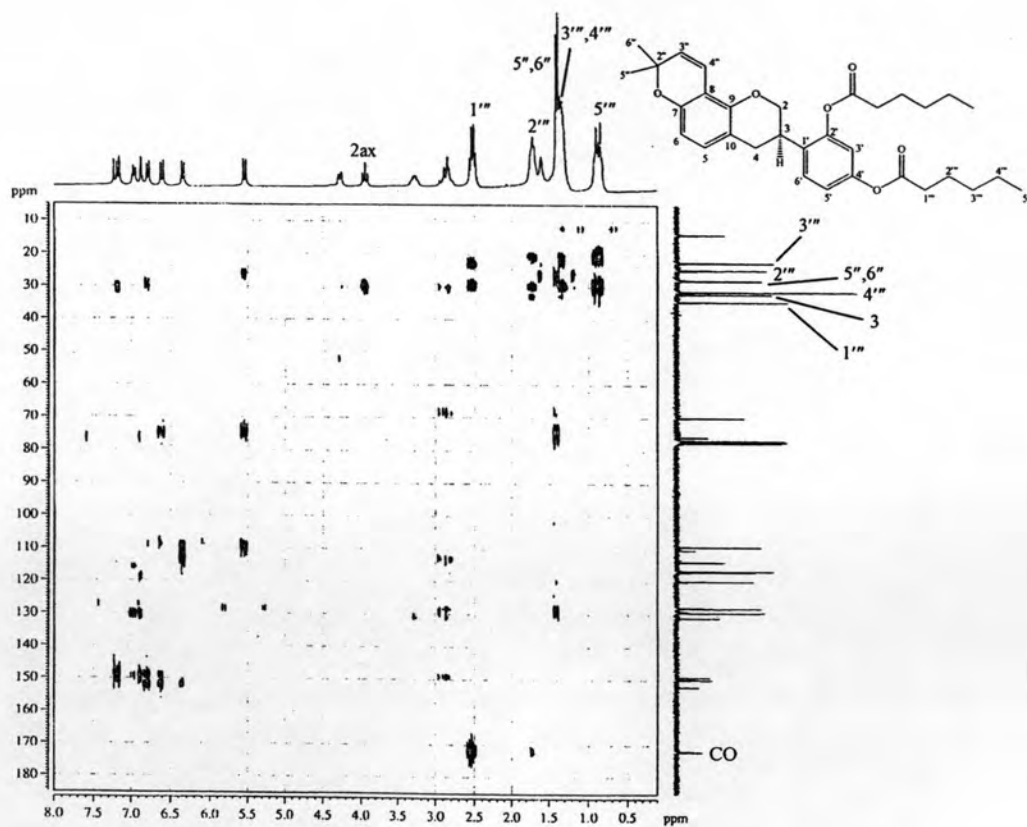


Figure 40. The HMBC spectrum of glabridin dihexanoate (17) in  $\text{CDCl}_3$ .

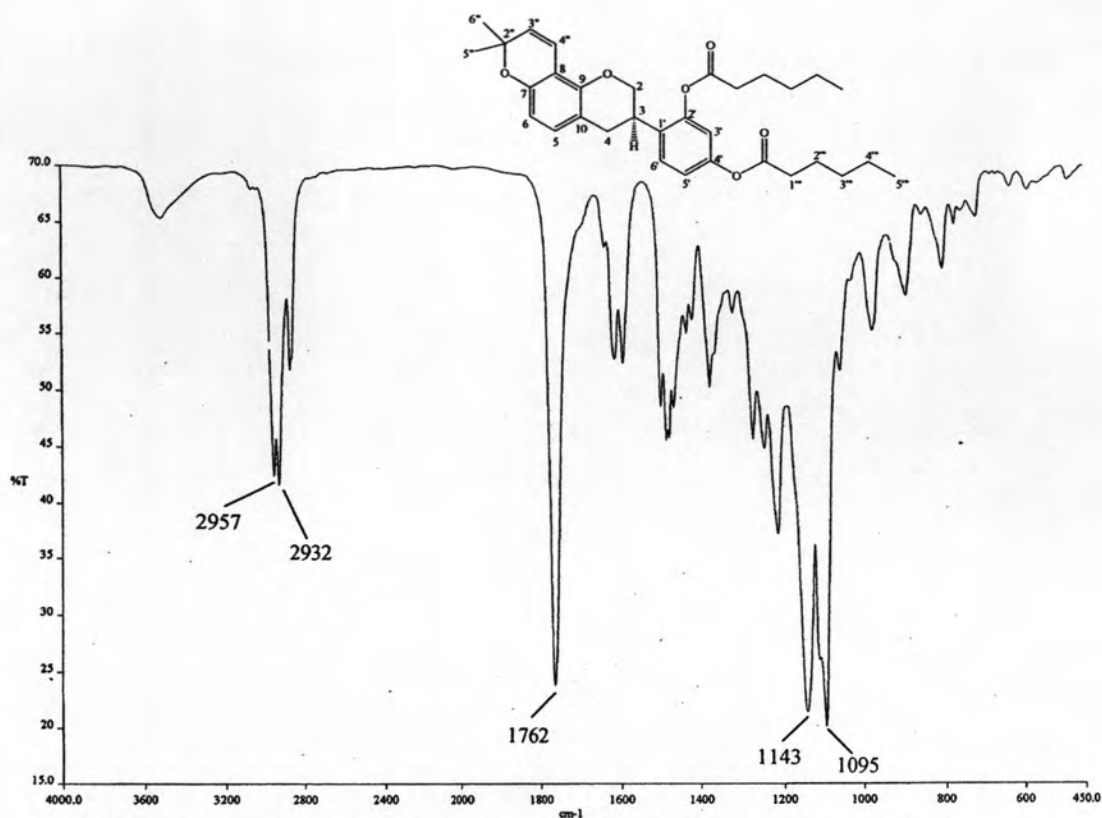


Figure 41. The infrared spectrum of glabridin dihexanoate (17).

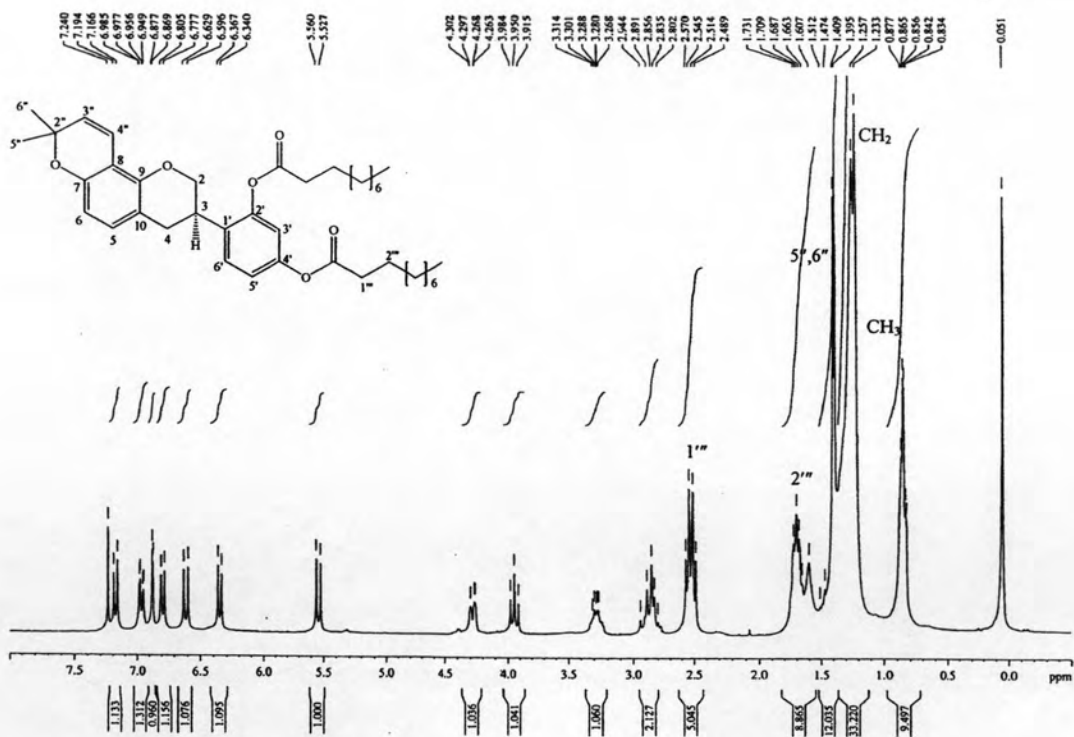


Figure 42. The 300 MHz <sup>1</sup>H-NMR spectrum of glabridin didecanoate (18) in CDCl<sub>3</sub>.



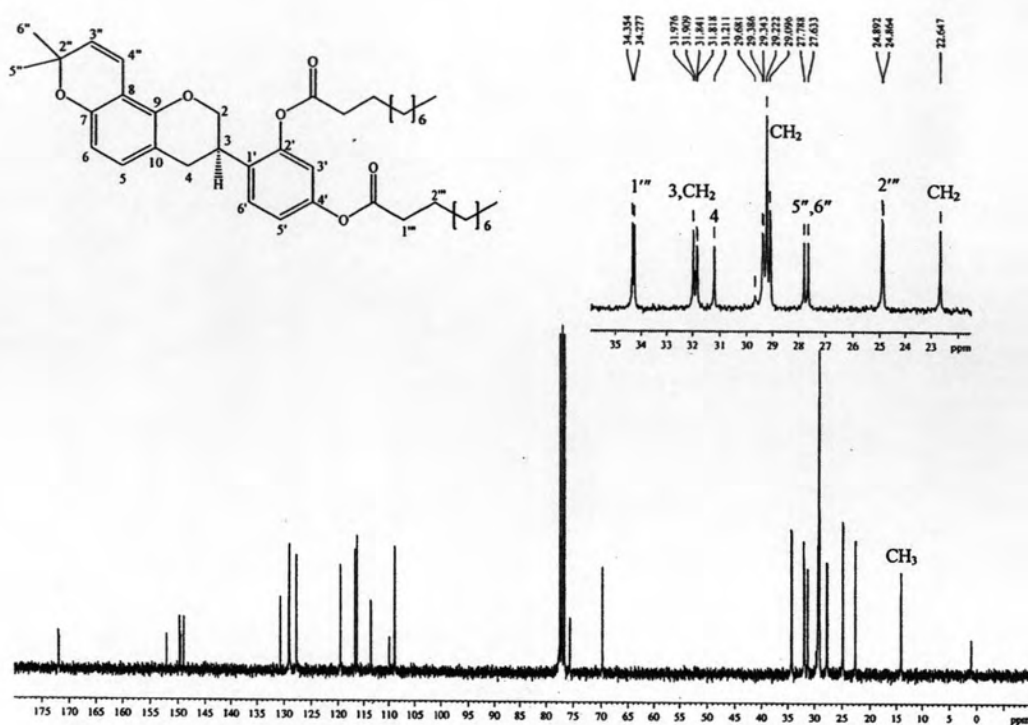


Figure 43. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin didecanoate (**18**) in  $\text{CDCl}_3$ .

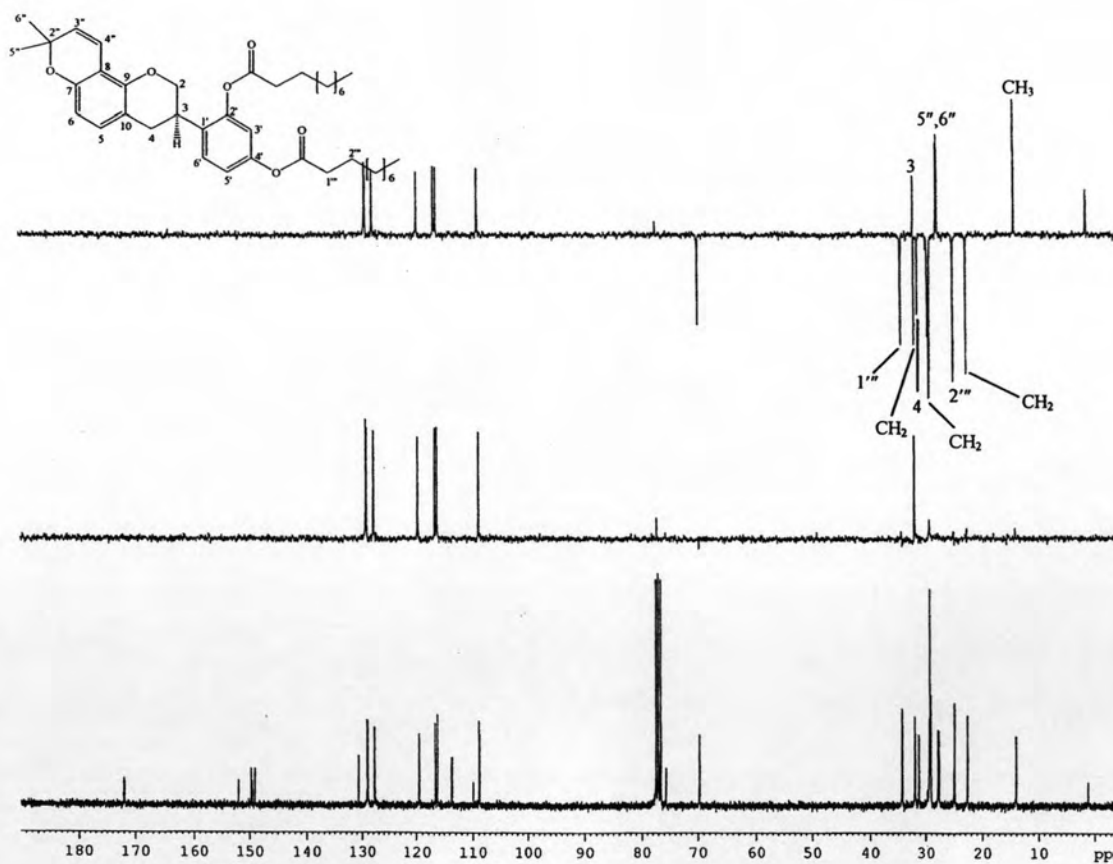


Figure 44. The DEPT  $90^\circ$  and  $135^\circ$  spectrum of glabridin didecanoate (**18**) in  $\text{CDCl}_3$ .

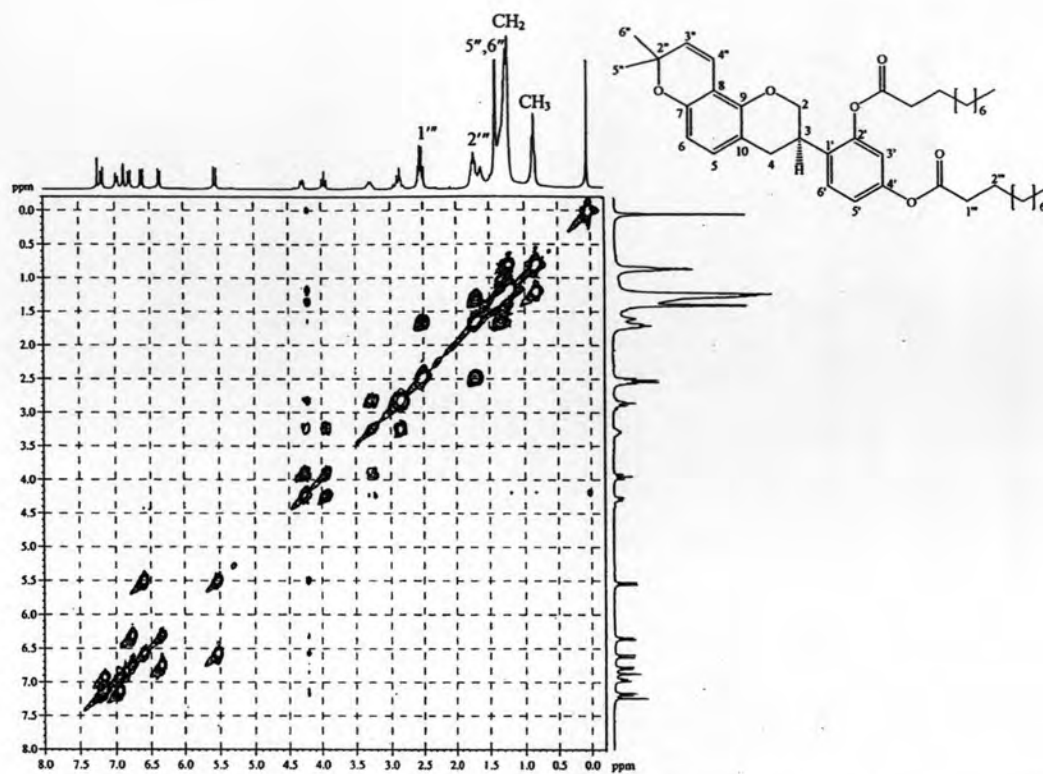


Figure 45. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin didecanoate (**18**) in  $\text{CDCl}_3$ .

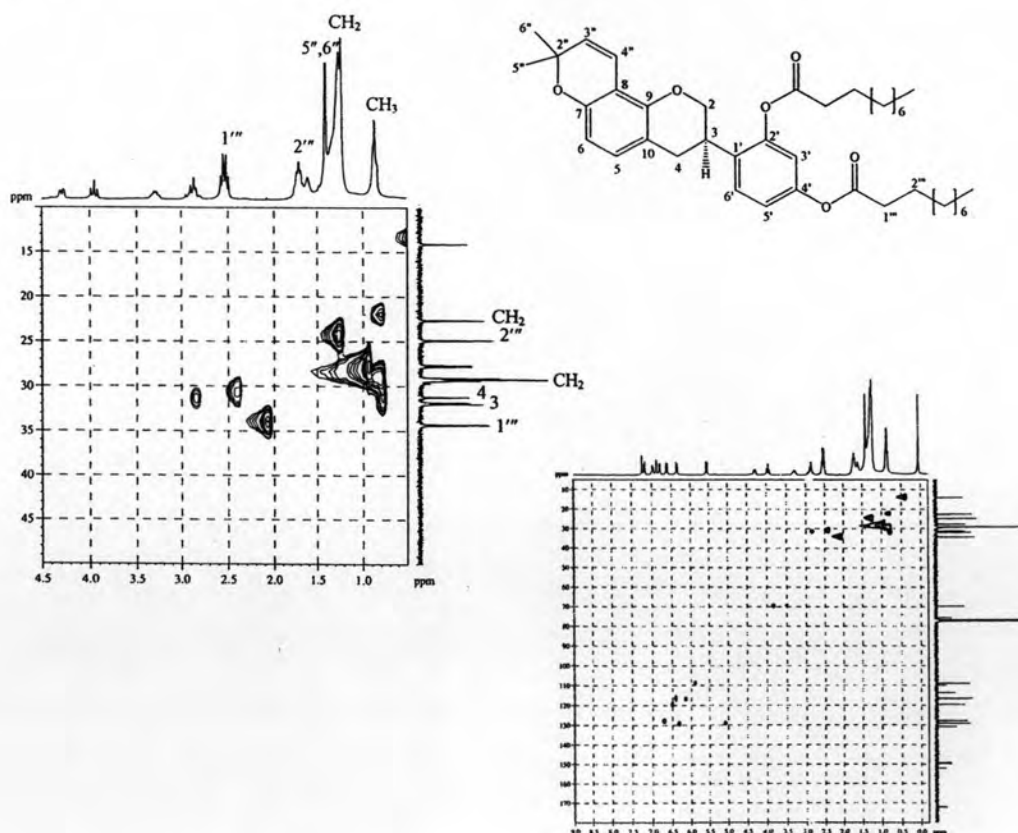


Figure 46. The HMQC spectrum of glabridin didecanoate (**18**) in  $\text{CDCl}_3$ .

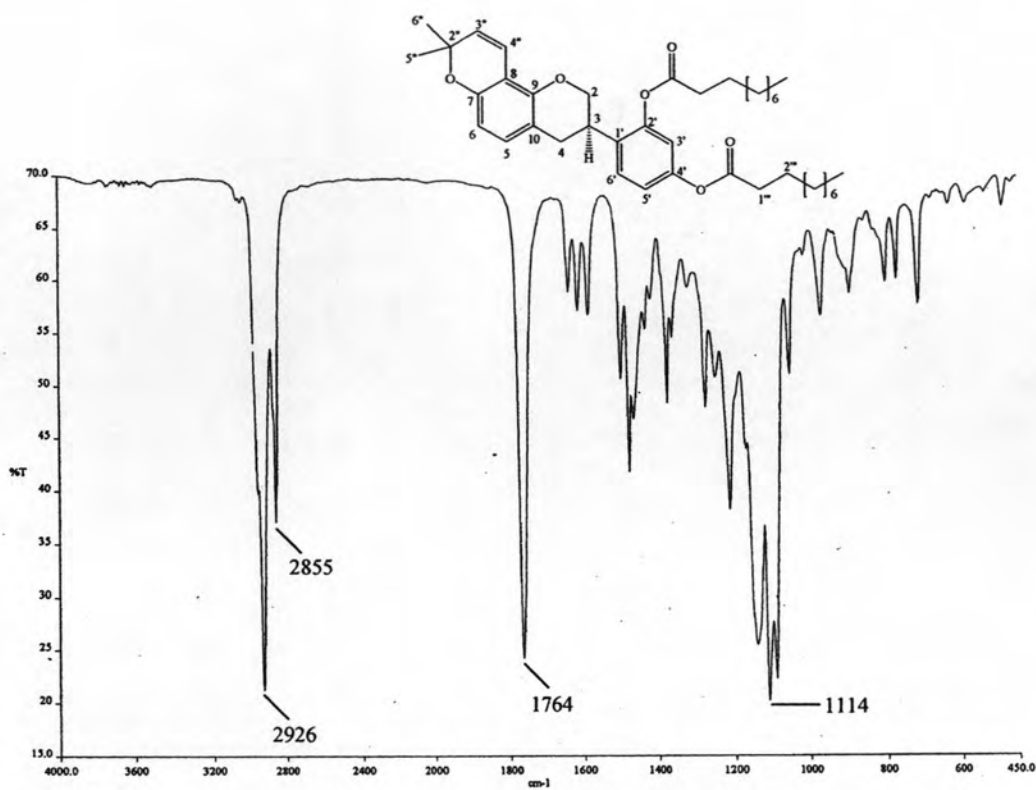


Figure 47. The infrared spectrum of glabridin didecanoate (18).

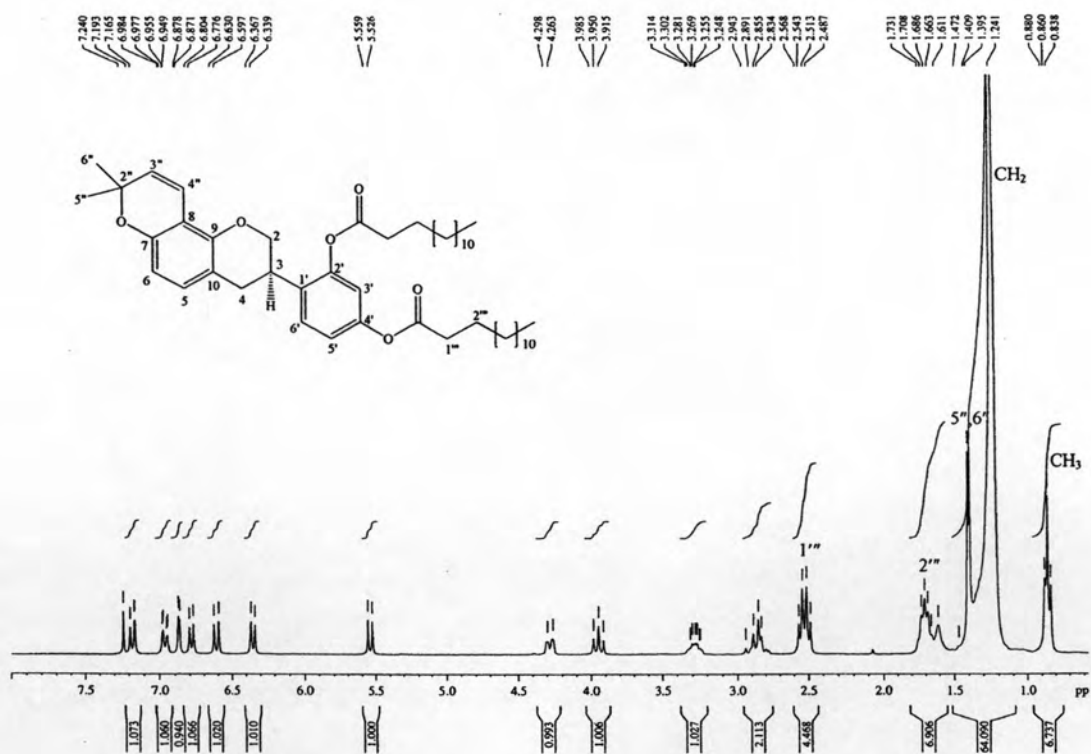


Figure 48. The 300 MHz <sup>1</sup>H-NMR spectrum of glabridin dipalmitate (19) in CDCl<sub>3</sub>.





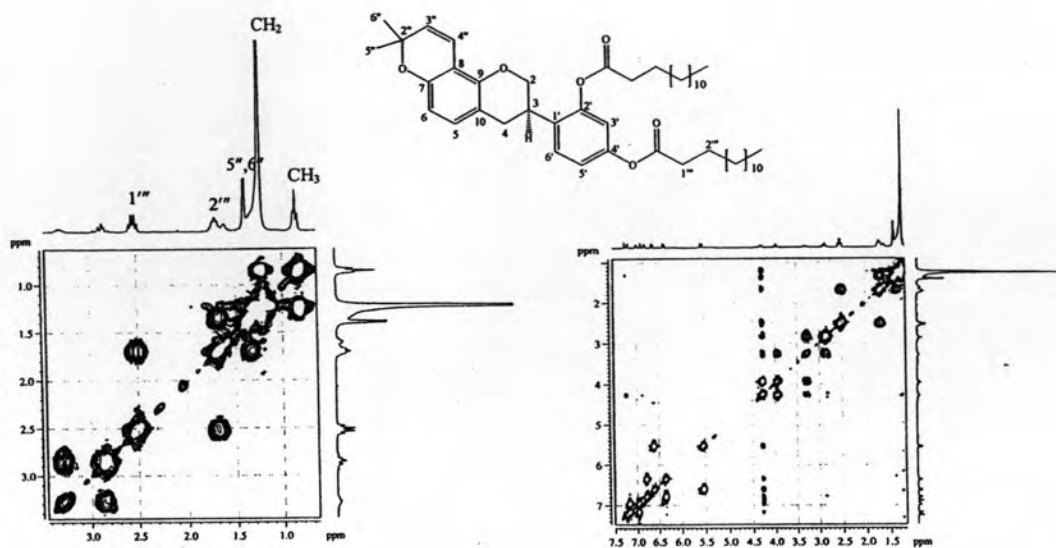


Figure 51. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin dipalmitate (19) in  $\text{CDCl}_3$ .

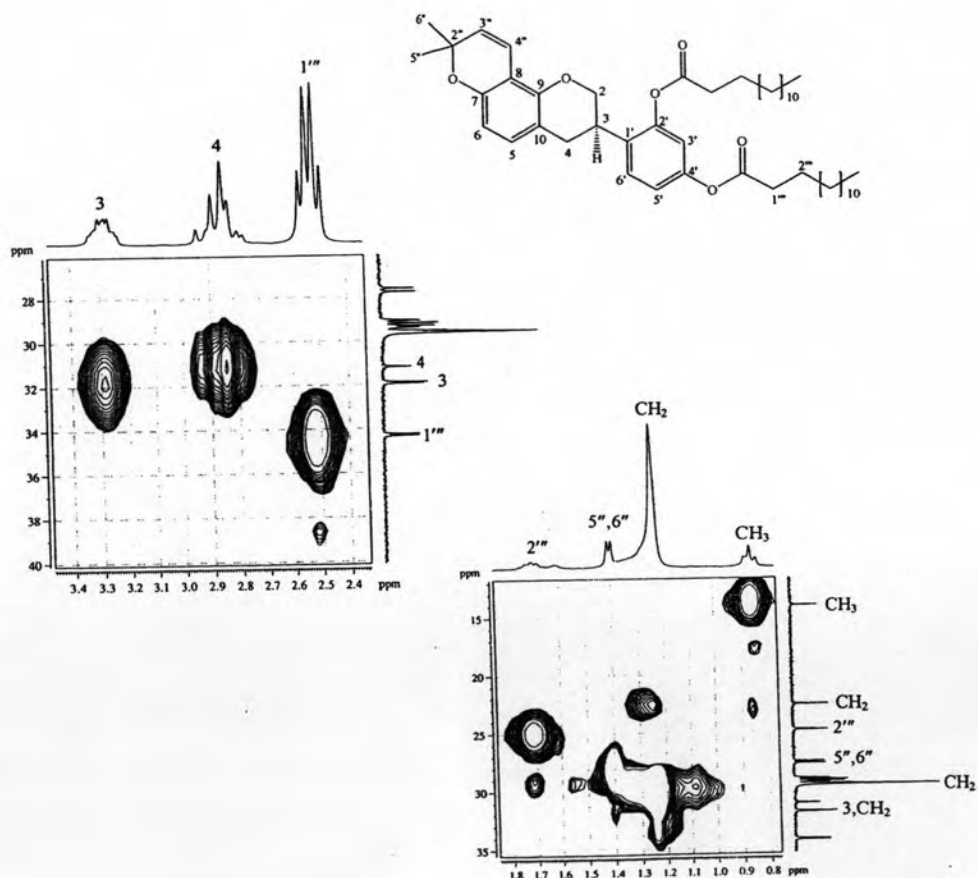


Figure 52. The HMQC spectrum of glabridin dipalmitate (19) in  $\text{CDCl}_3$ .

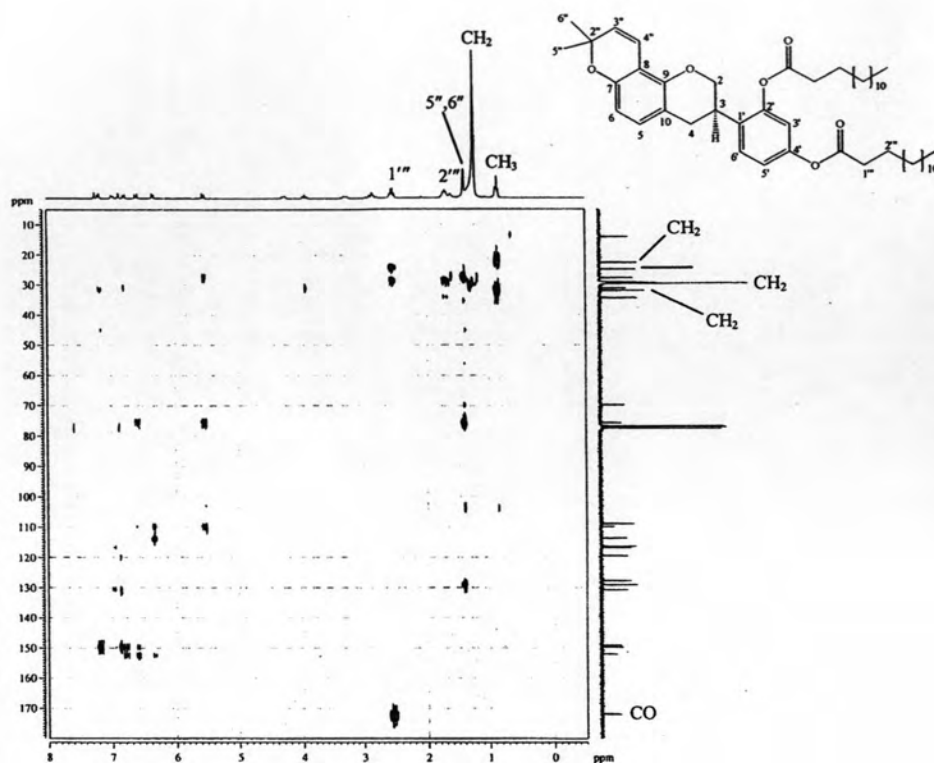


Figure 53. The HMBC spectrum of glabridin dipalmitate (19) in  $\text{CDCl}_3$ .

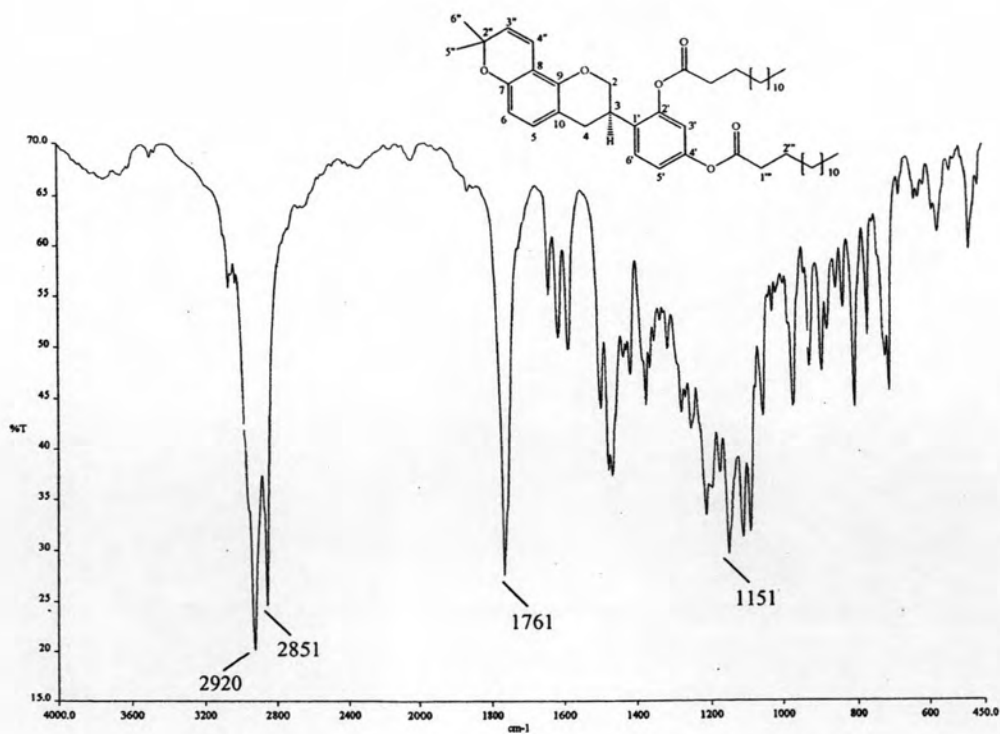


Figure 54. The infrared spectrum of glabridin dipalmitate (19).

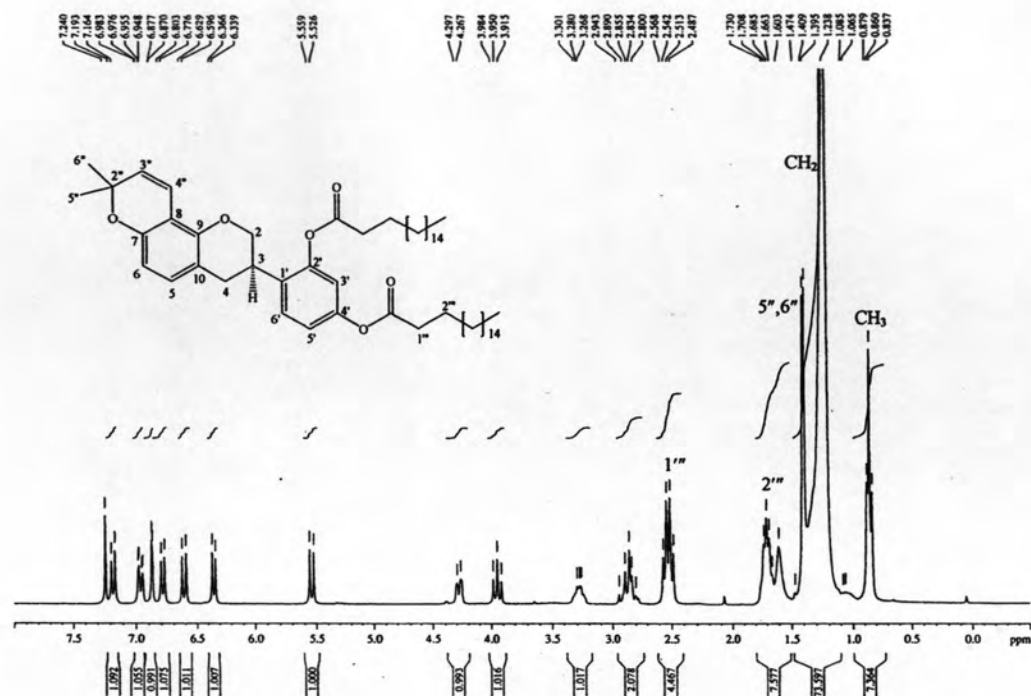


Figure 55. The 300 MHz  $^1\text{H}$ -NMR spectrum of glabridin distearate (20) in  $\text{CDCl}_3$ .

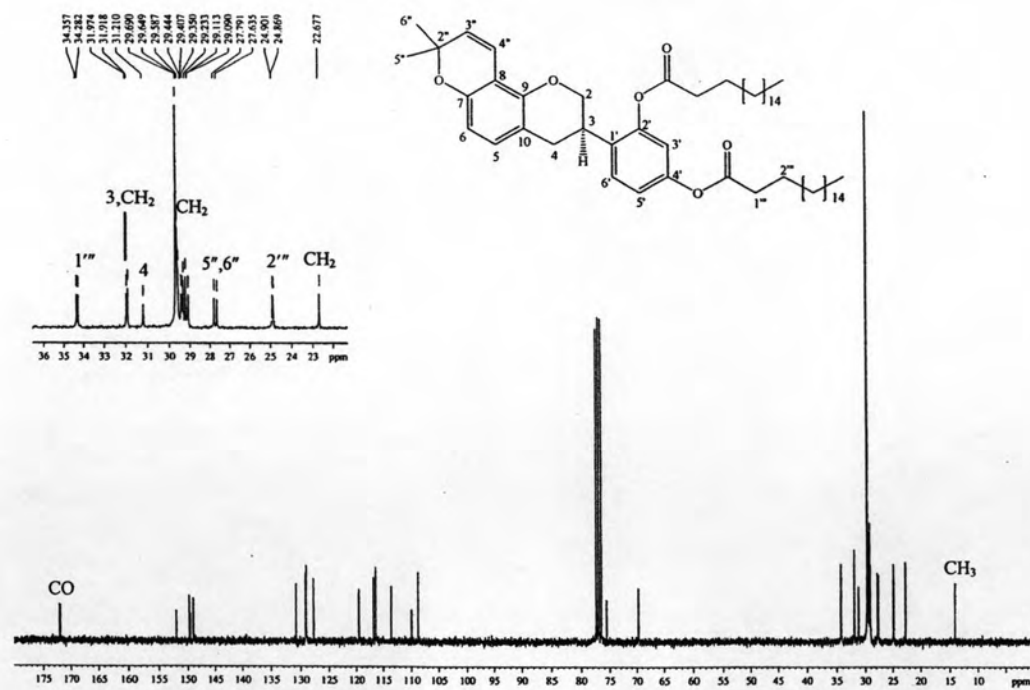


Figure 56. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin distearate (20) in  $\text{CDCl}_3$ .

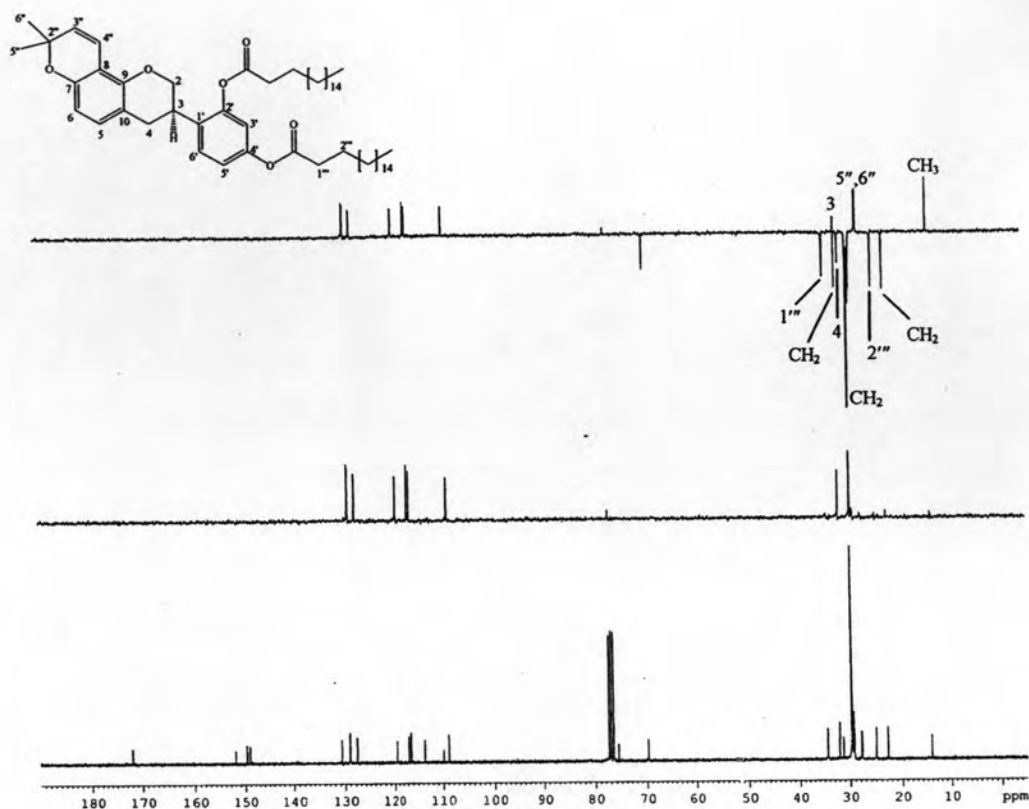


Figure 57. The DEPT 90° and 135° spectrum of glabridin distearate (**20**) in CDCl<sub>3</sub>.

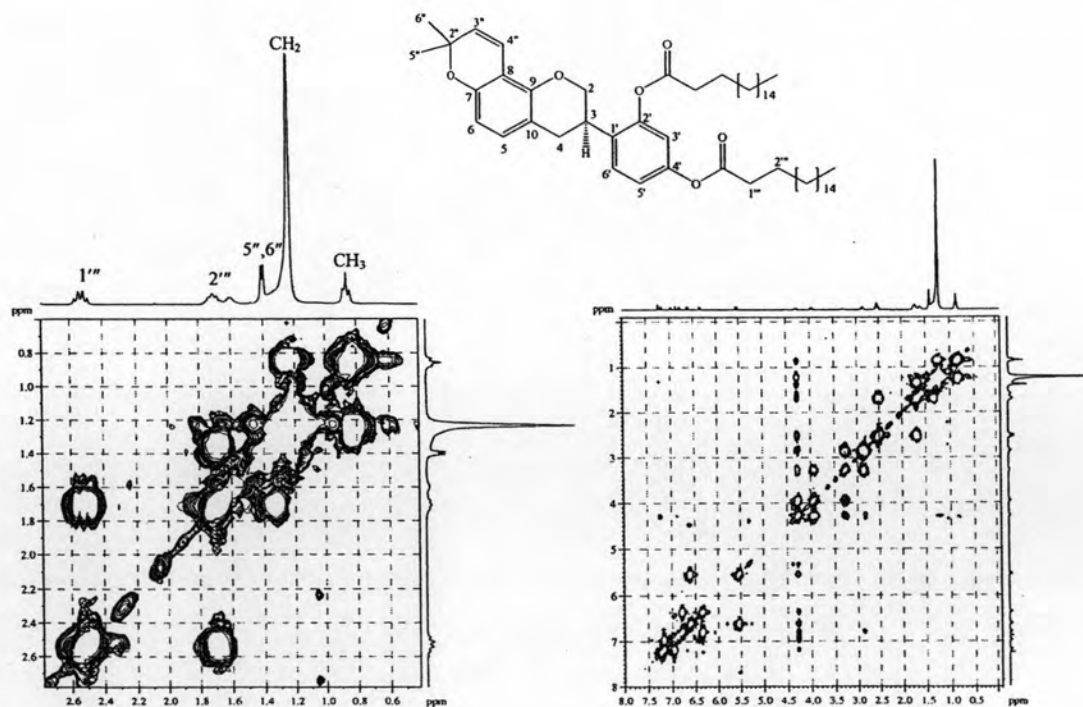


Figure 58. The <sup>1</sup>H-<sup>1</sup>H COSY spectrum of glabridin distearate (**20**) in CDCl<sub>3</sub>.

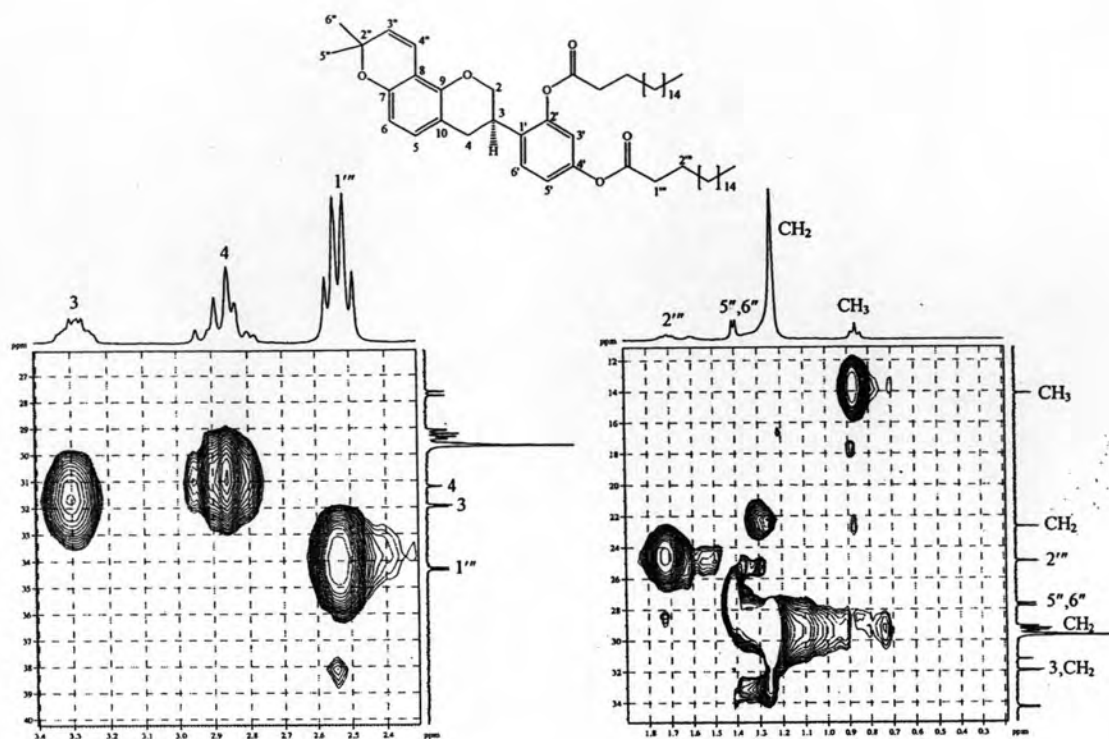


Figure 59. The HMQC spectrum of glabridin distearate (**20**) in  $\text{CDCl}_3$ .

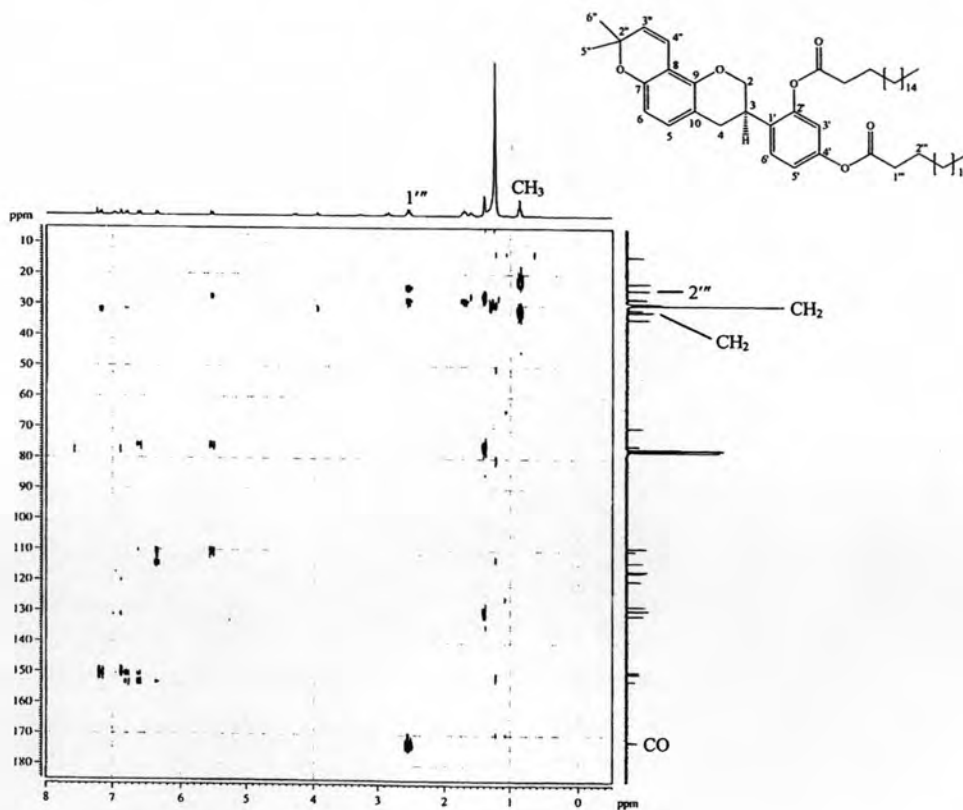


Figure 60. The HMBC spectrum of glabridin distearate (**20**) in  $\text{CDCl}_3$ .



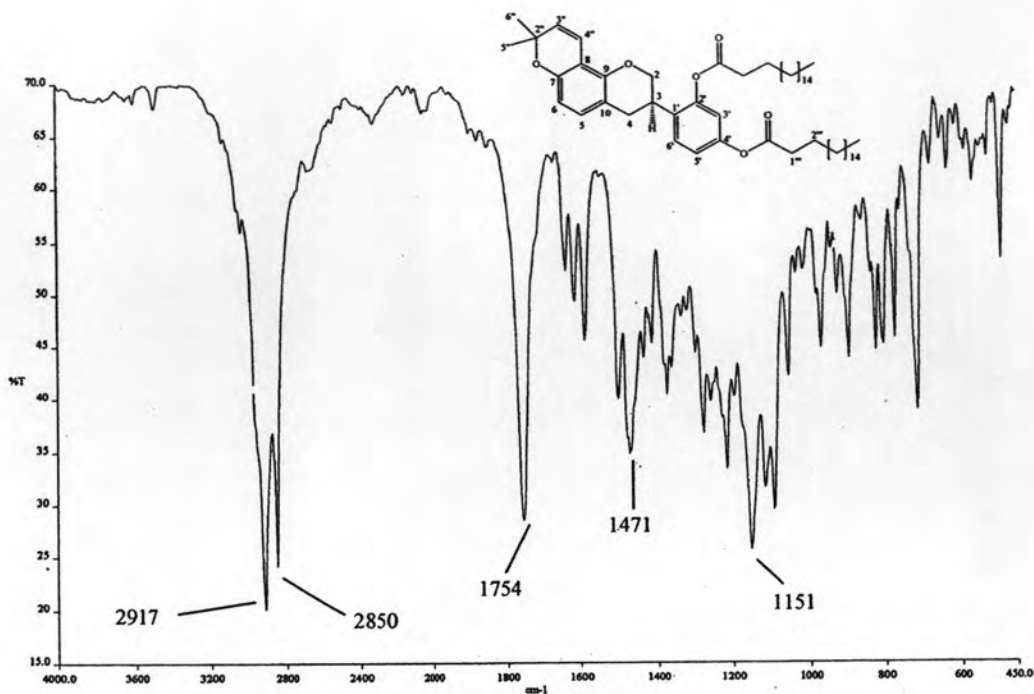


Figure 61. The infrared spectrum of glabridin distearate (20).

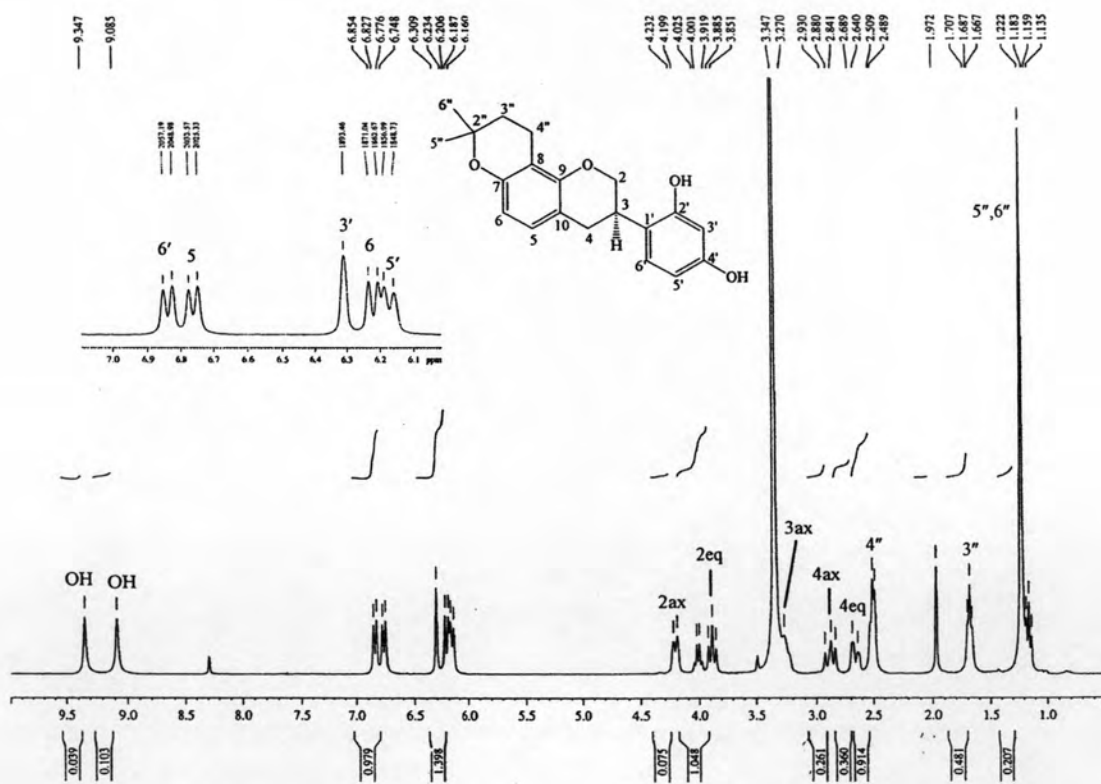


Figure 62. The 300 MHz  $^1\text{H}$ -NMR spectrum of 3'',4''-dihydroglabridin (21) in  $\text{DMSO-d}_6$ .

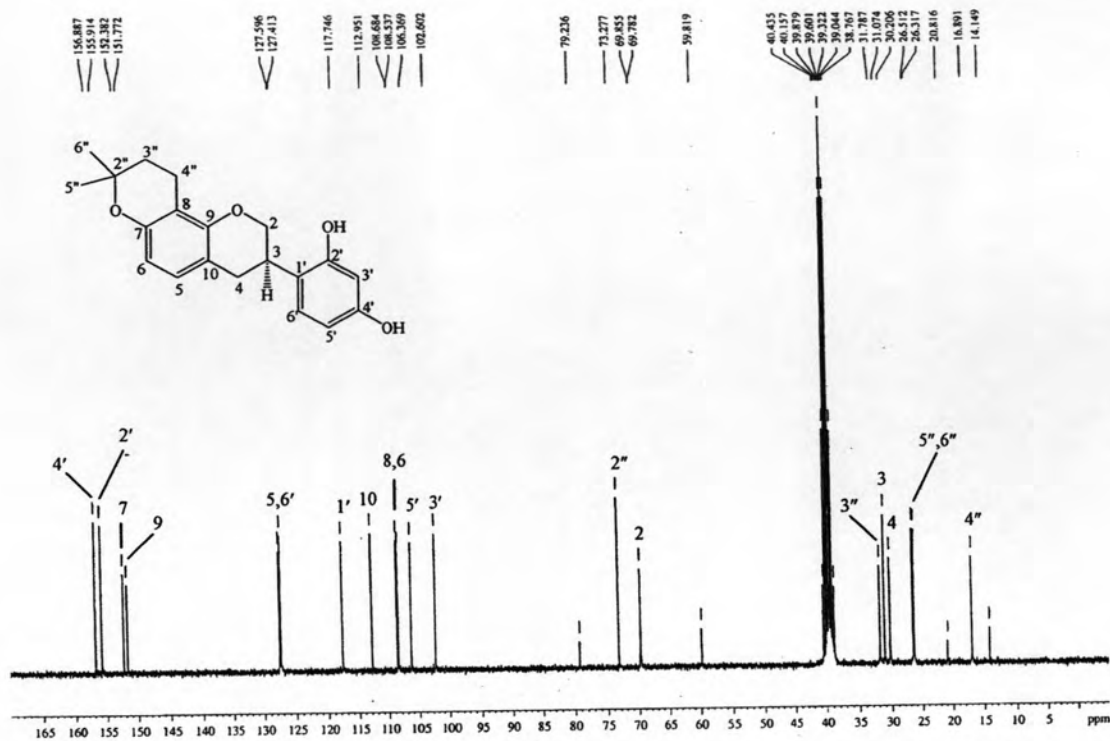


Figure 63. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 3'',4''-dihydroglabridin (**21**) in  $\text{DMSO-d}_6$ .

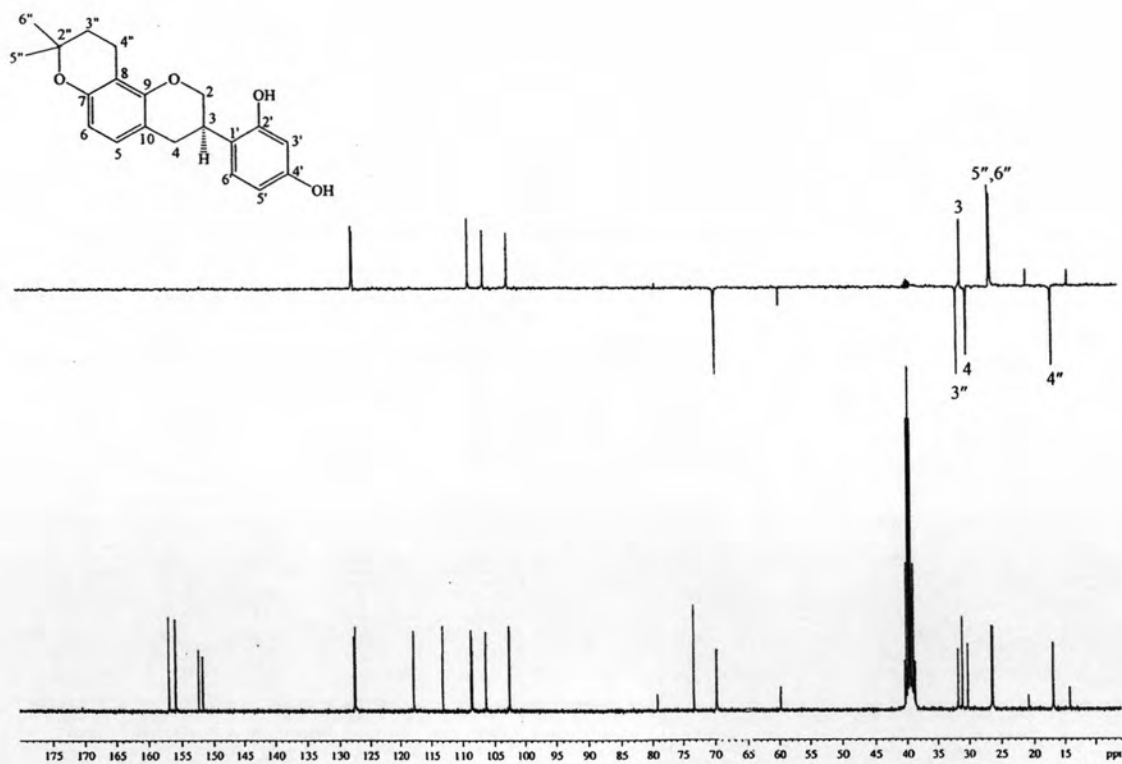


Figure 64. The DEPT  $135^\circ$  spectrum of 3'',4''-dihydroglabridin (**21**) in  $\text{DMSO-d}_6$ .

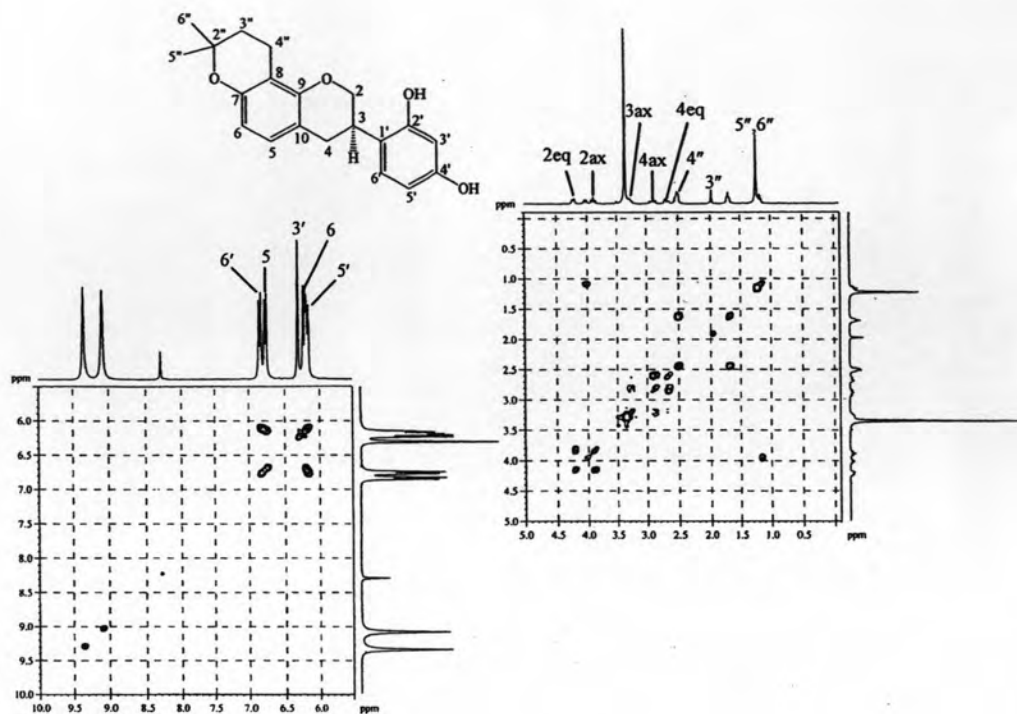


Figure 65. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of 3'',4''-dihydroglabridin (21) in  $\text{DMSO-d}_6$ .

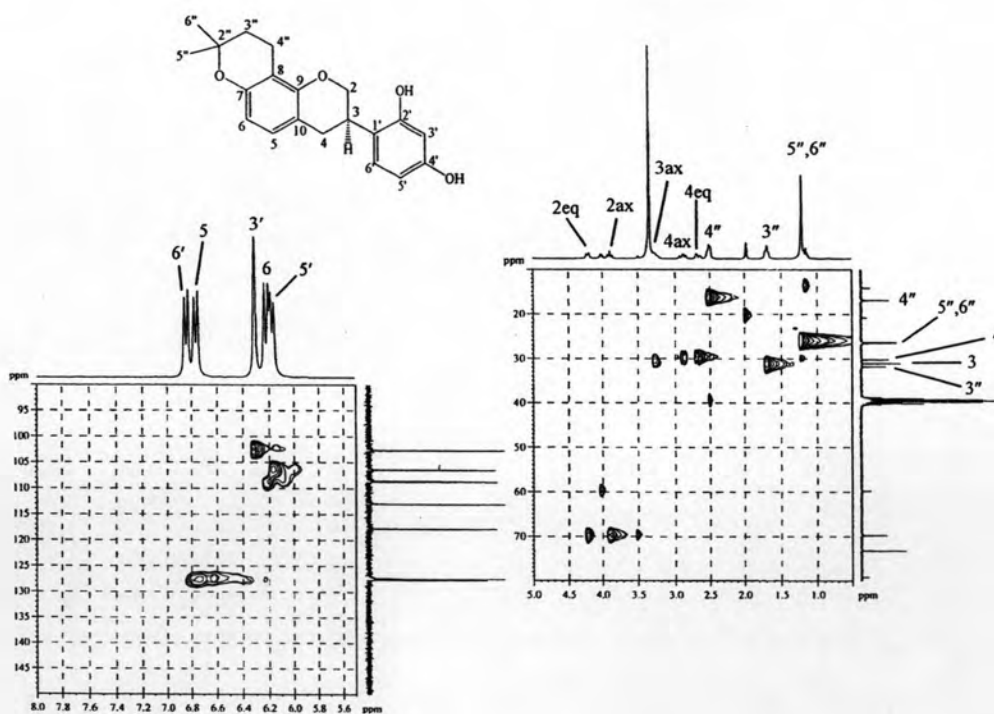


Figure 66. The HMQC spectrum of 3'',4''-dihydroglabridin (21) in  $\text{DMSO-d}_6$ .

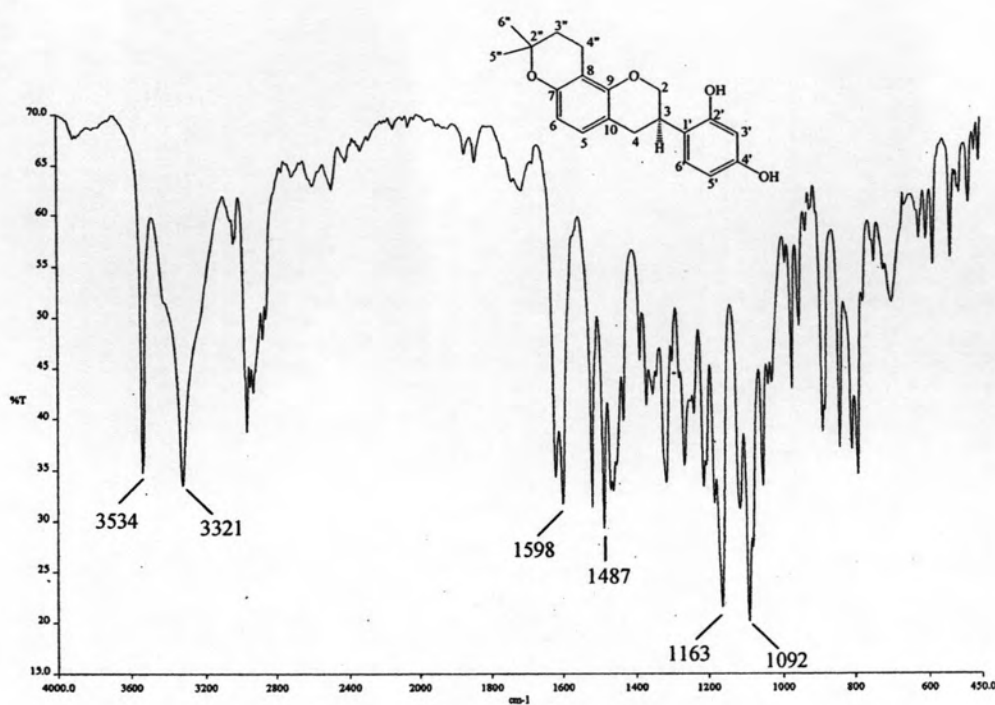


Figure 67. The infrared spectrum of 3'',4''-dihydroglabridin (**21**).

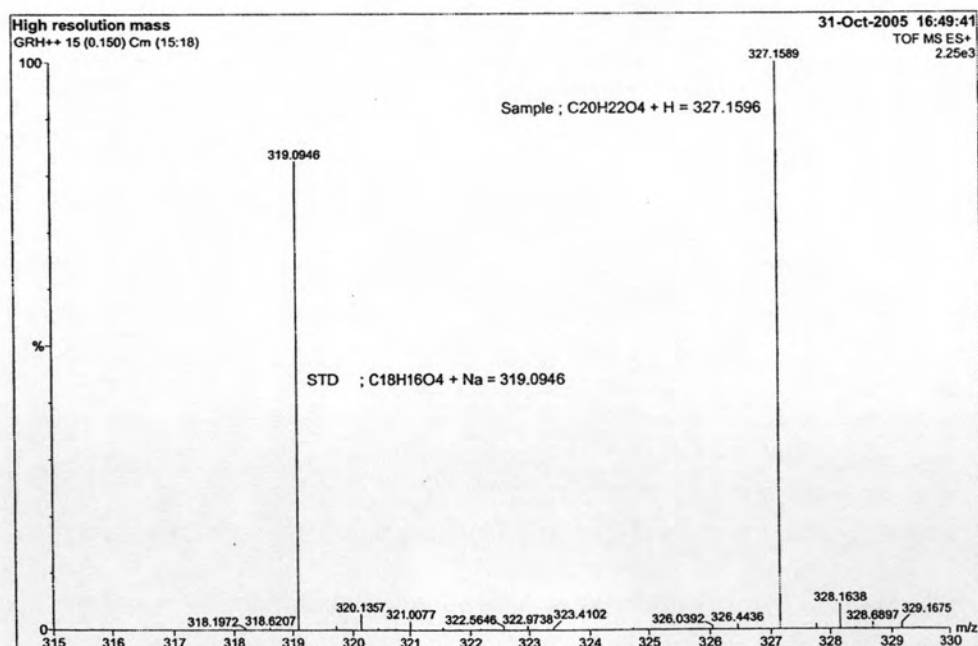


Figure 68. The TOF Mass spectrum of 3'',4''-dihydroglabridin (**21**).





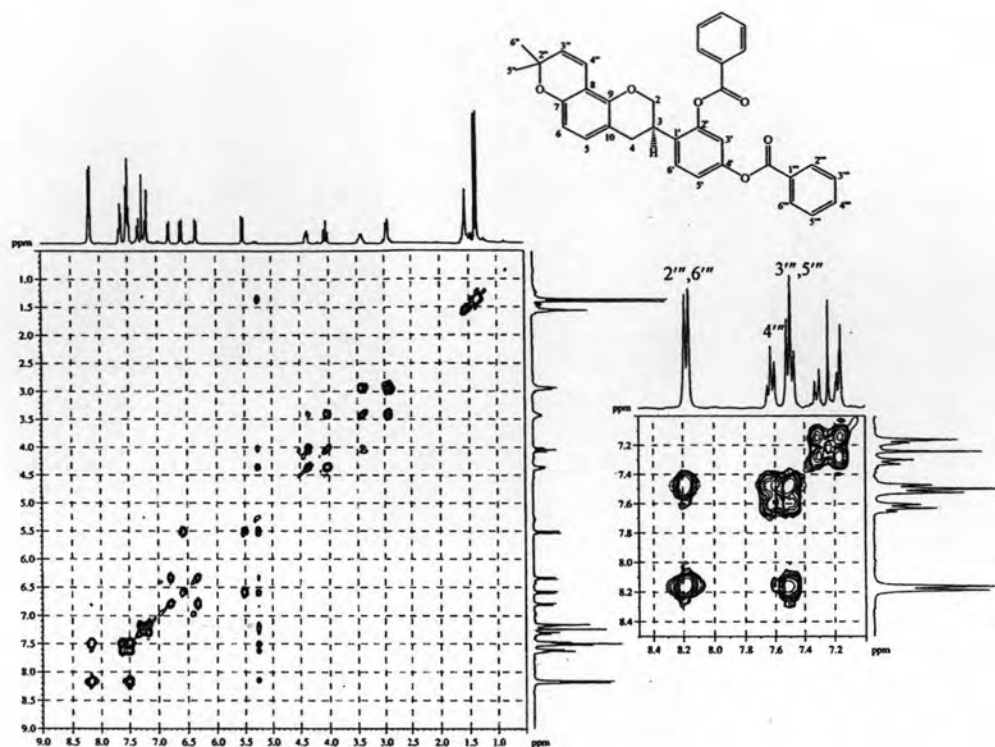


Figure 71. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-dibenzoate (**22**) in  $\text{CDCl}_3$ .

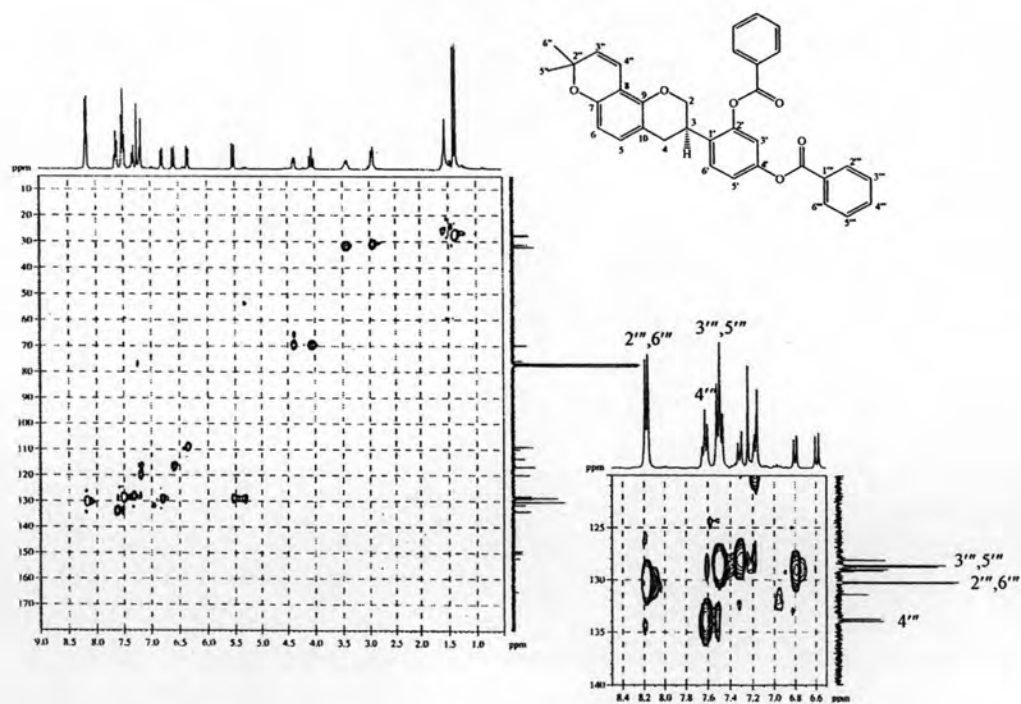


Figure 72. The HMQC spectrum of glabridin-2',4'-O-dibenzoate (**22**) in  $\text{CDCl}_3$ .

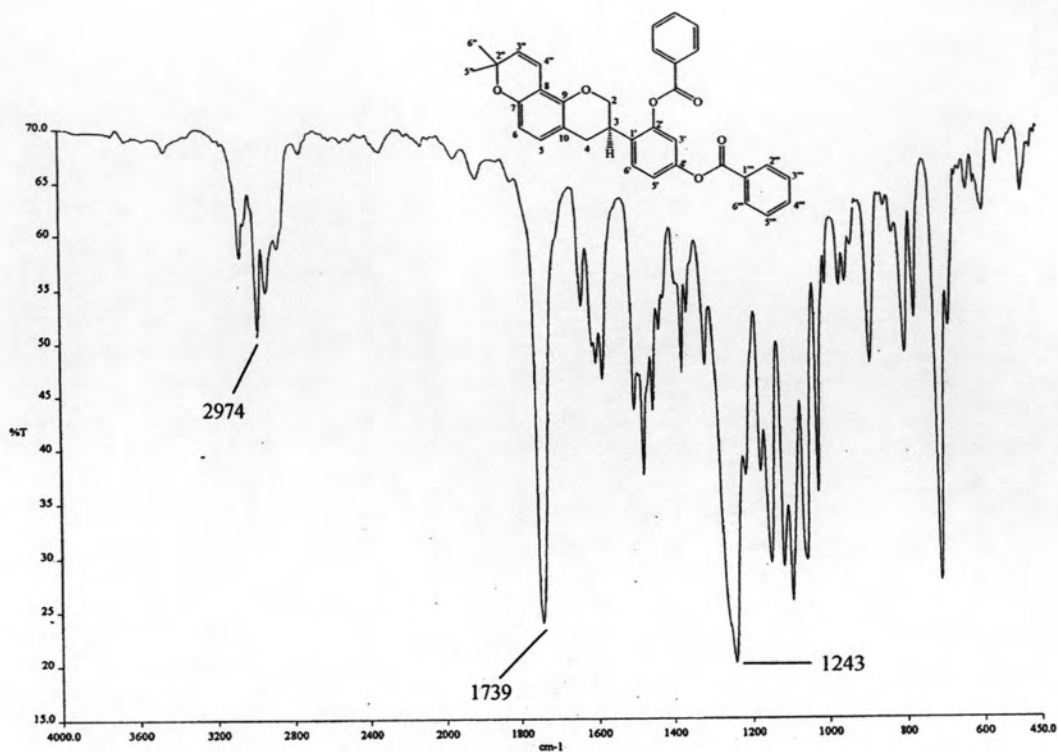


Figure 73. The infrared spectrum of glabridin-2',4'-O-dibenzoate (22).

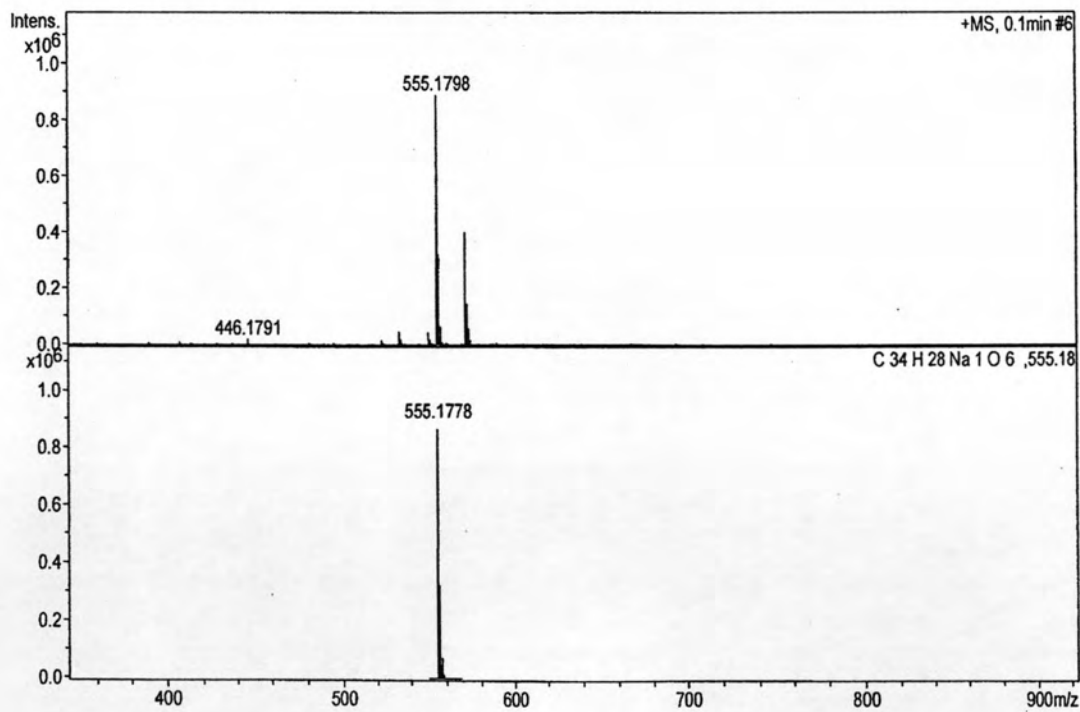


Figure 74. The TOF Mass spectrum of glabridin-2',4'-O-dibenzoate (22)

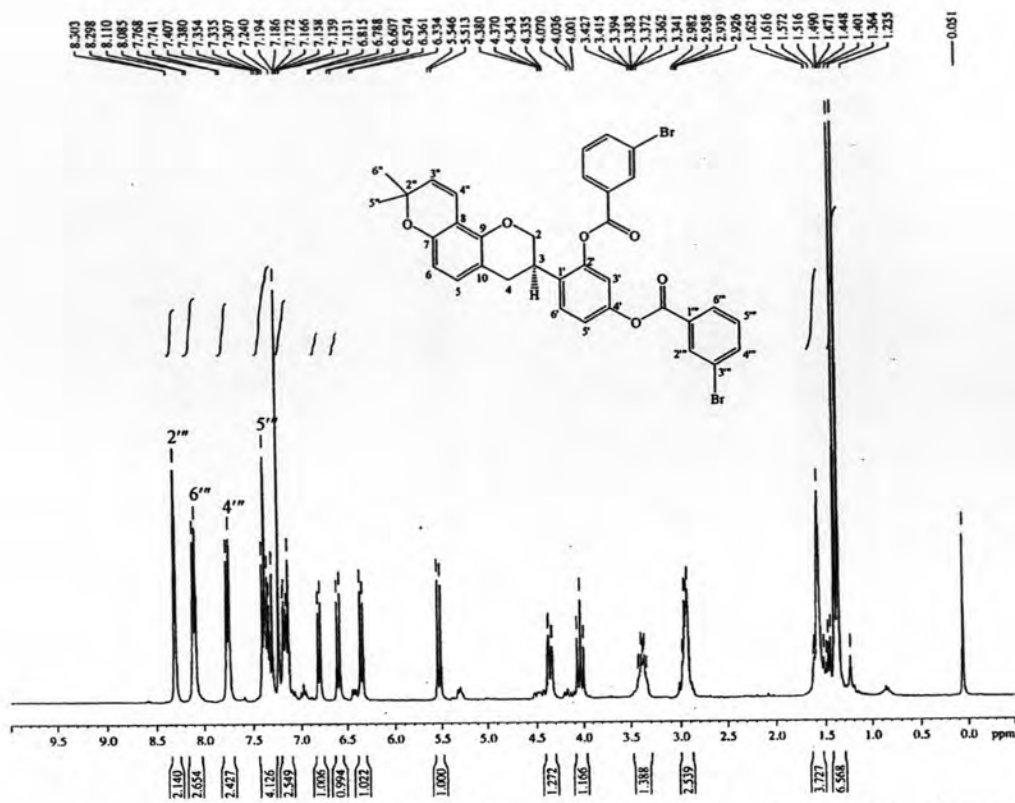


Figure 75. The 300 MHz  $^1\text{H-NMR}$  spectrum of glabridin-2',4'-O-di-3'''-bromobenzoate (**23**) in  $\text{CDCl}_3$ .

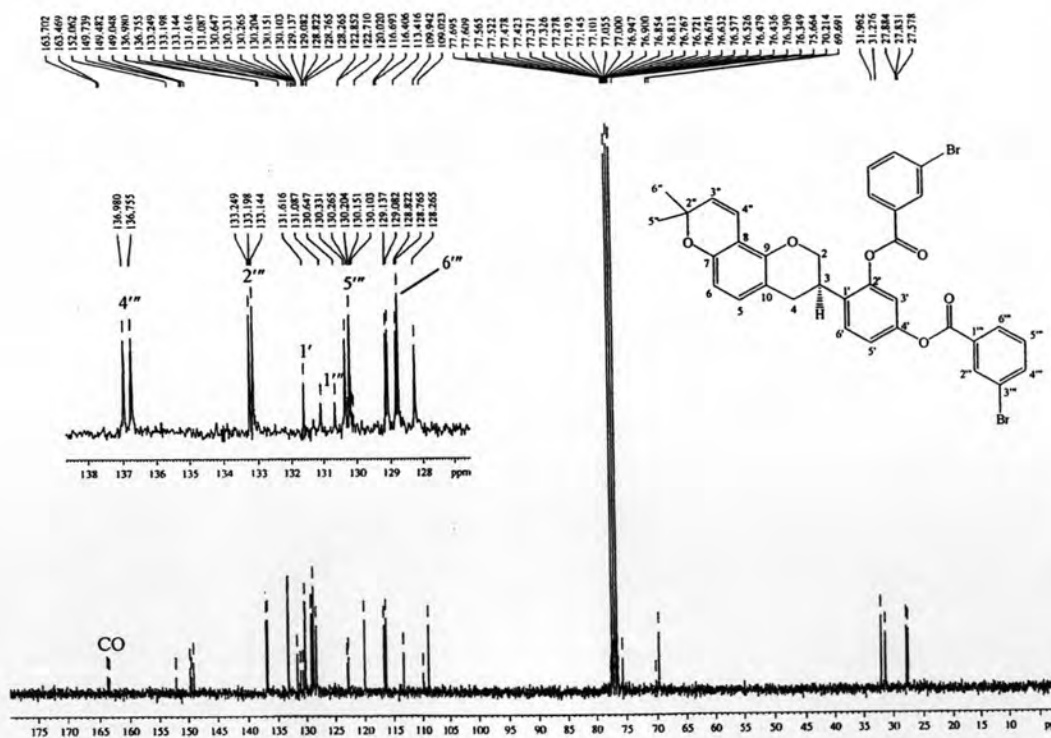


Figure 76. The 75 MHz  $^{13}\text{C-NMR}$  spectrum of glabridin-2',4'-O-di-3'''-bromobenzoate (**23**) in  $\text{CDCl}_3$ .

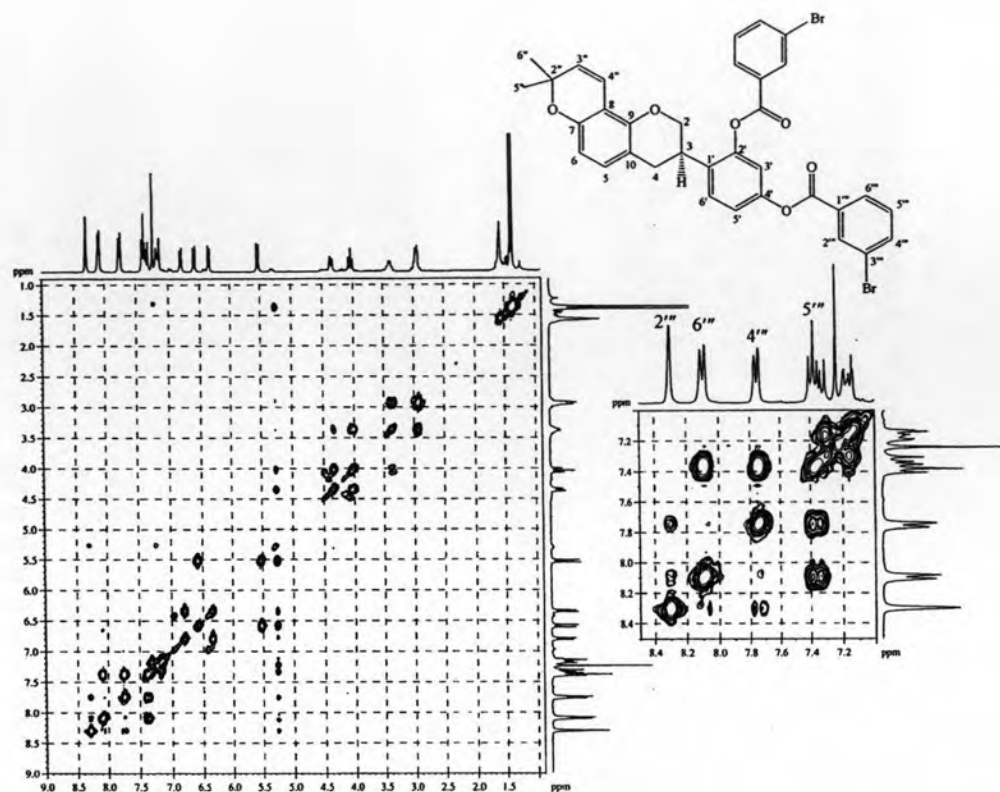


Figure 77. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-di-3'''-bromobenzoate (**23**) in  $\text{CDCl}_3$ .

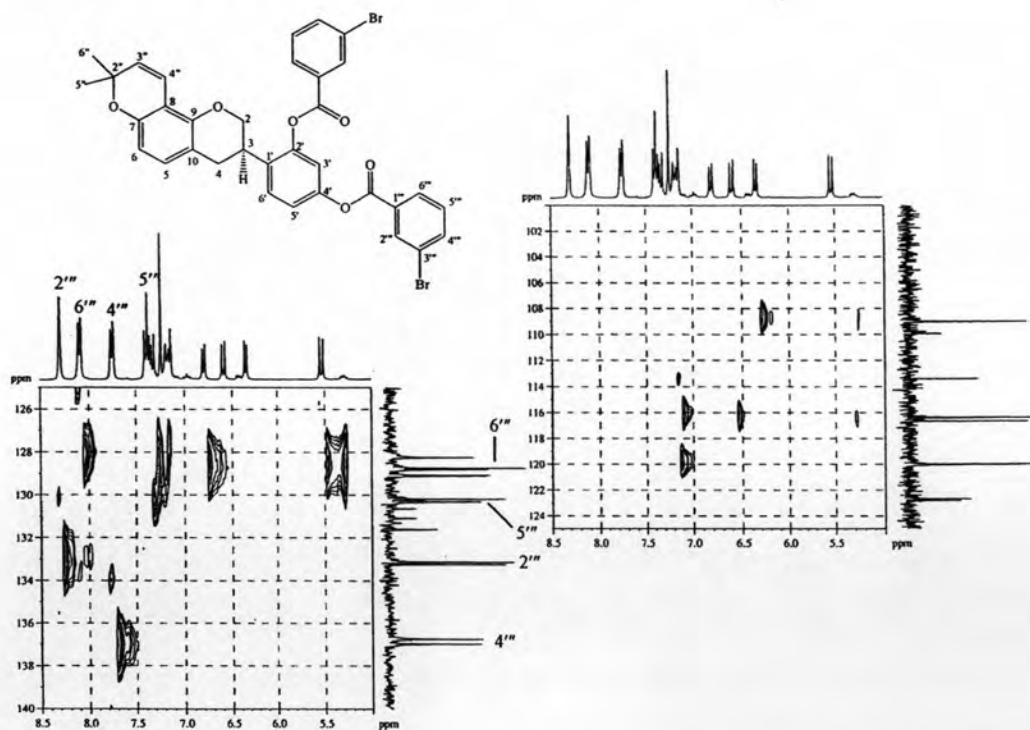


Figure 78. The HMQC spectrum of glabridin-2',4'-O-di-3'''-bromobenzoate (**23**) in  $\text{CDCl}_3$ .

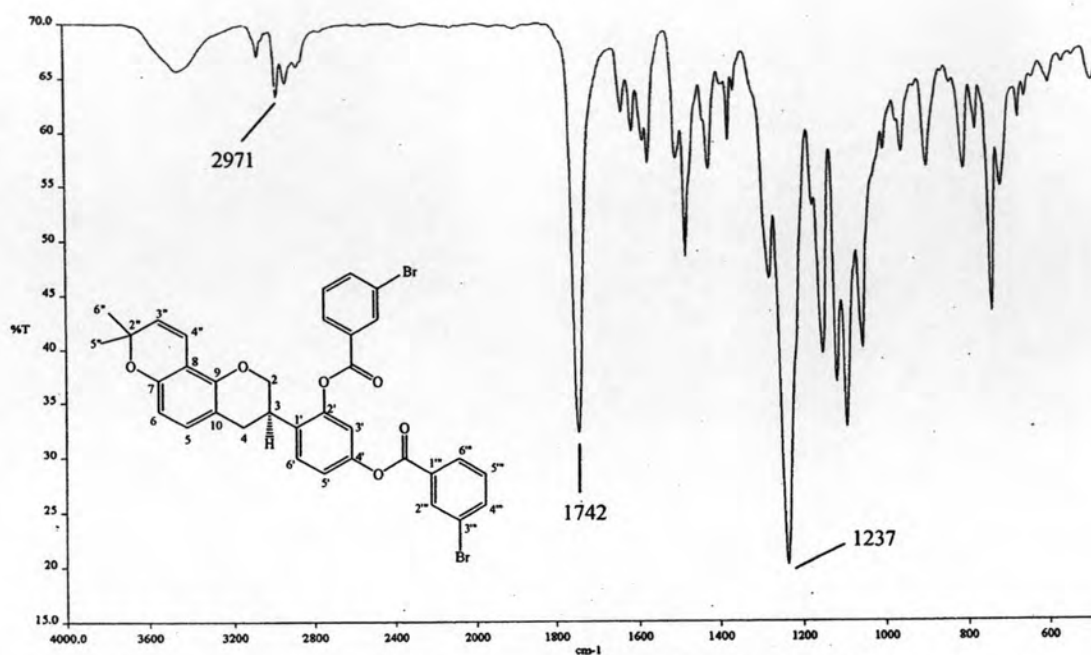


Figure 79. The infrared spectrum of glabridin-2',4'-O-di-3''-bromobenzoate (23).

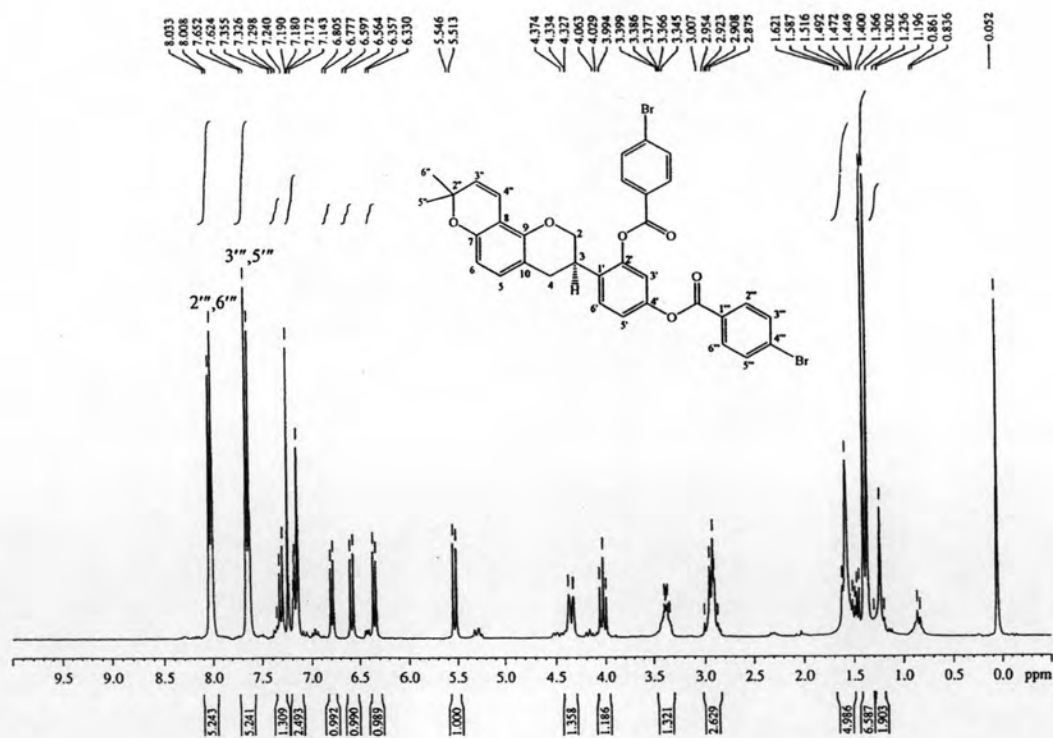


Figure 80. The 300 MHz <sup>1</sup>H-NMR spectrum of glabridin-2',4'-O-di-4''-bromobenzoate (24) in CDCl<sub>3</sub>.



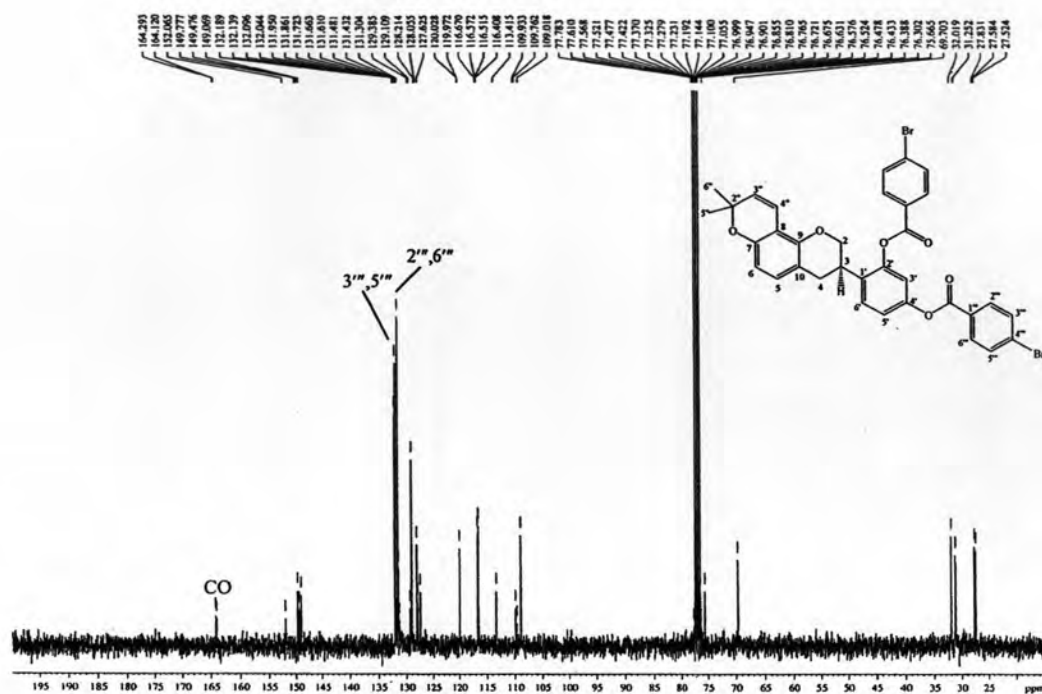


Figure 81. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin-2',4'-O-di-4'''-bromobenzoate (**24**) in  $\text{CDCl}_3$ .

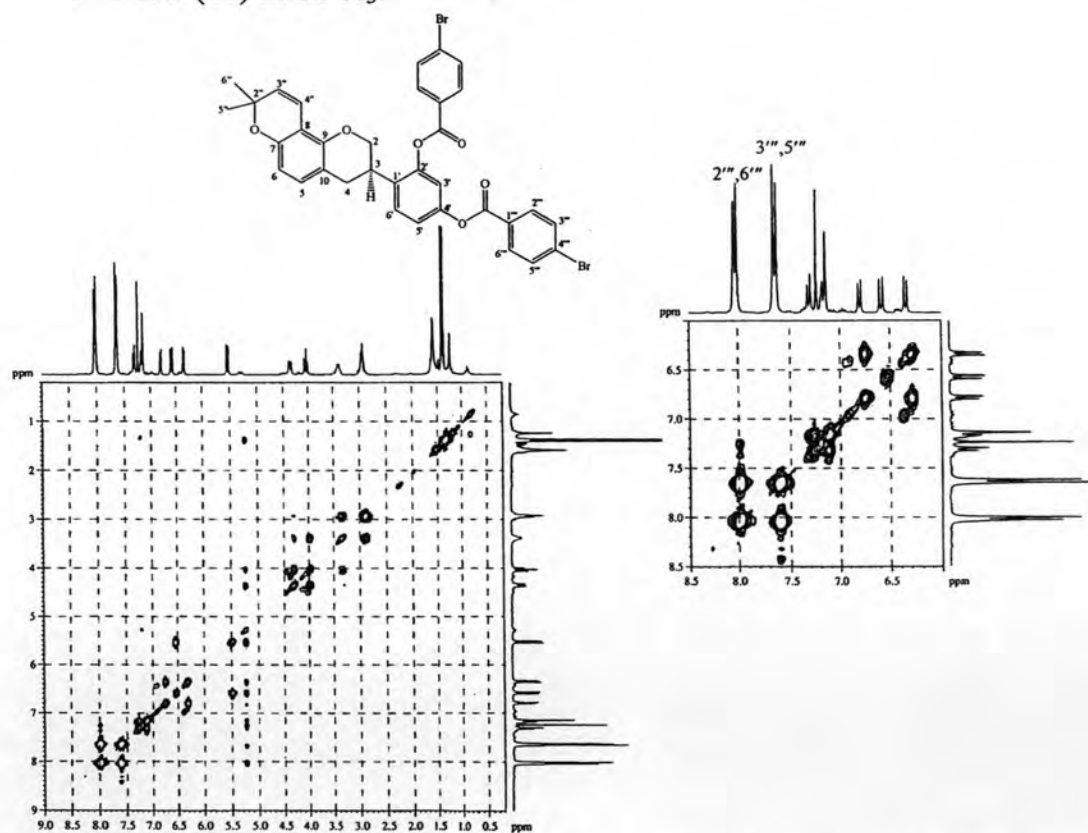


Figure 82. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-di-4'''-bromobenzoate (**24**) in  $\text{CDCl}_3$ .

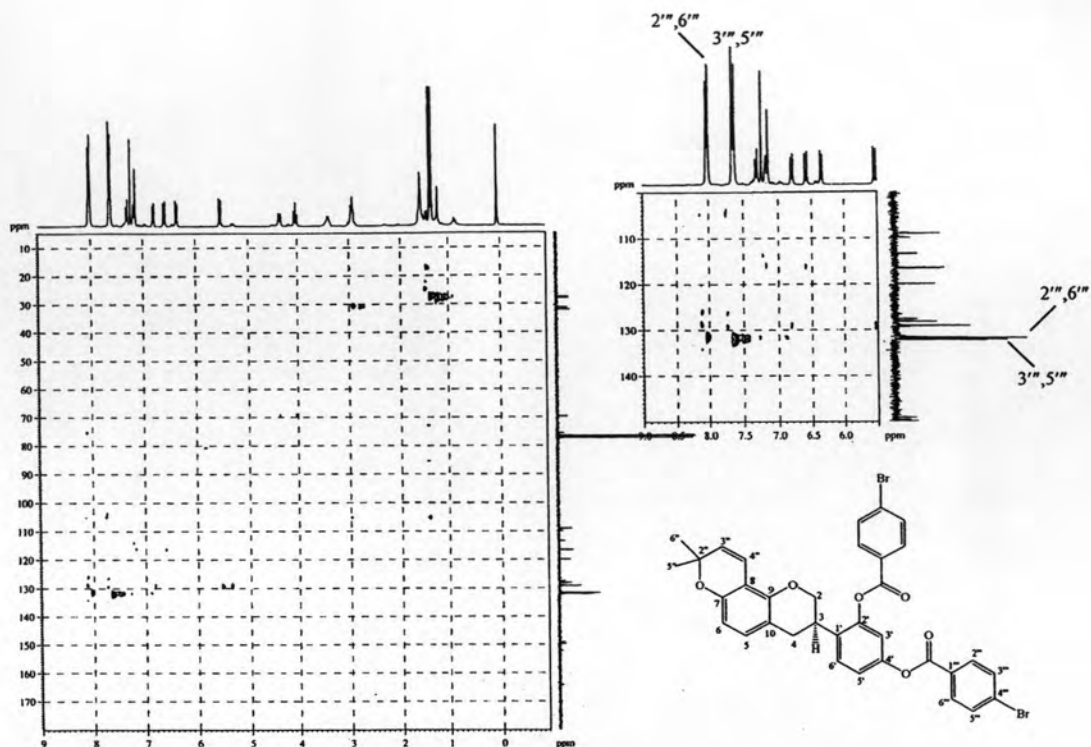


Figure 83. The HMQC spectrum of glabridin-2',4'-O-di-4'''-bromobenzoate (24) in  $\text{CDCl}_3$ .

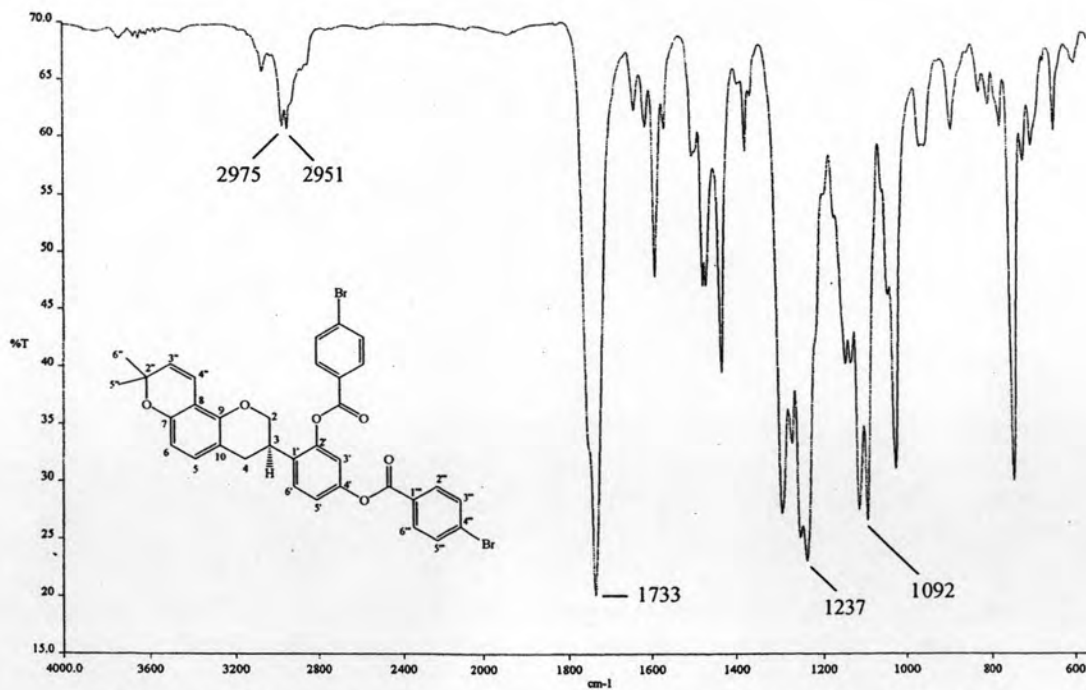


Figure 84. The infrared spectrum of glabridin-2',4'-O-di-4'''-bromobenzoate (24).

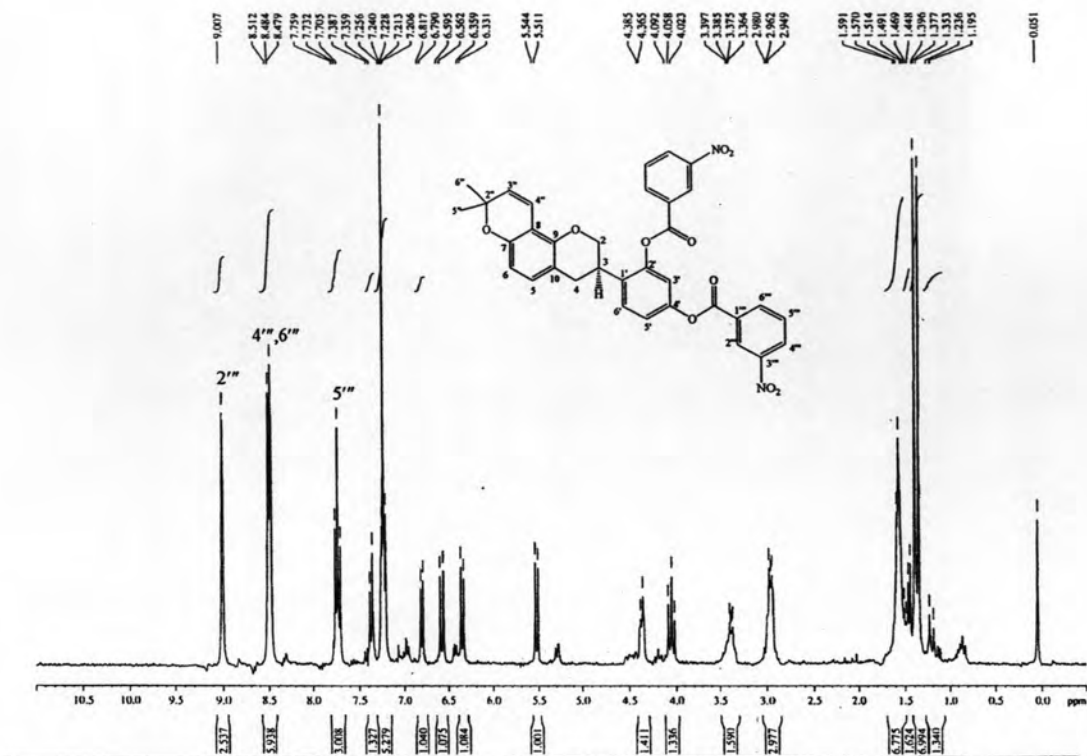


Figure 85. The 300 MHz  $^1\text{H-NMR}$  spectrum of glabridin-2',4'-O-di-3''-nitrobenzoate (**25**) in  $\text{CDCl}_3$ .

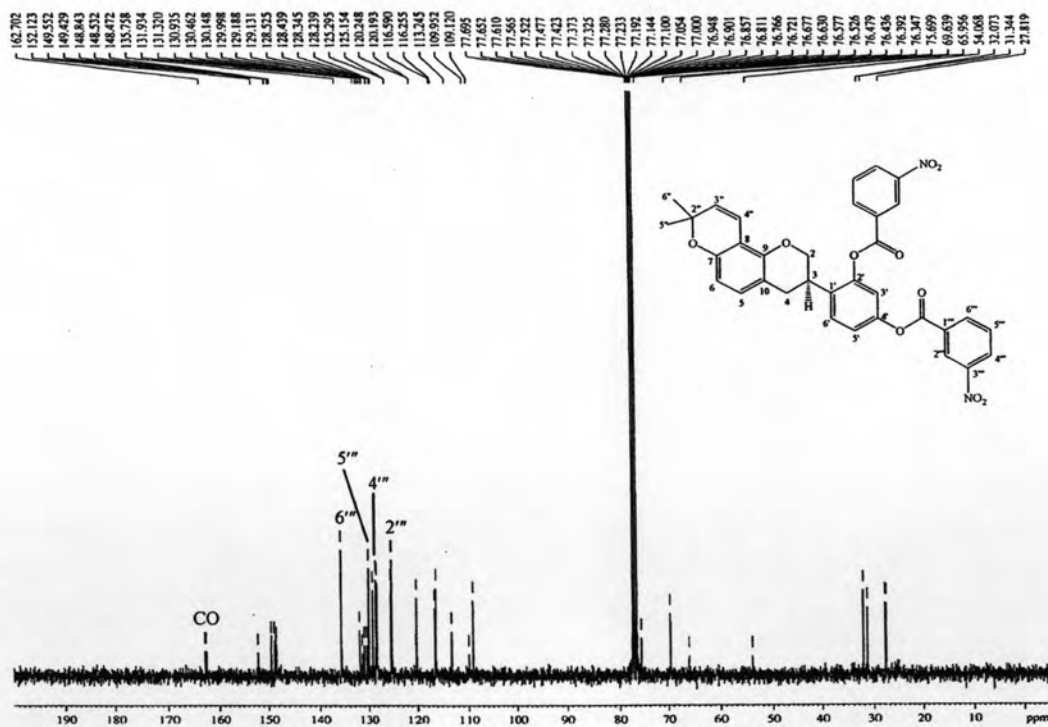


Figure 86. The 75 MHz  $^{13}\text{C-NMR}$  spectrum of glabridin-2',4'-O-di-3''-nitrobenzoate (**25**) in  $\text{CDCl}_3$ .

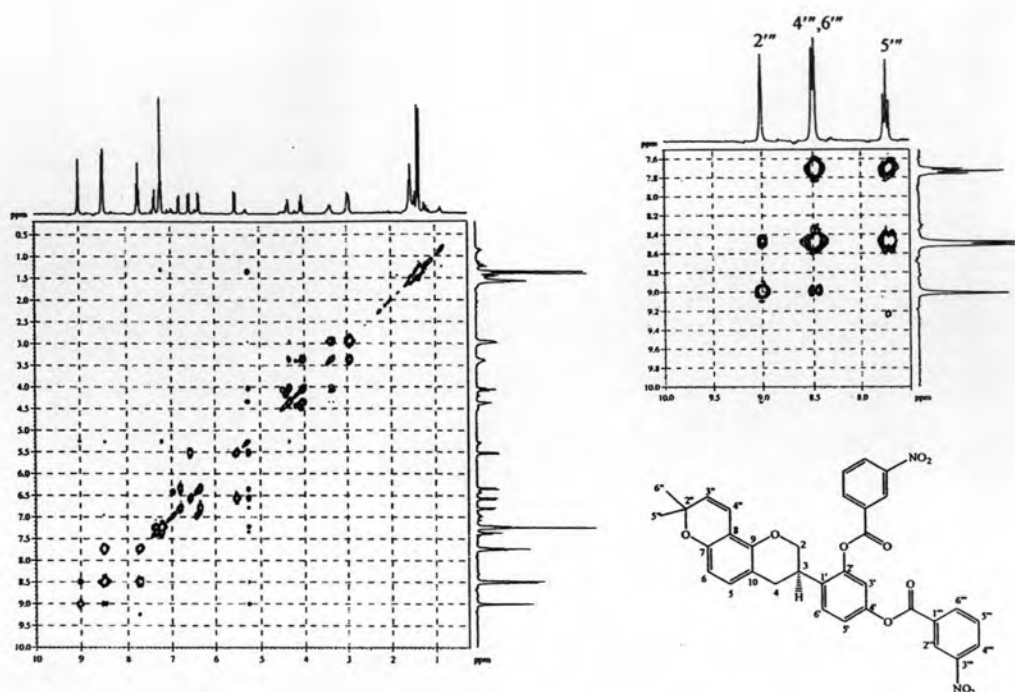


Figure 87. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-di-3''-nitrobenzoate (**25**) in  $\text{CDCl}_3$ .

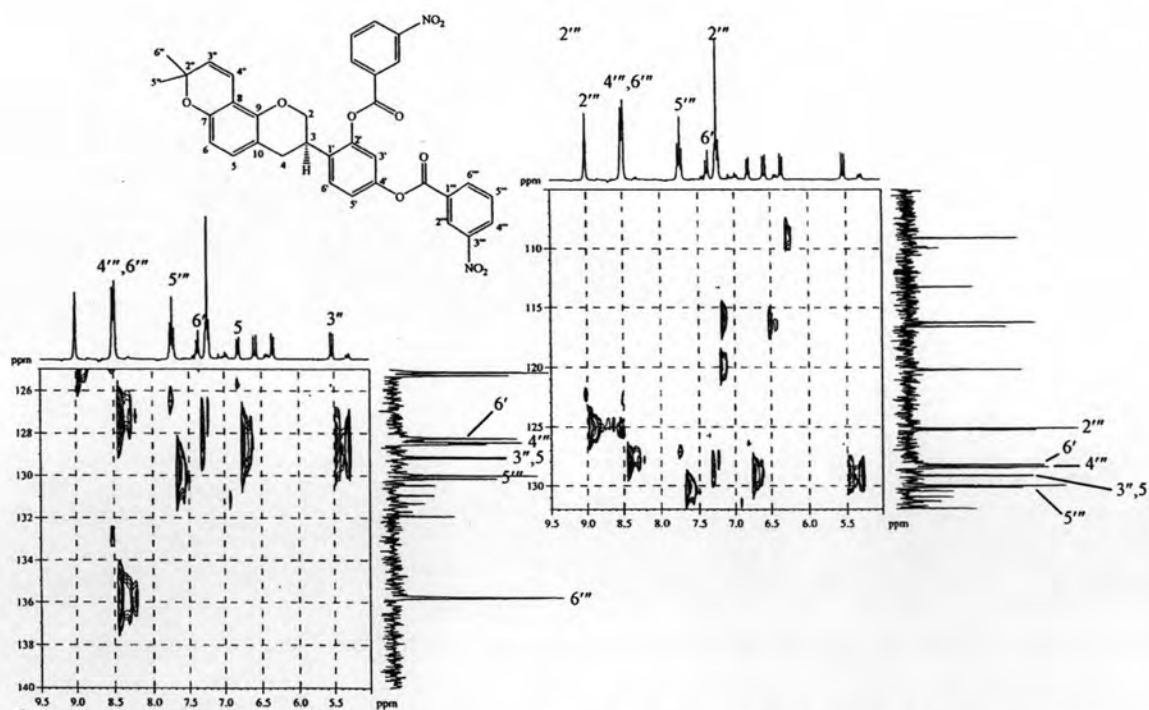


Figure 88. The HMQC spectrum of glabridin-2',4'-O-di-3''-nitrobenzoate (**25**) in  $\text{CDCl}_3$ .

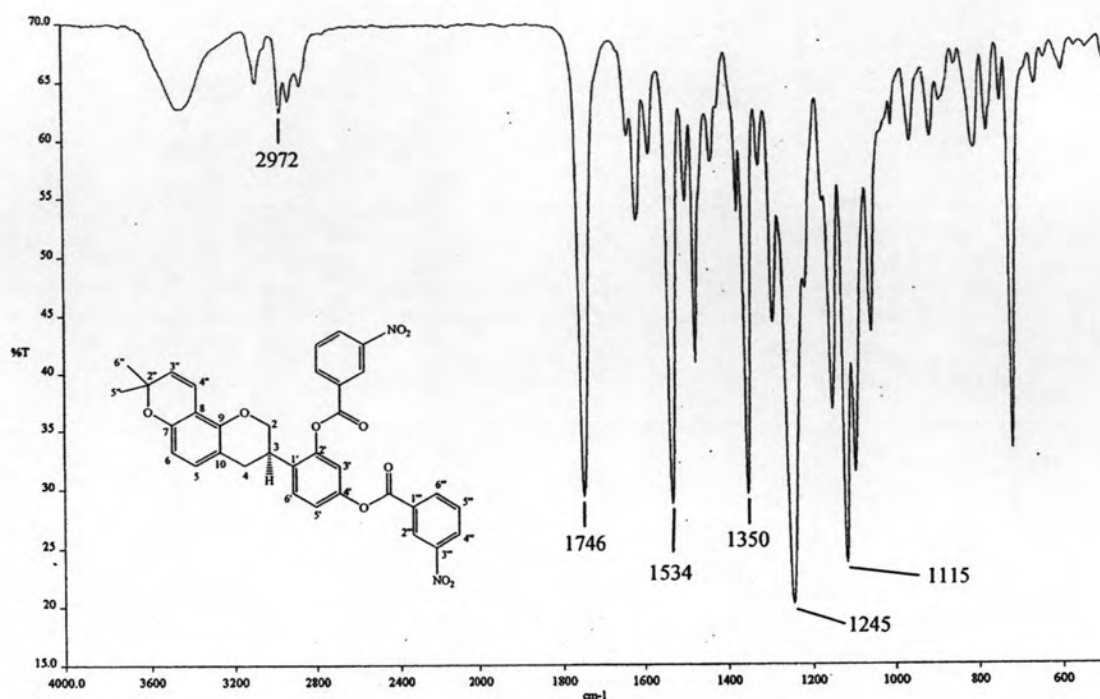


Figure 89. The infrared spectrum of glabridin-2',4'-O-di-3'''-nitrobenzoate (25).

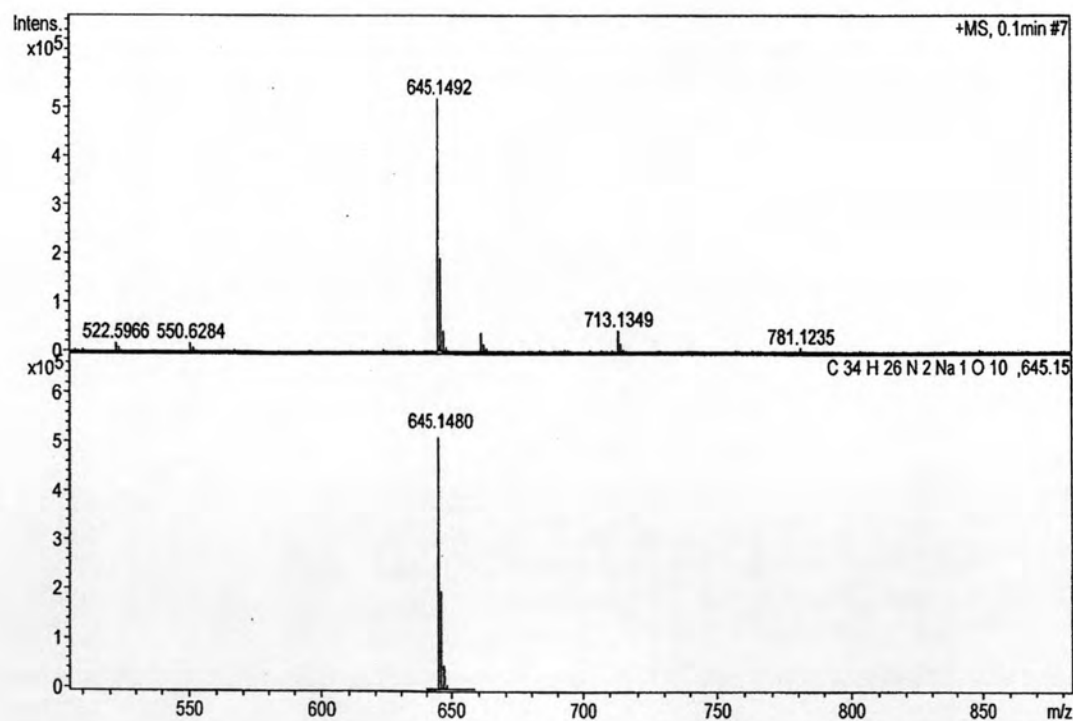


Figure 90 The TOF Mass spectrum of glabridin-2',4'-O-di-3'''-nitrobenzoate (25).

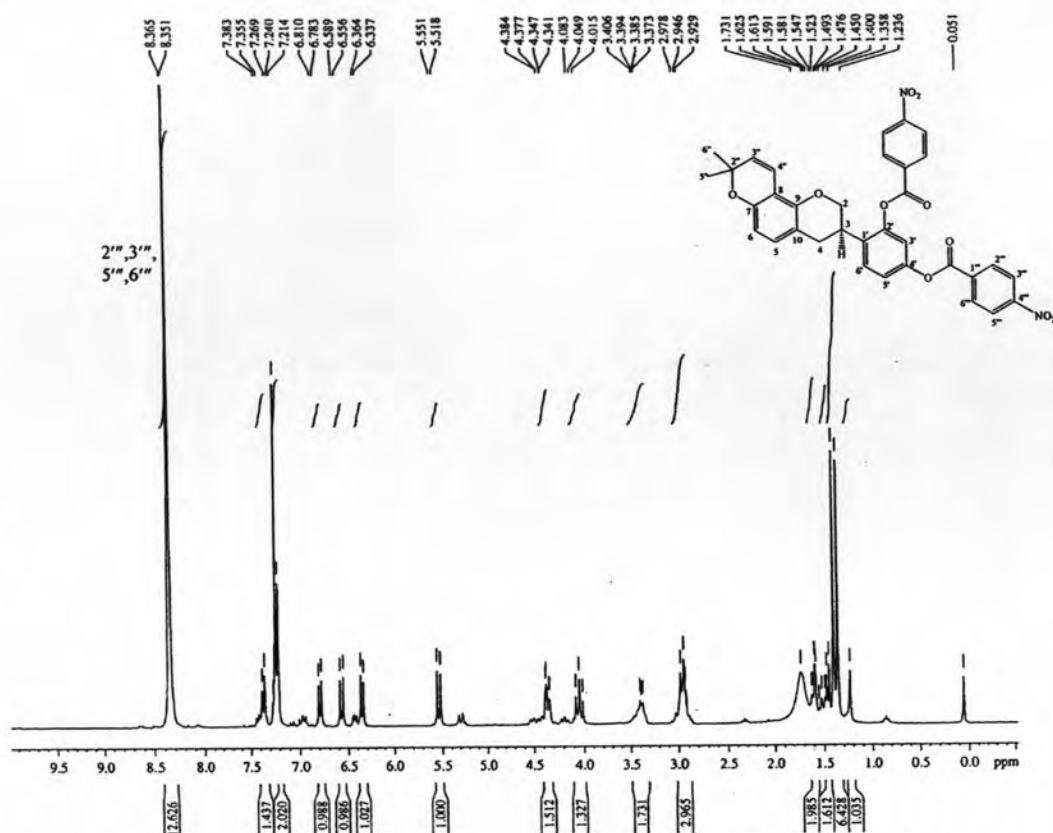


Figure 91. The 300 MHz  $^1\text{H-NMR}$  spectrum of glabridin-2',4'-O-di-4''-nitrobenzoate (**26**) in  $\text{CDCl}_3$ .

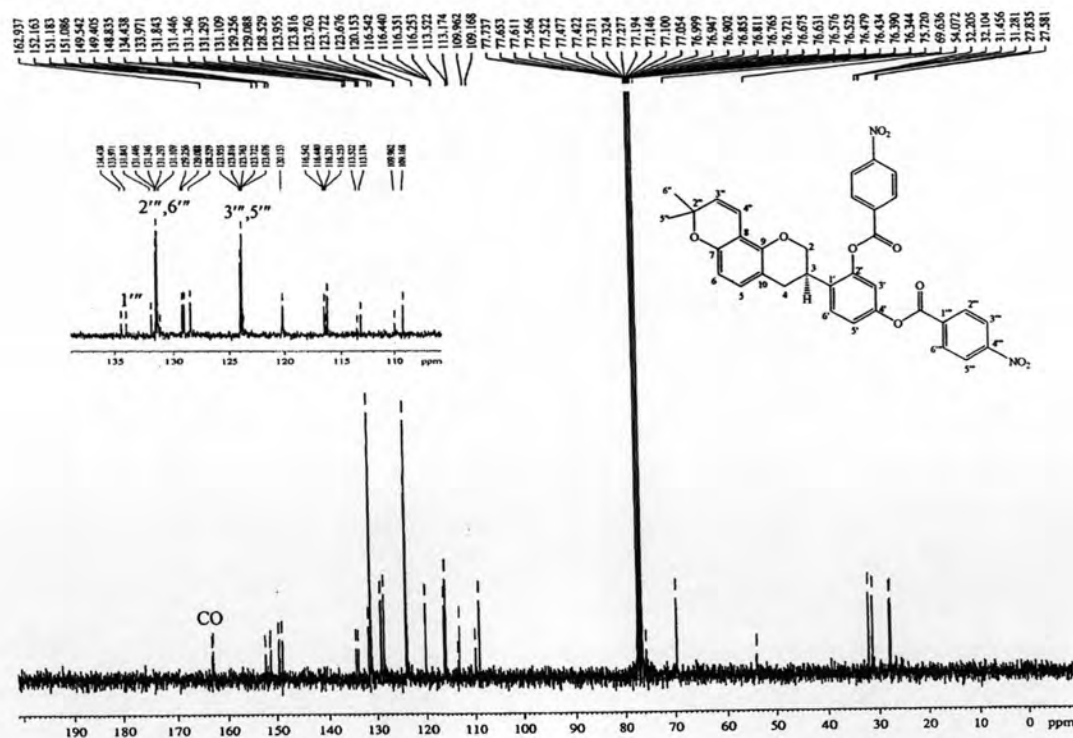


Figure 92. The 75 MHz  $^{13}\text{C-NMR}$  spectrum of glabridin-2',4'-O-di-4''-nitrobenzoate (**26**) in  $\text{CDCl}_3$ .



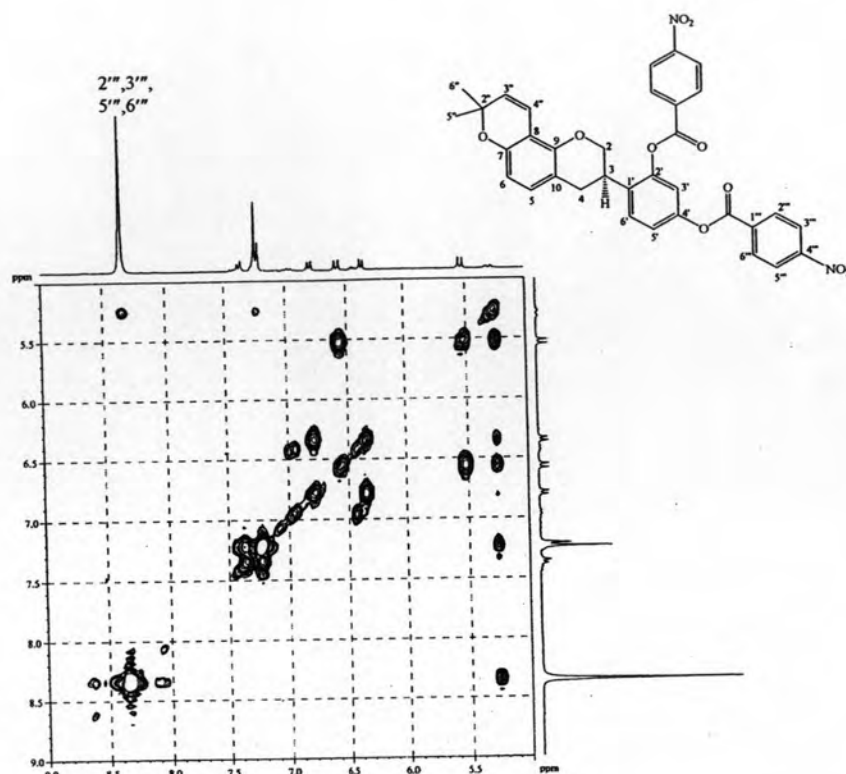


Figure 93. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-di-4'''-nitrobenzoate (**26**) in  $\text{CDCl}_3$ .

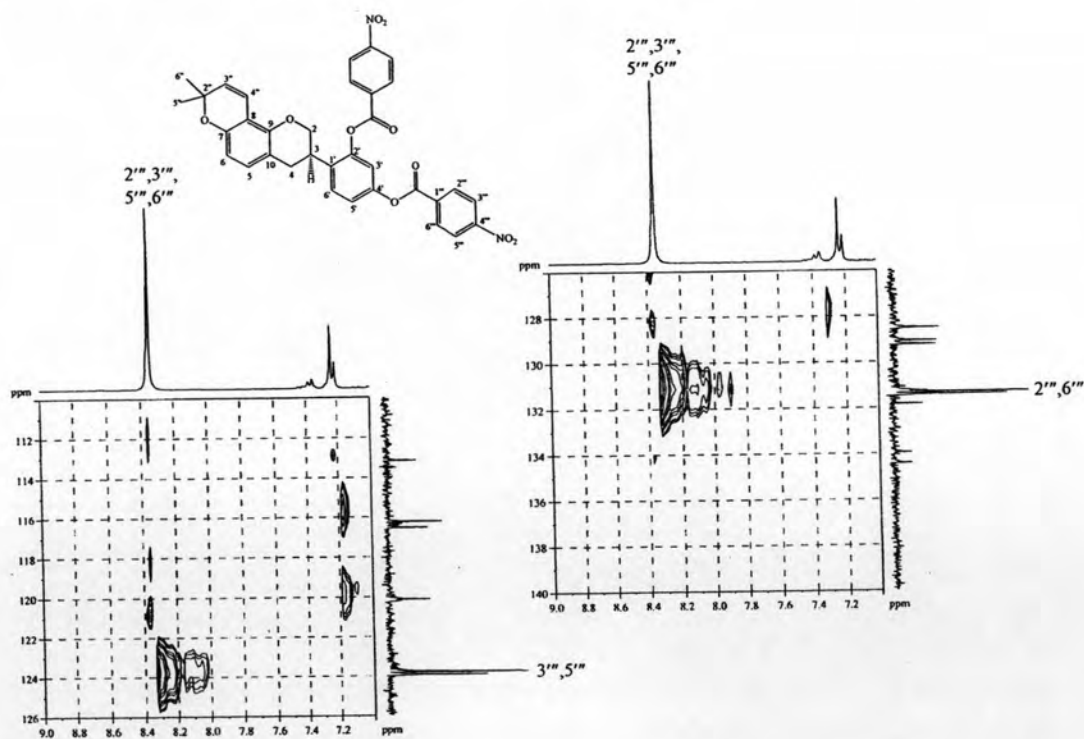


Figure 94. The HMQC spectrum of glabridin-2',4'-O-di-4'''-nitrobenzoate (**26**) in  $\text{CDCl}_3$ .

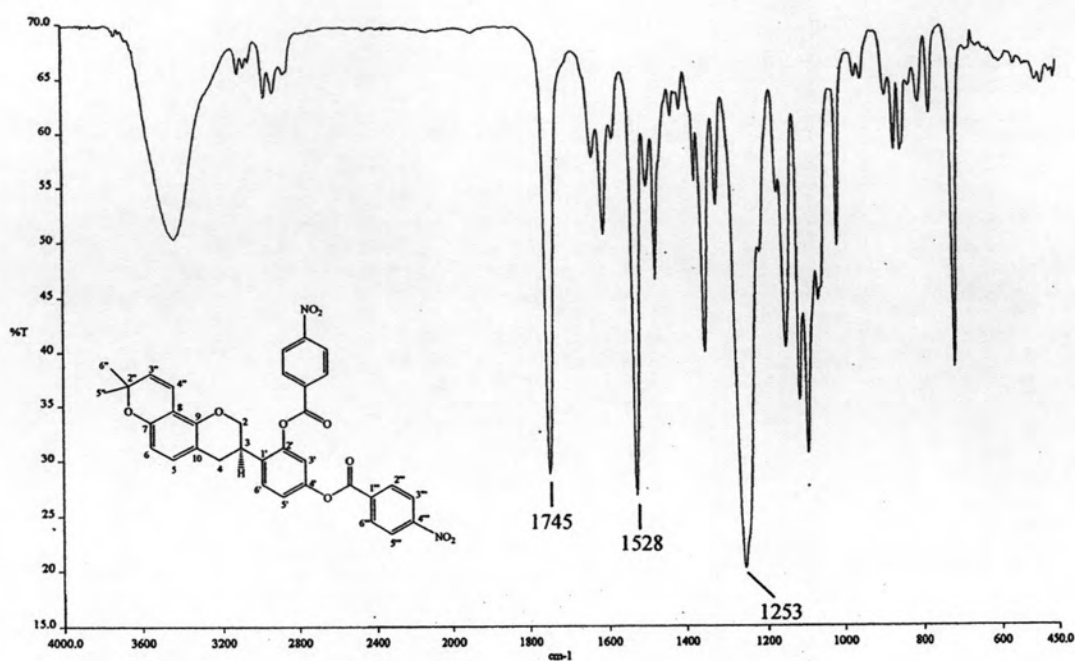


Figure 95. The infrared spectrum of glabridin-2',4'-O-di-4'''-nitrobenzoate (26).

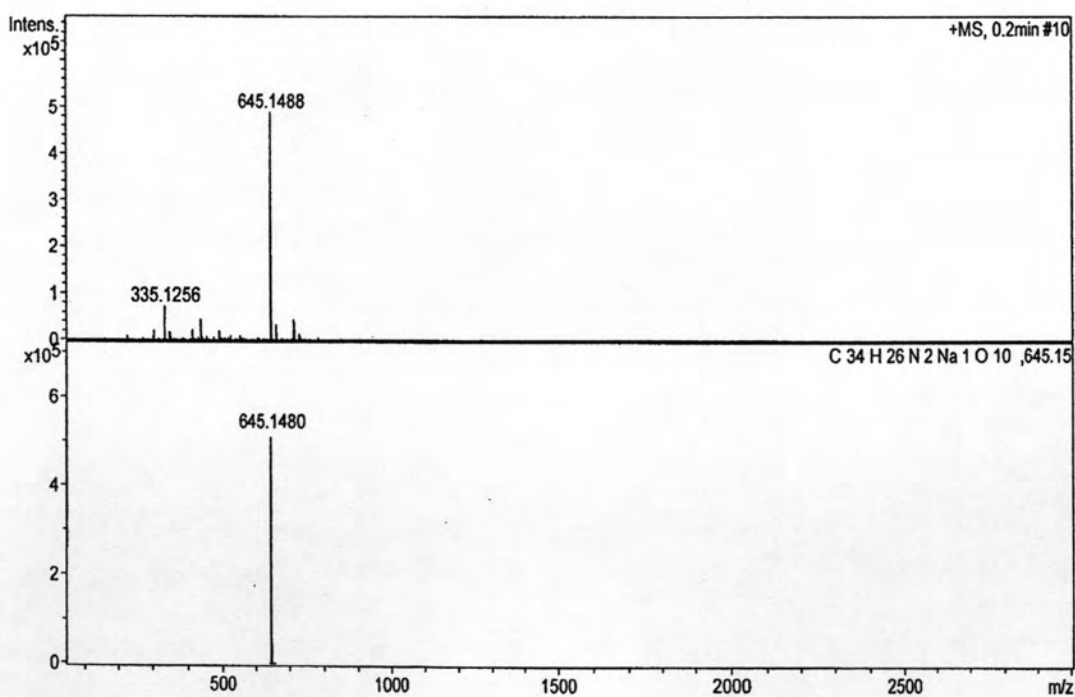


Figure 96. The TOF Mass spectrum of glabridin-2',4'-O-di-4'''-nitrobenzoate (26).

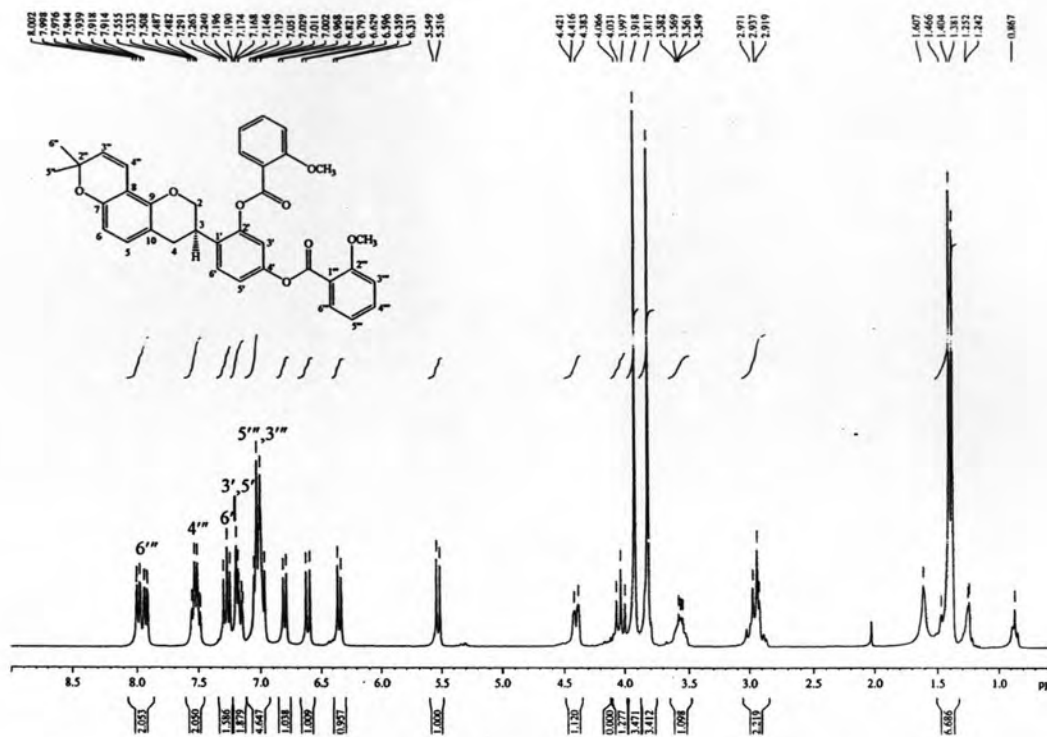


Figure 97. The 300 MHz  $^1\text{H}$ -NMR spectrum of glabridin-2',4'-O-di-2'''-methoxybenzoate (27) in  $\text{CDCl}_3$ .

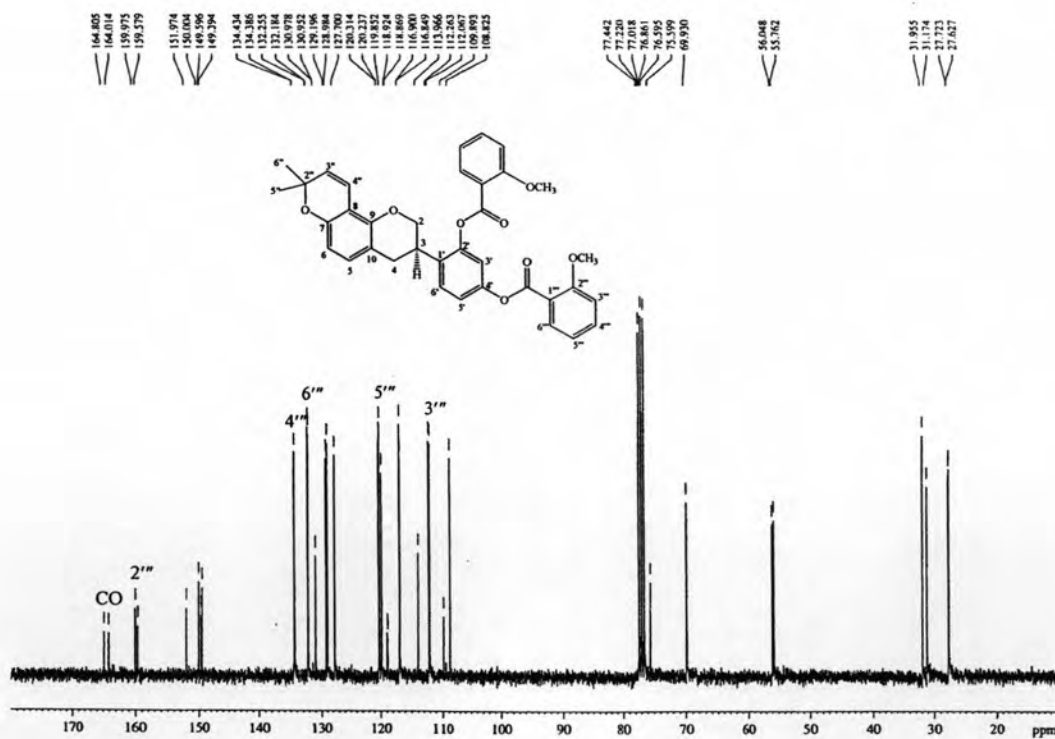


Figure 98. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin-2',4'-O-di-2'''-methoxybenzoate (27) in  $\text{CDCl}_3$ .

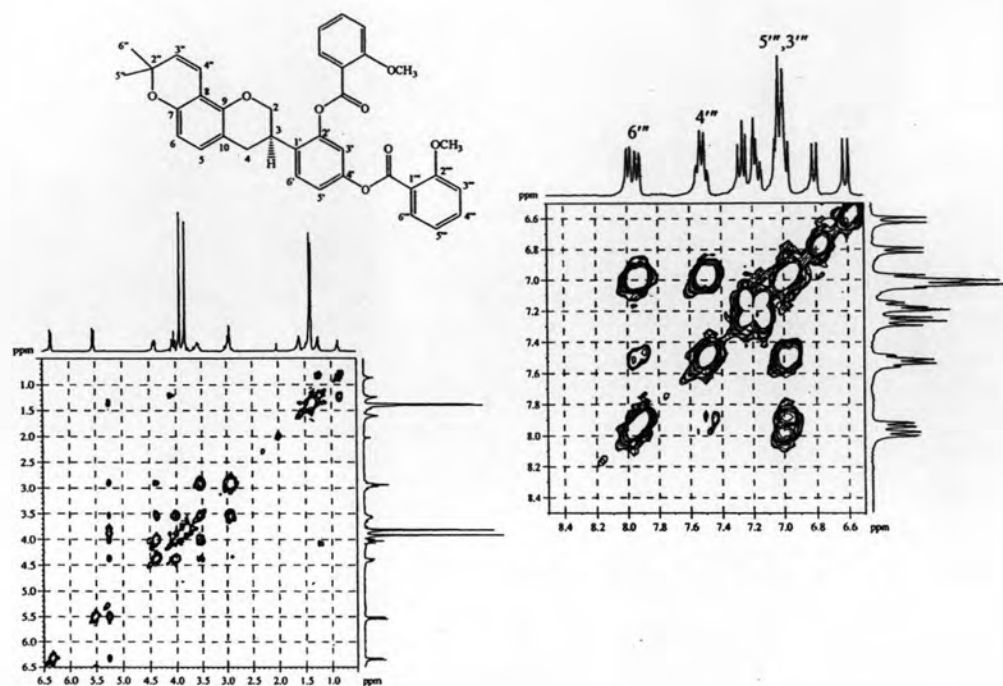


Figure 99. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-di-2'''-methoxybenzoate (**27**) in  $\text{CDCl}_3$ .

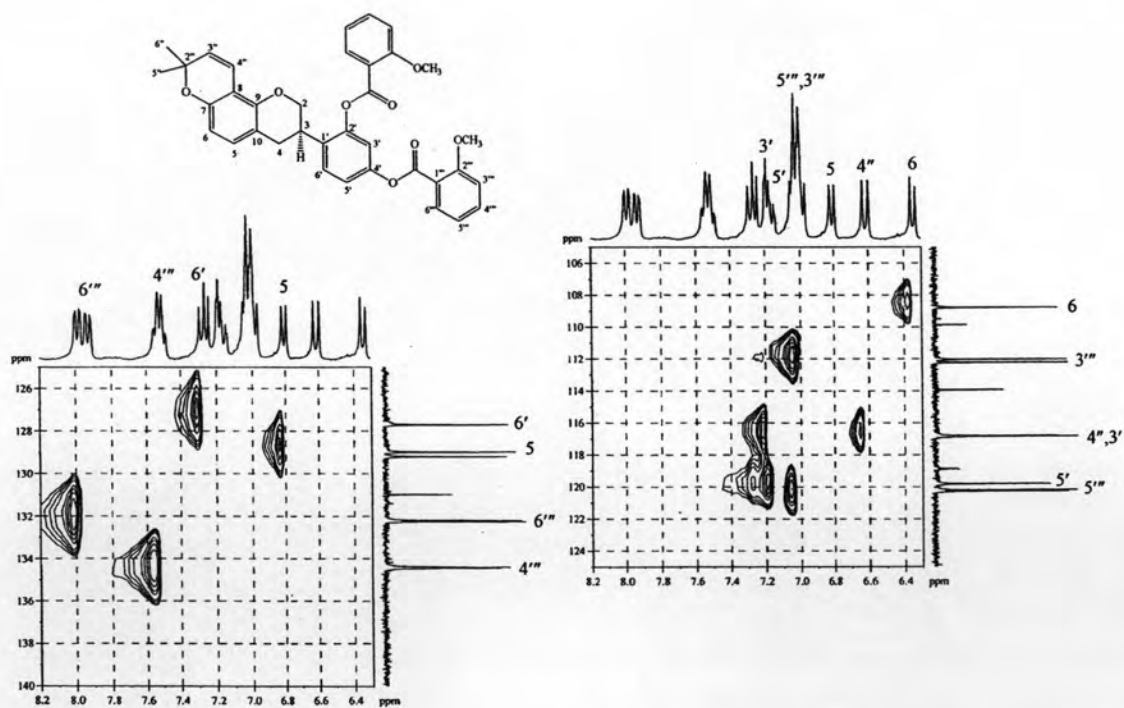


Figure 100. The HMQC spectrum of glabridin-2',4'-O-di-2'''-methoxybenzoate (**27**) in  $\text{CDCl}_3$ .

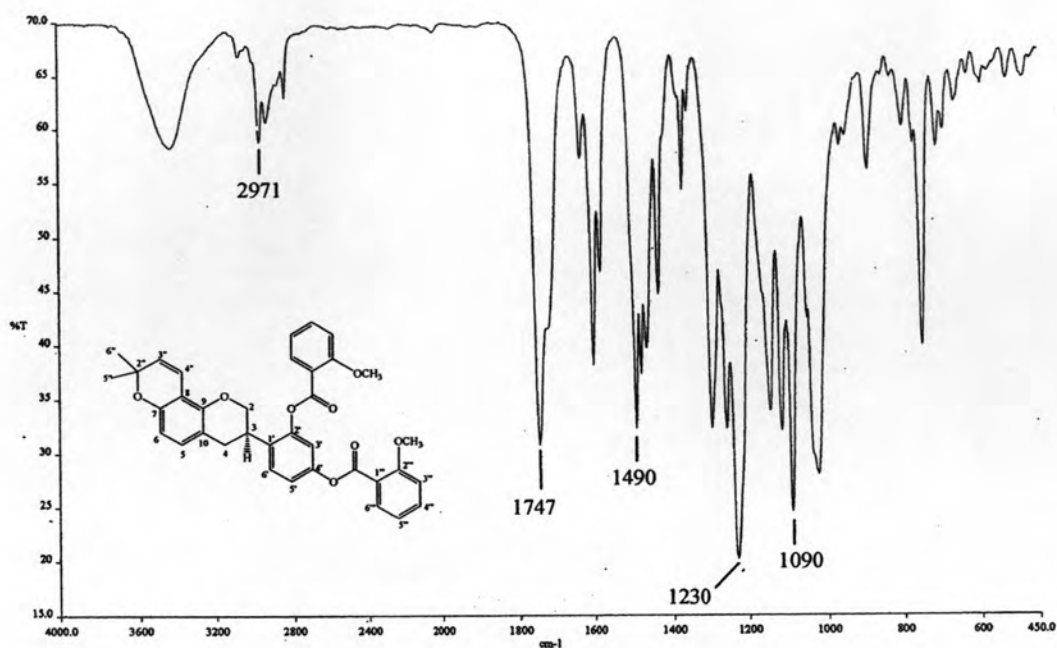


Figure 101. The infrared spectrum of glabridin-2',4'-O-di-2'''-methoxybenzoate (27).

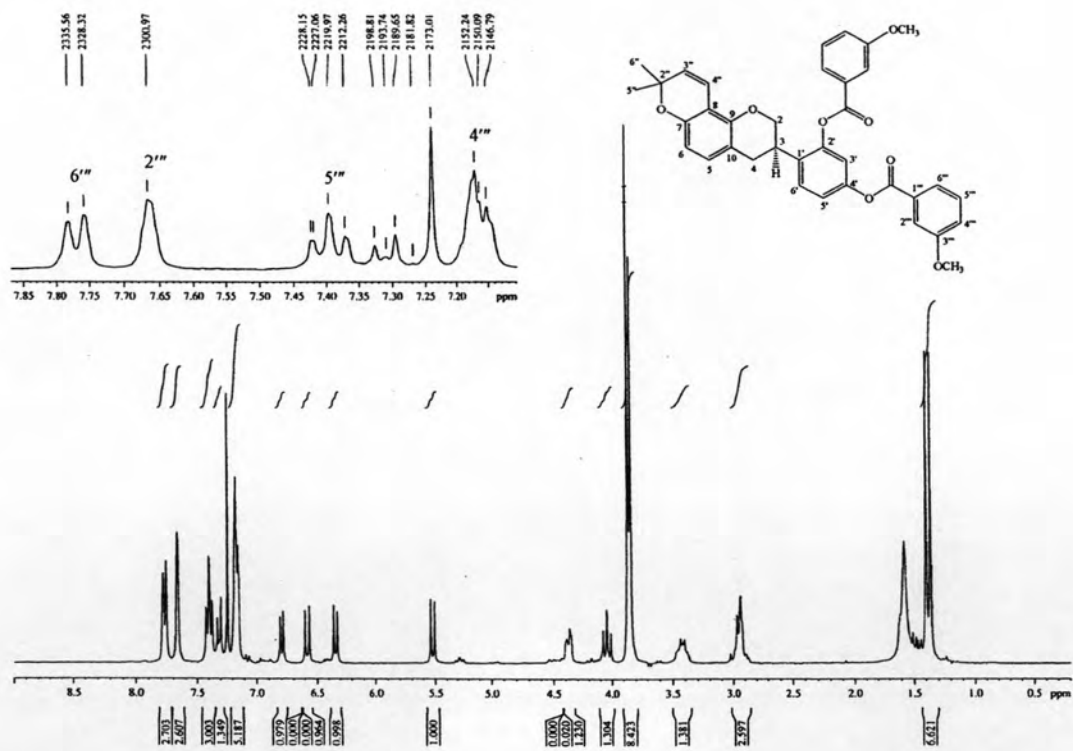


Figure 102. The 300 MHz  $^1\text{H-NMR}$  spectrum of glabridin-2',4'-O-di-3'''-methoxybenzoate (28) in  $\text{CDCl}_3$ .

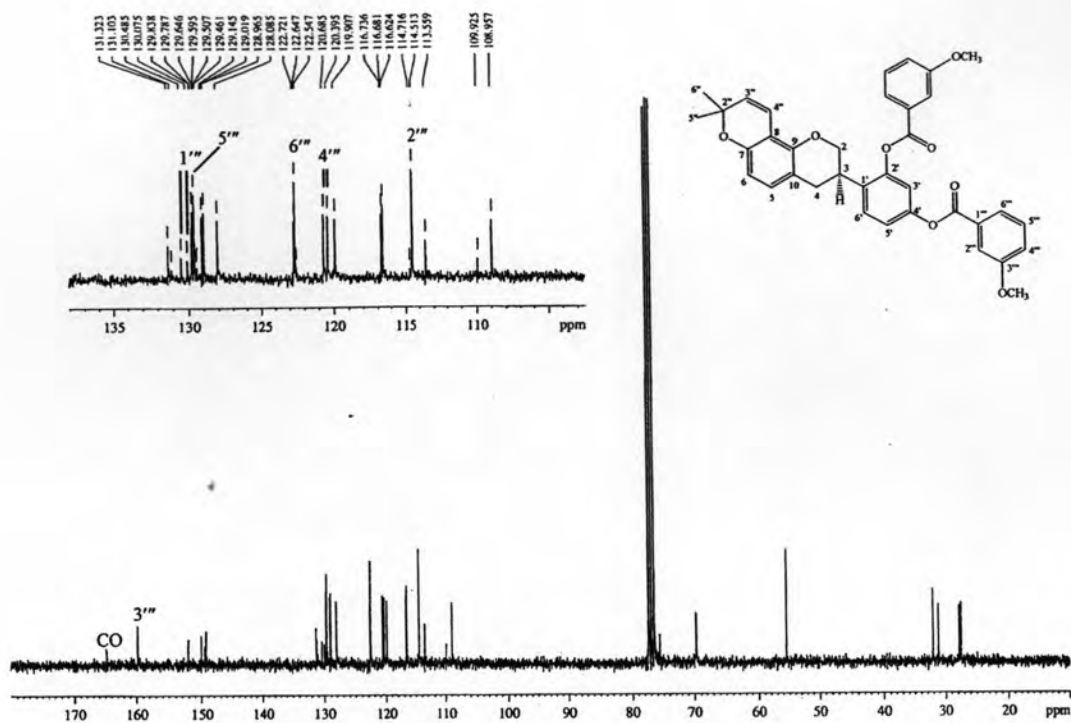


Figure 103. The 75 MHz  $^{13}\text{C}$ -NMR spectrum of glabridin-2',4'-O-di-3'''-methoxybenzoate (**28**) in  $\text{CDCl}_3$ .

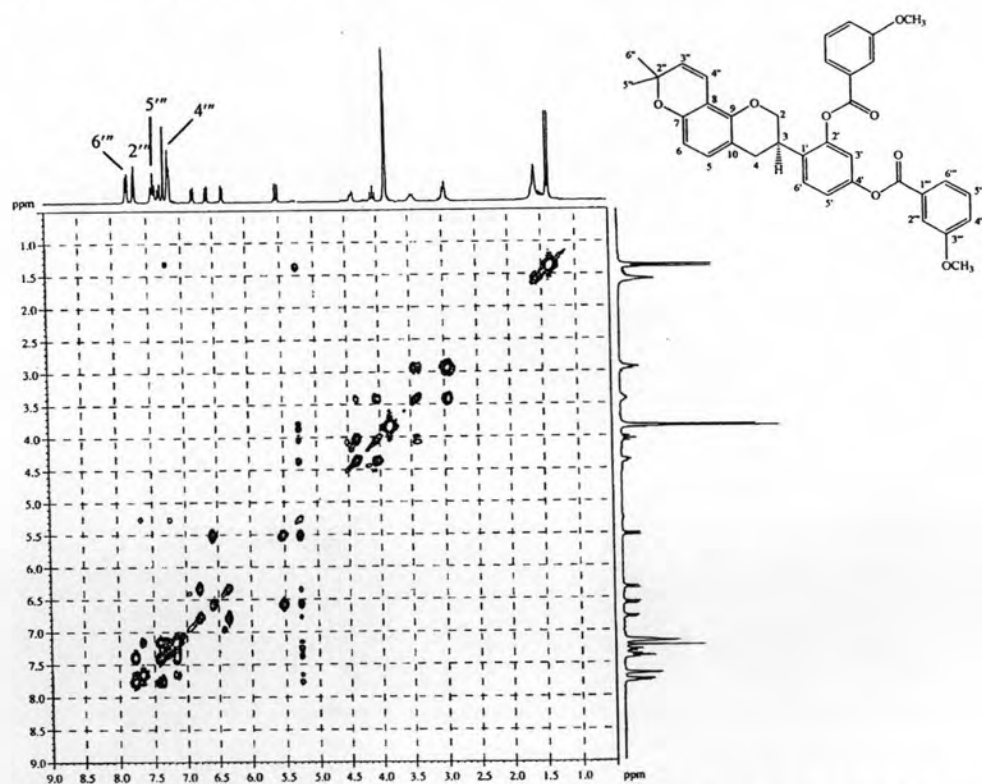


Figure 104. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of glabridin-2',4'-O-di-3'''-methoxybenzoate (**28**) in  $\text{CDCl}_3$ .



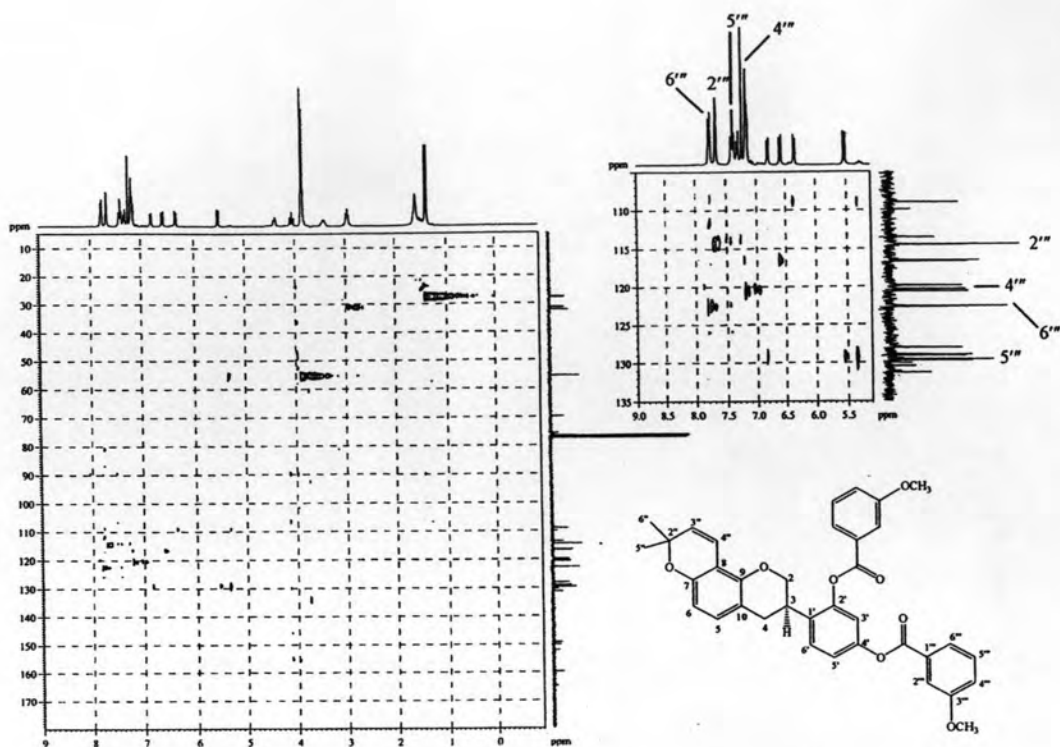


Figure 105. The HMQC spectrum of glabridin-2',4'-O-di-3'''-methoxybenzoate (28) in  $\text{CDCl}_3$ .

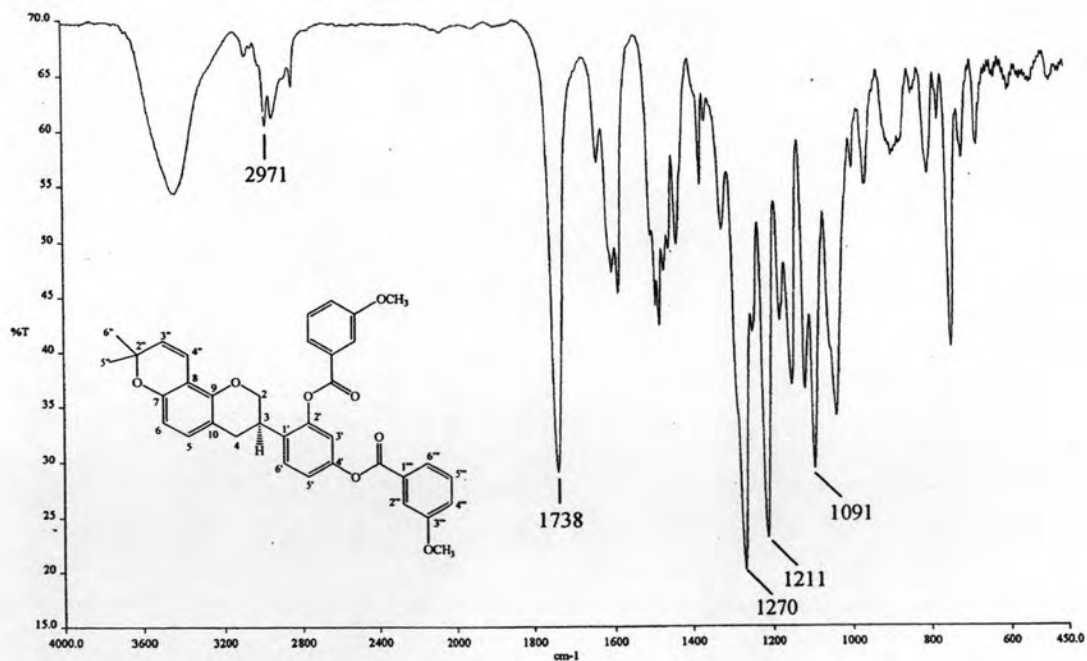


Figure 106. The infrared spectrum of glabridin-2',4'-O-di-3'''-methoxybenzoate (28).

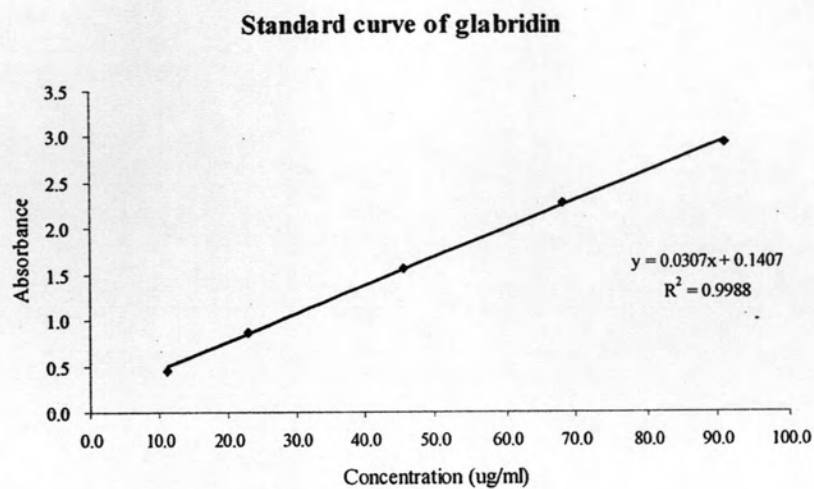


Figure 107. Calibration curve of glabridin (4) obtained from the UV absorption at 280 nm.

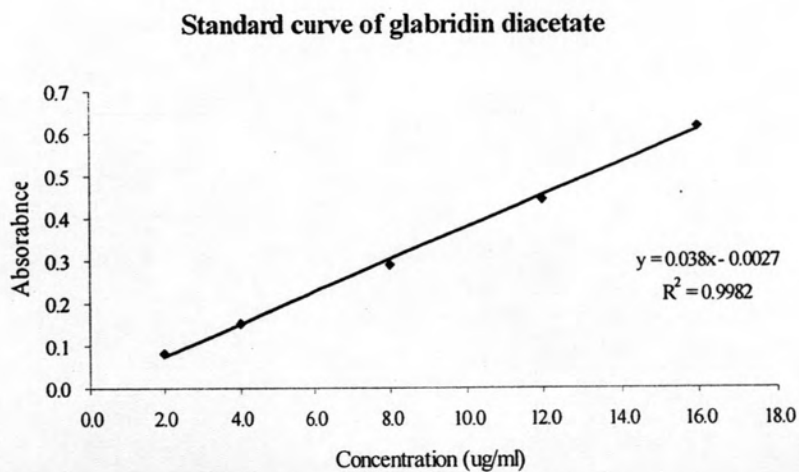


Figure 108. Calibration curve of glabridin diacetate (16) obtained from the UV absorption at 280 nm.

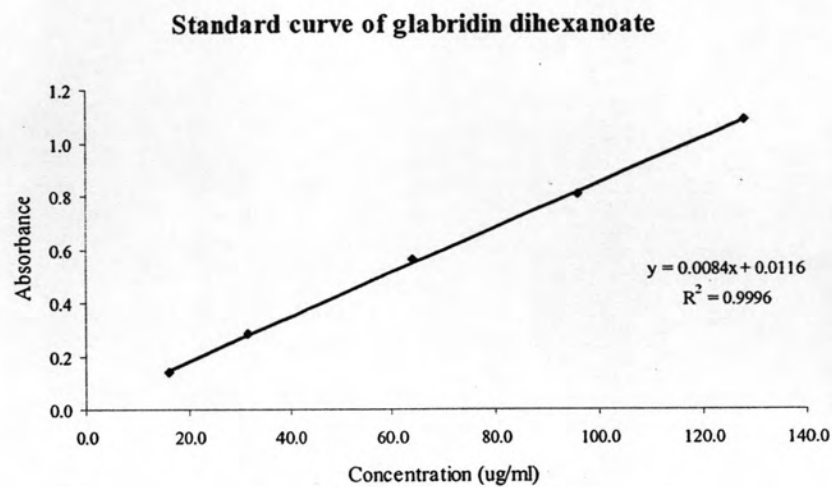


Figure 109. Calibration curve of glabridin dihexanoate (17) obtained from the UV absorption at 280 nm.

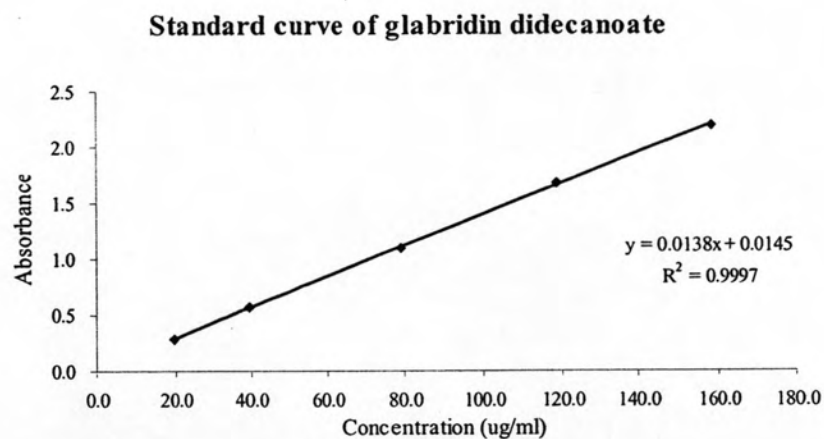


Figure 110. Calibration curve of glabridin didecanoate (18) obtained from the UV absorption at 280 nm.

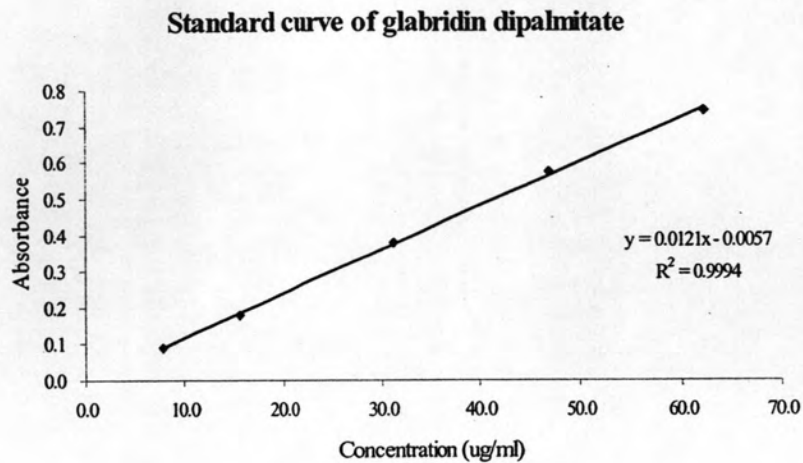


Figure 111. Calibration curve of glabridin dipalmitate (19) obtained from the UV absorption at 280 nm.

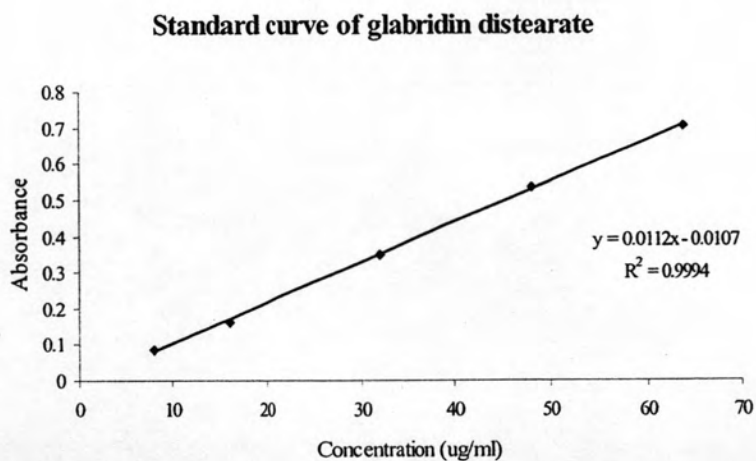


Figure 112. Calibration curve of glabridin distearate (20) obtained from the UV absorption at 280 nm.

12527837X

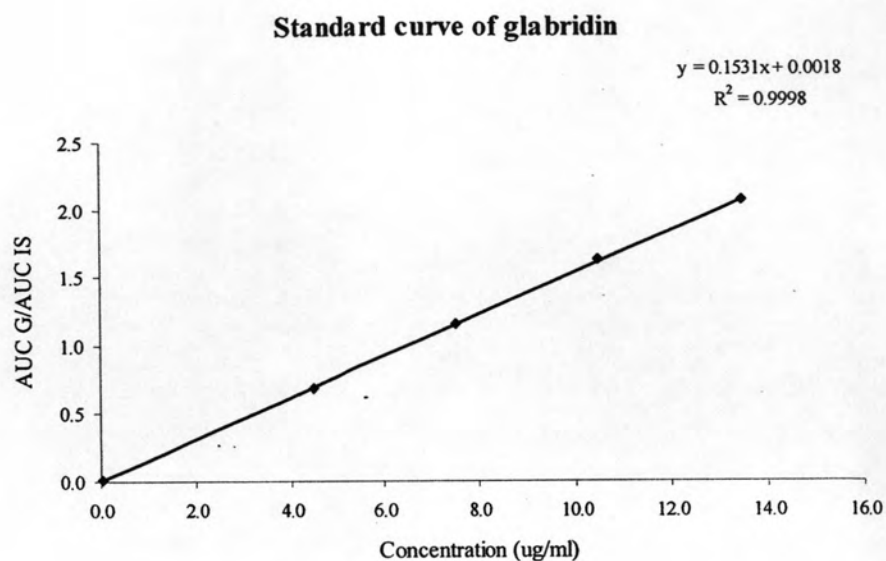


Figure 113. Calibration curve of glabridin (4) obtained from the AUC G / AUC IS ratio.

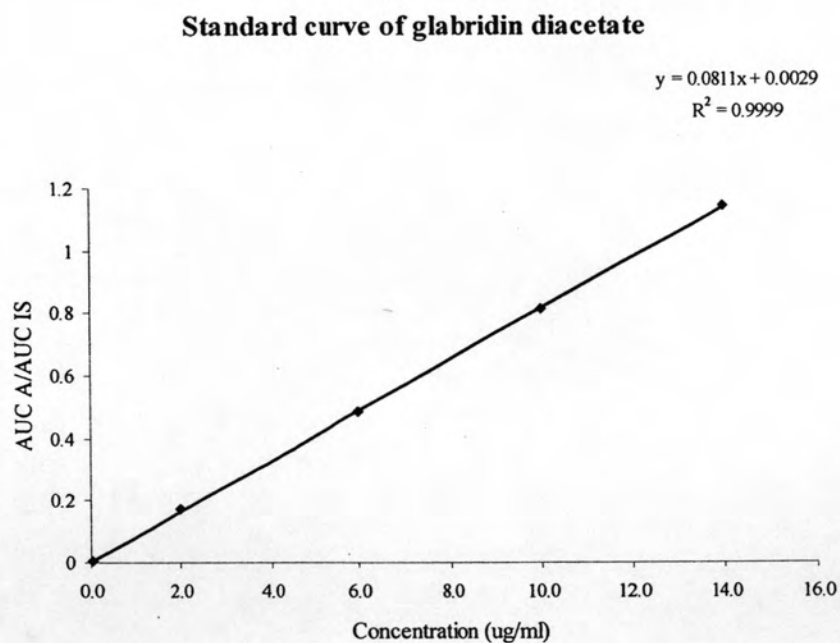


Figure 114. Calibration curve of glabridin diacetate (16) obtained from the AUC A / AUC IS ratio.

## VITA

Miss. Warunee Jirawattanapong was born on August 28, 1963 in Songkhla, Thailand. She received her Bachelor of Science in Pharmacy with second class honor in 1987 from the Faculty of Pharmacy, Prince of Songkla University and Master of Science in Pharmacy in 1995 from the Faculty of Pharmaceutical Sciences, Chulalongkorn University, Thailand. At present, she is working for Medicinal Plant Research Institute, the Department of Medical Sciences, Ministry of Public Health.