8 References

[1] Giersiepen, K.; Heitmann, C.; Janhsen, K.; Lange, C.: Gesundheitsberichterstattung des Bundes — Heft 25 — „Brustkrebs", **2005**, Robert Koch-Institut, Berlin. ISBN 3-89606-157-7.

[2] Edwards, D. P.: Regulation of signal transduction pathways by estrogen and progesterone. *Annu. Rev. Physiol*., **2005**, 67, 335-376.

[3] Song, R. X.; Barnes, C. J.; Zhang, Z.-G.; Bao, Y.-D.; Kumar, R.; Santen, R. J.: The role of Shc and insulin-like growth factor 1 receptor in mediating the translocation of estrogen receptor alpha to the plasma membrane. *Proc. Natl. Acad. Sci. USA*, **2004**, 101 (7), 2076-2081.

[4] Yager, J. D.: Endogenous estrogens as carcinogens through metabolic activation. *J. Natl. Cancer Inst. Monogr.*, **2000**, 27, 67-73.

[5] Dubey, R. K.; Jackson, E. K.: Cardiovascular protective effects of 17beta-estradiol metabolites. *J. Appl. Physiol.*, **2001**, 91, 1868-1883.

[6] Glasnapp, A.: Natural Estrogens: A Review of the Primary Literature. *International Journal of Pharmaceutical Compounding*, **2000**, 1-8.

[7] Cosman, F.; Lindsay, R.: Selective estrogen receptor modulators: Clinical spectrum. *Endocr. Rev.*, **1999**, 20, 418-434.

[8] Haddow, A.; Watkinson, J. M.; Paterson, E.: Influence of synthetic oestrogens upon advanced malignant disease. *Br. Med. J.*, **1944**, 2, 393-398.

[9] Katzenellenbogen, B. S.; Montano, M. M.; Ekena, K.; Herman, M. E.; Mclnerney, E. M.: Antiestrogens: Mechanisms of action and resistance in breast cancer. *Breast Cancer Res. Treat.*, **1997**, 44, 23-38.

[10] Osborne, C. K.; Zhao, H.; Fuqua, S. A. W.: Selective estrogen receptor modulators: structure, function, and clinical use. *J. Clin. Oncol.*, **2000**,18, 3172-3186.

[11] Balfour, J. A.; Goa, K. L.: Raloxifene. *Drugs Aging*, **1998**, 12, 335-341.

[12] Mckeage, K.; Curran, M. P.; Plosker, G. L.: Fulvestrant. A Review of its Use in Hormone Receptor-Positive Metastatic Breast Cancer in Postmenopausal Women with Disease Progression following Antiestrogen Therapy. *Drugs*, **2004**, 64(6), 633-648.

[13] Jensen, E. V.; Jocobson, H. I.: Basic guides to the mechanism of estrogen action. *Recent Prog. Horm. Res.*, **1962**, 18, 387-414.

[14] Jensen, E. V.; Block, G. E.; Smith, S.; Kyser, K.; DeSombre, E. R.: Estrogen receptors and breast cancer response to adrenalectomy. *Natl. Cancer Inst. Monogr.*, **1971**, 34, 55-70.

[15] Macgregor, J. I.; Jordan, V. C.: Basic guide to the mechanisms of antiestrogen action. *Pharmacol. Rev.*, **1998**, 50(2), 151-196.

[16] Green, S.; Walter, P.; Kumar, V.; Krust, A.; Bornert, J. M.; Argos, P.; Chambon, P.: Human oestrogen receptor cDNA: sequence, expression and homology to v-erb-A. *Nature*, **1986**, 320, 134-139.

[17] Greene, G. L.; Gilna, P.; Waterfield, M.; Baker, A.; Hort, Y.; Shine, J.: Sequence and expression of human estrogen receptor complementary DNA. *Science*, **1986**, 231, 1150-1154.

[18] Kuiper, G. G. J. M.; Enmark, E. ; Pelto-Huikko, M.; Nilsson, S.; Gustafsson, J-A.: Cloning of a novel estrogen receptor expressed in rat prostate and ovary. *Proc. Natl. Acad. Sci. USA*, **1996**, 93, 5925-5930.

[19] Mosselman, S.; Polman, J.; Dijkema, R.: ERβ: identification and characterization of a novel human estrogen receptor. *FEBS Lett.*, **1996**, 392, 49-53.

[20] Gustafsson, J.-Å.: Estrogen receptor beta--a new dimension in estrogen mechanism of action. *J. Endocrinol.*, **1999**, 163**,** 379-383.

[21] McDonnell, D. P.; Norris, J. D.: Connections and regulation of the human estrogen receptor. *Science*, **2002**, 296, 1642-1644.

[22] Persson, I.: Estrogens in the causation of breast, endometrial and ovarian cancers - evidence and hypotheses from epidemiological findings. *J. Steroid Biochem. Mol. Biol.*, **2000**, 74, 357-364.

[23] Kong, E. H.; Pike, A. C. W.; Hubbard, R. E.: Structure and mechanism of the oestrogen receptor. *Biochem. Soc. Trans.*, **2003**, 31, 56-59.

[24] Menasce, L. P.; White, G. R.; Harrison, C. J.; Boyle, J. M.: Localization of the estrogen receptor locus (ESR) to chromosome 6q25.1 by FISH and a simple post-FISH banding technique. *Genomics*, **1993**, 17, 263-265.

[25] Ogawa, S.; Inoue, S.; Watanabe, T. ; Hiroi, H.; Orimo, A.; Hosoi, T.; Ouchi, Y.; Muramatsu, M.: The complete primary structure of human estrogen receptor beta (hER beta) and its heterodimerization with ER alpha in vivo and in vitro. *Biochem. Biophys. Res. Com.*, 1998, 243, 122-126.

[26] Ruff, M.; Gangloff, M.; Wurtz, J. M.; Moras, D.: Estrogen receptor transcription and transactivation: Structure-function relationship in DNA- and ligand-binding domains of estrogen receptors. *Breast Cancer Res.*, **2000**, 2, 353-359.

[27] Muramatsu, M.; Inoue, S.: Estrogen receptors: how do they control reproductive and non reproductive functions? *Biochem. Biophys. Res. Commun.*, **2000**, 270, 1-10.

[28] Pettersson, K.; Gustafsson J.-Å.: Role of estrogen receptor beta in estrogen action. *Annu. Rev. Physiol.*, **2001**, 63, 165-92.

[29] Chen, D.-S.; Pace, P. E.; Coombes, R. C.; Ali, S.: Phosphorylation of human estrogen receptor alpha by protein kinase A regulates dimerization. *Mol. Cell. Biol.*, **1999**, 19, 1002-1015.

[30] Tsai, M. J.; O'Malley, B. W.: Molecular mechanisms of action of steroid/thyroid receptor superfamily members. *Annu. Rev. Biochem.*, **1994**, 63, 451-486.

[31] Kumar, V.; Chambon, P.: The estrogen receptor binds tightly to its responsive element as a ligand-induced homodimer. *Cell*, **1988**, 55, 145-156.

[32] Kumar, V.; Green, S.; Stack, G.; Berry, M.; Jin, J-R.; Chambon, P.: Functional domains of the estrogen receptor. *Cell*, **1987**, 51, 941-951.

[33] Wingender, E.: Gene Regulation in Eukaryotes. 12. Steroid / Thyroid Hormone Receptors. – Weinheim; New York; Basel; Cambridge; Tokyo: VCH, **1993**, 282

[34] Brzozowski, A. M.; Pike, A. C. W.; Dauter, Z.; Hubbard, R. E.; Bonn, T.; Engstrom, O.; Ohman, L.; Greene, G. L.; Gustafsson, J. A.; Carlquist, M.: Molecular basis of agonism and antagonism in the oestrogen receptor. *Nature*, **1997**, 389, 753-758.

[35] Pike, A. C. W.; Brzozowski, A. M.; Hubbard, R. E.; Bonn, T.; Thorsell, A. G.: Structure of the ligand-binding domain of oestrogen receptor beta in the presence of a partial agonist and a full antagonist. *EMBO J.*, **1999**, 18, 4608-4618.

[36] Bourguet, W.; Ruff, M.; Chambon, P.; Gronemeyer, H.; Moras, D.: Crystal structure of the ligand-binding domain of the human nuclear receptor RXR-alpha. *Nature*, **1995**, 375, 377-382.

[37] Danielian, P. S.; White, R.; Lees, J. A.; Parker, M. G.: Identification of a conserved region required for hormone dependent transcriptional activation by steroid hormone receptors. *EMBO J.*, **1992**, 11, 1025-1033.

[38] Moras, D.; Gronemeyer, H.: The nuclear receptor ligand-binding domain: structure and function. *Curr. Opin. Cell Biol.*, **1998**, 10, 384-391.

[39] McInerney, E. M.; Katzenellenbogen, B. S.: Different regions in activating function-1 of the human estrogen receptor required for antiestrogen- and estradioldependent transcription activation. *J. Biol. Chem.*, **1996**, 271, 24172-24178.

[40] Tzukerman, M. T.; Esty, A.; Santiso-Mere, D.; Danelian, D.; Parker, M. G.; Stein, R. B.; Pike, J. W.; McDonnell, D. P.: Human estrogen receptor transactivational capacity is determined by both cellular and promoter context and mediated by two functionally distinct intramolecular regions. *Mol. Endocrinol.*, **1994**, 8, 21-30.

[41] Berry, M.; Metzger, D.; Chambon, P.: Role of the two activating domains of the estrogen receptor in the cell-type and promoter-context dependent agonist activity of the antioestrogen 4-hydroxytamoxifen. *EMBO J.*, **1990**, 9, 2811-2818.

[42] Kuiper, G. G.; Carlsson, B.; Grandien, K.; Enmark, E.; Haggblad, J.; Nilsson, S.; Gustafsson, J. A.: Comparison of the ligand binding specificity and transcript tissue distribution of estrogen receptors alpha and beta. *Endocrinology*, **1997**, 138, 863-870.

[43] Shao, W.-L.; Brown, M.: Advances in estrogen receptor biology: prospects for improvements in targeted breast cancer therapy. *Breast Cancer Res.*, **2004**, 6, 39-52.

[44] Hall, J. M.; Couse, J. F.; Korach, K. S.; The multifaceted mechanisms of estradiol and estrogen receptor signaling. *J. Biol. Chem.*, **2001**, 276, 36869-36872.

[45] Pratt, W. B.; Toft, D. O.: Steroid receptor interactions with heat shock protein and immunophilin chaperones. *Endocr. Rev.*, **1997**, 18, 306-360.

[46] White, R.; Parker, M. G.: Molecular mechanisms of steroid hormone action. *Endocr.-Relat. Cancer*, **1998**, 5, 1-14.

[47] Paige, L. A.; Christensen, D. J.; Gron, H.; Norris, J. D.; Gottlin, E. B.; Padilla, K. M.; Chang, C.; Ballas, L. M.; Hamilton, P. T.; McDonnell, D. P.; Fowlkes, D. M.: Estrogen receptor (ER) modulators each induce distinct conformational changes in ER alpha and ER beta. *Proc. Natl. Acad. Sci. USA.*, **1999**, 96, 3999-4004.

[48] McDonnell, D. P.; Clemm, D. L.; Herman, T.; Goldman, M. E.; Pike, J. W.: Analysis of estrogen receptor function in vitro reveals three distinct classes of antiestrogens. *Mol. Endocrinol.*, **1995**, 9, 659-669.

[49] Wijayaratne, A. L.; Nagel, S. C.; Paige, L. A.; Christensen, D. J.; Norris, J. D.; Fowlkes, D. M.; McDonnell, D. P.: Comparative Analyses of Mechanistic Differences Among Antiestrogens. *Endocrinology*, **1999**, 140, 5828-5840.

[50] Wijayaratne, A. L.; McDonnell, D. P.: The human estrogen receptor-alpha is a ubiquitinated protein whose stability is affected differentially by agonists, antagonists, and selective estrogen receptor modulators. *J. Biol. Chem.*, **2001**, 276, 35684-35692.

[51] Pinzone, J. J.; Stevenson, H.; Strobl, J. S.; Berg, P. E.: Molecular and cellular determinants of estrogen receptor alpha expression. *Mol. Cell. Biol.*, **2004**, 24, 4605-4612.

[52] Cowley, S. M.; Hoare, S.; Mosselman, S.; Parker, M. G.: Estrogen receptors α and β form heterodimers on DNA. *J. Biol. Chem.*, **1997**, 272, 19858-19862.

[53] Pace, P.; Taylor, J.; Suntharalingam, S.; Coombes, R. C.; Ali, S.: Human estrogen receptor beta binds DNA in a similar to and dimerizes with estrogen receptor alpha. *J. Biol. Chem.*, **1997**, 272, 25832-25838.

[54] Paech, K.; Webb, P.; Kuiper, G. G. J. M.; Nilsson, S.; Gustafsson, J.-Å.; Kushner, P. J.; Scanlan, T. S,: Differential ligand activation of estrogen receptors ERa and ERb at AP1 sites. *Science*, **1997**, 277, 1508-1510.

[55] Webb, P.; Nguyen, P.; Valentine, C.; Lopez, G. N.; Kwok, G. R.; McInerney, E.; Katzenellenbogen, B. S.; Enmark, E.; Gustafsson, J.-A.; Nilsson, S.; Kushner, P. J.: The estrogen receptor enhances AP-1 activity by two distinct mechanisms with different requirements for receptor transactivation functions. *Mol. Endocrinol.*, **1999**, 13, 1672-1685.

[56] Safe, S.: Transcriptional activation of genes by 17 beta-estradiol through estrogen receptor-Sp1 interactions. *Vitam. Horm.*, **2001**, 62, 231-52.

[57] Katzenellenbogen, B. S.; Katzenellenbogen, J. A.: Estrogen receptor transcription and transactivation: Estrogen receptor alpha and estrogen receptor beta: regulation by selective estrogen receptor modulators and importance in breast cancer. *Breast Cancer Res.*, **2000**, 2, 335-344.

[58] Klinge, C. M.; Jernigan, S. C.; Mattingly, K. A.; Risinger, K. E.; Zhang, J.: Estrogen response element-dependent regulation of transcriptional activation of estrogen receptors alpha and beta by coactivators and corepressors. *J. Mol. Endocrinol.*, **2004**, 33, 387-410.

[59] Klinge, C. M.: Estrogen receptor interaction with co-activators and co-repressors. *Steroids*, **2000**, 65, 227-251.

[60] Rosenfeld, M. G.; Glass, C. K.: Coregulator codes of transcriptional regulation by nuclear receptors. *J. Biol. Chem.*, **2001**, 276, 36865-36868.

[61] Ogryzko, V. V.; Schiltz, R. L.; Russanova, V.; Howard, B. H.; Nakatani, Y.: The transcriptional coactivators p300 and CBP are histone acetyltransferases. *Cell*, **1996**, 87, 953-959.

[62] Kingston, R. E.; Narlikar, G. J.: ATP-dependent remodeling and acetylation as regulators of chromatin fluidity. *Genes Dev.*, **1999**, 13, 2339-2352.

[63] Orphanides, G.; Reinberg, D.: RNA polymerase II elongation through chromatin. *Nature*, **2000**, 407, 471-475.

[64] Heery, D. M.; Kalkhoven, E.; Hoare, S.; Parker, M. G.: A signature motif in transcriptional co-activators mediates binding to nuclear receptors. *Nature*, **1997**, 387, 733-736.

[65] Lanz, R. B.; McKenna, N. J.; Onate, S. A.; Albrecht, U.; Wong, J.; Tsai, S. Y.; Tsai. M. J.; O'Malley, B. W.: A steroid receptor coactivator, SRA, functions as an RNA and is present in an SRC-1 complex. *Cell*, **1999**, 97, 17-27.

[66] Endoh, H.; Maruyama, K.; Masuhiro, Y.; Kobayashi, Y.; Goto, M.; Tai, H.; Yanagisawa, J.; Metzger, D.; Hashimoto, S.; Kato, S.: Purification and identification of p68 RNA helicase acting as a transcriptional coactivator specific for the activation function 1 of human estrogen receptor α. *Mol. Cell. Biol.*, **1999**, 19, 5363-5372.

[67] Watanabe, M.; Yanagisawa, J.; Kitagawa, H.; Takeyama, K.; Ogawa, S.; Arao, Y.; Suzawa, M.; Kobayashi, Y.; Yano, T.; Yoshikawa, H.; Masuhiro, Y.; Kato, S.: A subfamily of RNA-binding DEAD-box proteins acts as an estrogen receptor α coactivator through the N-terminal activation domain (AF-1) with an RNA coactivator, SRA. *EMBO J.*, **2001**. 20, 1341-1352.

[68] Shang, Y.; Hu, X.; DiRenzo, J.; Lazar, M. A.; Brown, M.: Cofactor dynamics and sufficiency in estrogen receptor-regulated transcription. *Cell*, **2000**, 103, 843-852.

[69] Huang, H. J.; Norris, J. D.; McDonnell, D. P.: Identification of a negative regulatory surface within estrogen receptor α provides evidence in support of a role for corepressors in regulating cellular responses to agonists and antagonists. *Mol. Endocrinol.*, **2002**, 16, 1778-1792.

[70] Moggs, J. G.; Orphanides, G.: Estrogen receptors: orchestrators of pleiotropic cellular responses. *EMBO reports*, **2001**, 2, 775-781.

[71] Cosma, M. P.: Ordered Recruitment: Gene-Specific Mechanism of Transcription Activation. *Mol. Cell*, **2002**, 10, 227-236.

[72] Beekman, J. M.; Allan, G. F.; Tsai, S. Y.; Tsai, M.-J.; O'Malley, B. W.: Transcriptional activation by the estrogen receptor requires a conformational change in the ligand binding domain. *Mol. Endocrinol.*, **1993**, 7, 1266-1274.

[73] McKenna, N. J.; O'Malley, B. W.: An issue of tissues: divining the split personalities of selective estrogen receptor modulators. *Nat. Med.*, **2000**, 6, 960-962.

[74] McKenna, N. J.; Lanz, R. B.; O'Malley, B. W.: Nuclear receptor coregulators: cellular and molecular biology. *Endocr. Rev.*, **1999**, 20, 321-344.

[75] Shiau A. K.; Barstad, D.; Loria, P. M.; Cheng, L.; Kushner, P. J.; Agard, D. A.; Greene, G. L.: The Structural Basis of Estrogen Receptor/Coactivator Recognition and the Antagonism of This Interaction by Tamoxifen. *Cell*, **1998**, 95(7), 927-937.

[76] Shiau, A. K.; Barstad, D.; Radek, J. T.; Meyers, M. J.; Nettles, K. W.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A.; Agard, D. A.; Greene, G. L. : Structural characterization of a subtype-selective ligand reveals a novel mode of estrogen receptor antagonism. *Nat. Struct. Biol.*, **2002**, 9(5), 359-64.

[77] Pike, A. C. W.; Brzozowski, A. M.; Hubbard, R. E.; Bonn, T.; Thorsell, A. G.; Engstrom, O.; Ljunggren, J.; Gustafsson, J.-Å.; Carlquist, M.: Structure of the ligand-binding domain of oestrogen receptor beta in the presence of a partial agonist and a full antagonist. *EMBO J.*, **1999**, 18(17), 4608-4618.

[78] Pike, A. C.; Brzozowski, A. M.; Walton, J.; Hubbard, R. E.; Thorsell, A. G.; Li, Y. L.; Gustafsson, J. A.; Carlquist, M.: Structural insights into the mode of action of a pure antiestrogen. *Structure*, **2001**, 9, 145-153.

[79] Shang, Y.; Brown, M.: Molecular determinants for the tissue specificity of SERMs. *Science*, **2002**, 295, 2465-2468.

[80] Dauvois, S.; White, R.; Parker, M. G.: The antiestrogen ICI 182 780 disrupts estrogen receptor nucleocytoplasmic shuttling. *J. Cell Sci.*, **1993**, 106, 1377-1388.

[81] Dutertre, M.; Smith, C. L.: Molecular mechanisms of selective estrogen receptor modulator (SERM) action. *J. Pharmacol. Exp. Ther.*, **2000**, 295, 431-437.

[82] Mitlak, B. H.; Cohen, F. J.: In search of optimal long-term female hormone replacement: The potential of selective estrogen receptor modulators. *Horm. Res.*, **1997**, 48, 155-163.

[83] Lubczyk, V.; Bachmann, H.; Gust, R.: Investigations on estrogen receptor binding. The estrogenic, antiestrogenic, and cytotoxic properties of C2-alkyl-substituted 1,1-bis(4-hydroxyphenyl)-2-phenylethenes. *J. Med. Chem.*, **2002**, 45, 5358-5364.

[84] Lubczyk, V.; Bachmann, H.; Gust, R.: Antiestrogenically active 1,1,2-tris(4-hydroxyphenyl)alkenes without basic side chain: synthesis and biological activity. *J. Med. Chem.*, **2003**, 46, 1484-1491.

[85] Walter, G.; Liebl, R.; von Angerer, E.: Stilbene-based inhibitors of estrone sulfatase with a dual mode of action in human breast cancer cells. *Arch. Pharm. (Weinheim)*, **2004**, 337(12), 634-644.

[86] Sanoh, S.; Kitamura, S.; Sugihara, K.; Fujimoto, N.; Ohta, S.: Estrogenic Activity of Stilbene Derivatives. *J. Health Sci.*, **2003**, 49 (5), 359-367.

[87] Le Corre, L.; Chalabi, N.; Delort, L.; Bignon, Y.-J.; Bernard-Gallon, D. J.: Resveratrol and breast cancer chemoprevention: molecular mechanisms. *Mol. Nutr. Food Res.*, **2005**, 49, 462-471.

[88] Ulrich, S.; Wolter, F.; Stein, J. M.: Molecular mechanisms of the chemopreventive effects of resveratrol and its analogs in carcinogenesis. *Mol. Nutr. Food Res.*, **2005**, 49, 452-461.

[89] Levenson, A. S. ; Gehm, B. D.; Pearce, S. T.; Horiguchi, J.; Simons, L. A.; Ward III, J. E.; Jameson, J. L.; Jordan, V. C.: Resveratrol acts as an estrogen receptor (ER) agonist in breast cancer cells stably transfected with ER alpha. *Int. J. Cancer*, **2003**, 104, 587-596.

[90] Roberti, M.; Pizzirani, D.; Simoni, D.; Rondanin, R.; Baruchello, R.; Bonora, C.; Buscami, F.; Grimaudo, S.; Tolomeo, M.: Synthesis and biological evaluation of resveratrol and analogues as apoptosis-inducing agents. *J. Med. Chem.*, **2003**, 46, 3546-3554.

[91] Lion, C. J.; Matthews, C. S.; Stevens, M. F. G.; Westwell, A. D.: Synthesis, antitumor evaluation, and apoptosis-inducing activity of hydroxylated (E)-stilbenes. *J. Med. Chem.*, **2005**, 48, 1292-1295.

[92] Schertl, S.; Hartmann, R. W.; Batzl-Hartmann, C.; Schlemmer, R.; Spruß, T.; Bernhardt, G.; Gust, R.; Schönenberger, H.: 1-(2,6-Dichloro-4-hydroxyphenyl)-2-phenylethanes ─ New Biologiical Response Modifiers for the Therapy of Breast Cancer. Synthesis and Evaluation of Estrogenic/Antiestrogenic Properties. *Arch. Pharm. Pharm. Med. Chem.*, **2001**, 334, 125-137.

[93] Gust, R.: unpublished results.

[94] Gust, R.; Burgmeister, Th.; Mannschreck, A.; Schönenberger, H.: Aqua[1-(2,6-dichloro-4-hydroxyphenyl)-2-phenylethylenediamine](sulfato)platinum-(II) complexes with variable substituents in the 2-phenyl ring. 1. Synthesis and antitumor and estrogenic properties. J. *Med. Chem.*, **1990**, 33 (9), 2535-2544.

[95] Gust, R.: Aqua[1,1-bis(4-hydroxyphenyl)-1,2-diamino-2-phenylethane]-sulfatoplatinum(II), a New Compound for the Treatment of the Mammary Carcinoma. *Arch. Pharm. (Weinheim)*, **1994**, 327, 49-54.

[96] Becker, K. B.: Synthesis of Stilbenes. *Synthesis*, **1983**, 341-368.

[97] von Rauch, M.: *Dissertation*, Free University Berlin, **2003**, 30.

[98] Wiglenda, Th.: *Dissertation*, Free University Berlin, **2004**, 34.

[99] Simchen, G.: Aldehyde durch Aufbaureaktion unter C-C-Neuknuepfung. Houben-Weyl, Methoden der Organischen Chemie, Aldehyde. E3. Stuttgart, New York: Thieme **1983**, 19-27.

[100] Fanghänel, E.; Bartossek, H.; Lochter, Th.; Baumeister, U.; Hartung, H.: 4-(1-Methyl-2-sulfamoylvinyl)pyrazoles by Ring Transformation of 1,1-Dioxo-2H-1,2-thiazine-4-carbaldehydes with Hydrazines. *J. prakt. Chem.*, **1997**, 339, 277-283.

[101] Lenoir, D.: The Application of Low-Valent Titanium Reagents in Organic Synthesis. *Synthesis*, **1989**, 883-897.

[102] McMurry, J. E: Carbonyl-Coupling Reactions Using Low-Valent Titanium. *Chem. Rev.*, **1989**, 89, 1513-1524.

[103] Castedo, L.; Saá, J. M.; Suau, R.; Tojo, G.: Selective Reductive Carbonyl Couplings with Titanium. *J. Org. Chem.*, **1981**, 46, 4292-4294.

[104] Ali, M. A.; Kondo, K.; Tsuda, Y.: Synthesis and Nematocidal Activity of Hydroxystilbenes. *Chem. Pharm. Bull.*, **1992**, 40(5), 1130-1136.

[105] Chen, T. L., Chan, T. H., Shaver, A.: Reactions of $Cp_2Ti(CO)_2$ with aldehydes and ketones. *J. Organometal. Chem.*, **1984**, 268(1), C1-C6.

[106] Richardson, W. H.: *Syn. Commun.*, **1981**, 11, 895.

[107] Mukaiyama, T.; Sato, T.; Hanna, J.: *Chem. Lett.*, **1973**, 1041.

[108] Lenoir, D.: Synthese tetrasubstituierter Ethylene durch reduktive Kupplung von Ketonen mittels Titan(II)-salzen. Zur Anwendung der Methode. *Synthesis*, **1977**, 553-554.

[109] Coe, P. L.; Scriven, C. E.: Crossed Coupling of Functionalised Ketones by Low Valent Titanium (The McMurry Reaction): A New Stereoselective Synthesis of Tamoxifen. *J. Chem. Soc. Perkin Trans. I*, **1986**, 475-477.

[110] Tierling, Th.: Synthesis of 6-[18F]fluoro-L-DOPA through nucleophilic 18F-fluoridation of carbonyl-activated aromatic amino acid, derivatives. "Berichte des Forschungszentrums Juelich (**2002**)", (Juel-3952), i-vi, 1-111. CAN 138:287905.

[111] Ranu, B. C.; Bhar, S.: Dealkylation of ethers. A Review. *Organic Preparations and Procedures Int.*, **1996**, 28 (4), 371-409.

[112] Node, M.; Nishide, K.; Fuji, K.; Fujita, E. : Hard Acid and Soft Nucleophile System. 2. Demethylation of Methyl Ethers of Alcohol and Phenol with an Aluminum Halide-Thiol System. *J. Org. Chem.*, **1980**, 45, 4275-4277.

[113] Nishide, K.; Ohsubi, S.-I.; Miyamoto, T.; Kumar, K.; Node, M.: Development of Odorless Thiols and Sulfides and Their Applications to Organic Synthesis. *Monatshefte fuer Chemie*, **2004**, 135, 189-200.

[114] Benton, F. L.; Dillon, T. E.: The Cleavage of Ethers with Boron Bromide. I. Some Common Ethers. *J. Am. Chem. Soc.*, **1942**, 64, 1128-1129.

[115] McOmie, J. F. W.; Watts, M. L.; West, D. E.: Demethylation of aryl methyl ethers by boron tribromide. *Tetrahedron*, **1968**, 24, 2289-2292.

[116] Wedemeyer, E.-F.: Ein und mehrwertige Phenole, Spaltung von Phenolethern. Houben-Weyl, Methoden der Organischen Chemie, Phenole. Teil 1, 6/1c. Stuttgart: Thieme **1976**, 340-358.

[117] Kirk, K. L.; Cantacuzène, D.; Collins, B.; Chen, G. T.; Nimit, Y.; Creveling, C. R: Syntheses and adrenergic agonist properties of ring-fluorinated isoproterenols. *J. Med. Chem.*, **1982**, 25 (6), 680-684.

[118] Borgulya, J.; Bruderer, H.; Bernauer, K.; Zürcher, G.; Da Prada, M.: Catechol-*O*-methyltransferase-Inhibiting Pyrocatechol Derivatives: Synthesis and Structure-Activity Studies. *Helvetica Chimica Acta*, **1989**, 72 (5), 952-968.

[119] Bennett, J. G., JR.; Bunce, S. C.: Cyclopropyl Analogs of Hexestrol and Diethylstilbestrol. *J. Org. Chem.*, **1960**, 25, 73-79.

[120] Staudinger, H.; Pfenninger, F. P.: Ueber die Einwirkung von Schwefeldioxyd auf Diphenyl-diazomethan. *Ber.*, **1916**, 49, 1941-1951.

[121] Smith, L. I.; Howard, K. L.: Diphenyldiazomethane (Methane, diazodiphenyl-). *Org. Syntheses*, **1955**, Coll. Vol. III, 351-352.

[122] Dodds, E. C.; Golberg, L.; Lawson, W.; Robinson, R.: Synthetic estrogenic compounds related to stilbene and diphenylethane I. *Proc. Roy. Soc. London, Ser. B*, **1939**, 127, 140-167.

[123] Schneider, M. R.; Schuderer, M. L.: 1-[4-(N,N-bis-beta-chloroethylcarbamoyloxy)-phenyl]-1,2-bis-(hydroxyphenyl)-but-1-enes: drugs specifically targeted against estrogen receptor positive mammary tumors. *Arch. Pharm.(Weinheim)*, **1990**, 323(4), 215-9.

[124] Schneider, M. R.; Schuderer, M. L.: Cytotoxic estrogens: anilin mustard linked 1,1,2-triphenylbut-1-enes with mammary tumor inhibiting activity. *Arch. Pharm.(Weinheim)*, **1989**, 322(1), 59-62.

[125] Lednicer, D.; Grostic, M. F.: Selective demethylation of deoxyanisoin. Mass spectra of the products. *J. Org. Chem.*, **1967**, 32 (10), 3251-3253.

[126] Middleton, W. J.; Metzger, D.; Snyder, J. A.: 1-Trifluoromethyl-1,2,2-triphenylethylenes. Synthesis and postcoital antifertility activity. *J. Med. Chem.*, **1971**, 14 (12), 1193-1197.

[127] Middleton, W. J.: 1-(Perfluoroalkyl)-1,2,2-triphenylethylenes. Patent: US 3712929, **1973**

[128] Hassner, A.: Alkyl, Aryl und Hetaryl-azide. Houben-Weyl, Methoden der Organischen Chemie, Organo-Stickstoff-Verbindungen I, Teil 2, E16a. Stuttgart, New York: Thieme **1990**, 1243-1290.

[129] Minisci, F.: *Acc. Chem. Res.*, **1975**, 8, 165.

[130] Pini, D.; Iuliano, A.; Rosini, C.; Salvadori, P.: An Efficient and Practical Route to Enantiomerically Pure (+)-(1R,2R)- and (–)-(1S,2S)-1,2-Diphenylethane-1,2-diamines. *Synthesis*, **1990**, 1023-1024.

[131] Müller, R.; Gust, R.; Klement, U.; Schönenberger, H.: Stereoisomeric Dichloro[1-(hydroxyphenyl)-2-phenyl-1,2-ethanediamine]platinum(II) Complexes, Part I: Synthesis. *Chem. Ber.*, **1991**, 124, 2381-2389.

[132] Brunner, H.; Schellerer, K.-M.: New porphyrin platinum conjugates for the cytostatic and photodynamic tumor therapy. *Inorganica Chimica Acta*, **2003**, 350 39-48.

[133] Fowler, F. W.; Hassner, A.; Levy, L.: Stereospecific Introduction of Azide Functions into Organic Molecules. *J. Am. Chem. Soc.*, **1967**, 89, 2077-2082.

[134] Caubere, P.; Forconi, H.: Process for preparation of polyazido alcohols from oxiranes, and preparation of derived polyamino alcohols. Can. Pat. Appl. **1993**, CA 2083465; *Chem. Abs.* **120**: 8208

[135] Scheurer, A.; Mosset, P.; Saalfrank, R. W.: Efficient synthesis of (2R,3R)-and (2S,3S)-2,3-diaminobutane-1,4-diol and their dibenzyl ethers. *Tetrahedron: Asymmetry*, **1997**, 8 (8), 1243-1251.

[136] Hassner, A.: Regiospecificity. A Useful Terminology in Addition and Elimination Reactions. *J. Org. Chem.*, **1968**, 33, 2684-2686.

[137] Hassner, A.; Teeter, J. S.: Phenyl Migration in Pseudohalogen Additions to 3,3,3-Triphenylpropene. *J. Org. Chem.*, **1970**, 35 (10), 3397-3401.

[138] Roellgen, F. W.: "Fast Atom Bombardment" – Massenspektrometrie. *Nachr. Chem. Tech. Lab.*, **1983**, 31 (3), 174-177

[139] Carpenter, H.: *Justus Liebigs Ann. Chem.*, **1898**, 302, 223.

[140] Mackewitz, Th.; Röper, M.; Breit, B.: Preparation of phosphabenzene compounds. Patent: US 6252117, **2001**.

[141] Chakravarti, D.; Roy, N: K.: Condensation of substituted acetophenones with methylene iodide. II. Formation of 1,5-diketones. *J. Indian Chem. Soc.*, **1964**, 41 (1), 65-68; *Chem. Abs.* **60**: 82606

[142] Huang, Z.-N.; Xu, B.-A.; Jin, S.; Fan, M.-G.: Facile Synthesis of Novel Photochromic 1,2-Diheteroaryl-Substituted Cycloalkyenes by Titanium-Induced Intramolecular Coupling Reaction. *Synthesis*, **1998**, 1092-1094

[143] Benetollo, F.; Busetti, V.; Marcuzzi, F.: Crystal structure of phenyl-substituted cyclopentenes. *J. Chem. Crystallogr.*, **1999**, 29 (10), 1127-1132.

[144] Feutrill, G. I.; Mirrington, R. N.: Reactions with thioethoxide ion in dimethylformamide: I. Selective demethylation of aryl methyl ethers. *Aust. J. Chem.*, **1972**, 25, 1719-1729.

[145] Youngdale, G. A.: Acetonitrile derivatives of heterocycles. Patent: S. African (**1968**), ZA 6800277; *Chem. Abs.* **70**: 68135.

[146] Mortensen, D. S.; Rodriguez, A. L.; Carlson, K. E.; Sun, J.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A.: Synthesis and biological evaluation of a novel series of furans: ligands selective for estrogen receptor alpha. *J. Med. Chem.*, **2001**, 44, 3838-3848.

[147] Radziszewski, B.: Ueber die Constitution des Lophins und verwandter Verbindungen. *Ber.*, **1882**, 15, 1493-1496.

[148] Davidson, D.; Weiss, M.; Jelling, M.: The action of ammonia on benzil. *J. Org. Chem.*, **1937**, 2, 319-327.

[149] Grimmett, M. R.: *Advan. in Heterocycl. Chem.*, **1970**, 12, 103-183.

[150] Gust, R.; Busch, S.; Keilitz, R.; Schmidt, K.; von Rauch, M.: Invesgations on the Influence of Halide Substituents on the Estrogen Receptor Interaction of 2,4,5-Tris(4-hydroxyphenyl)-imidazoles. *Arch. Pharm. Pharm. Med. Chem.*, **2003**, 336, 456-465.

[151] Soule, H. D.; Vasquez, J.; Long, A.; Albert, S.; Brennan, M.: *J. Natl. Cancer Inst.*, **1973**, 51, 1409-1413

[152] Brooks, S. C.; Locke, E. R.; Soule, H. D.: Estrogen receptor in a human cell line (MCF-7) from breast carcinoma. *J. Biol. Chem.*, **1973**, 248, 6251-6253

[153] Horwitz, K. B.; Kostloff, M. E.; McGuire, W. L.: *Steroids*, **1975**, 26, 785-788.

[154] Horwitz, K. B.; Zava, D. T.; Thilager, A. K.; Jensen, E. M.; McGuire, W. L.: Steroid receptor analyses of nine human breast cancer cell lines. *Cancer Res.*, **1978**, 38, 2434-2437.

[155] Walter, P.; Green, S.; Green, G.; Krust, A.; Bornert, J. M.; Jeltsch, J. M. et al: Cloning of the human estrogen receptor cDNA. *Proc. Natl. Acad. Sci. USA*, **1985**, 82, 7889-7893.

[156] Masiakowski, P. R.; Breathnach, J.; Bloch, J.; Gannon, F.; Drust, A.; Chambon, P.: Cloning of cDNA sequences of hormone-regulated genes from the MCF-7 human breast cancer cell line. *Nucleic Acids Res.*, **1982**, 10, 7895-7903.

[157] Watanabe, T.; Inoue, S.; Ogawa, S.; Ishii, Y.; Hiroi, H.; Ikeda, K.; Orimo, A.; Muramatsu, M.: Agonistic effect of tamoxifen is dependent on cell type, ERE-promoter context, and estrogen receptor subtype. *Biochem. Biophys. Res. Commun.*, **1997**, 236, 140-145.

[158] Gooch, J. L.; Yee, D.: Strain-specific differences in formation of apoptotic DNA ladders in MCF-7 breast cancer cells. *Cancer Lett.*, **1999**, 144, 31-37

[159] Burow, M. E.; Weldon, C. B.; Tang, Y.; Navar, G. L.; Krajewski, S.; Reed, J. C.; Hammond, T. G.; Clejan, S.; Beckmann, B. S.: Differences in susceptibility to tumor necrosis factor alpha-induced apoptosis among MCF-7 breast cancer cell variants. *Cancer Res.*, **1998**, 58, 4940-4946.

[160] Burdall, S. E.; Hanby, A. M.; Lansdown, M. R. J.; Speirs, V.: Breast cancer cell lines: friend or foe? *Breast Cancer Res.*, **2003**, 5(2), 89-95.

[161] Meyer, T.: *Diplomarbeit*, Universität Regensburg, **1992**.

[162] Meyer, T.; Koop, R.; von Angerer, E.; Schönenberger, H.; Holler, E.: A rapid luciferase transfection assay for transcription activation effects and stability control of estrogenic drugs in cell cultures. *J. Cancer Res. Clin. Oncol.*, **1994**, 120, 359-364.

[163] Koop, R.: *Dissertation*, Universität Regensburg, **1992**.

[164] Pink, J. J.; Jiang, S. Y.; Fritsch, M.; Jordan, V. C.: An estrogen-independent MCF-7 breast cancer cell line which contains a novel 80-kilodalton estrogen receptor-related protein. *Cancer Res.*, **1995**, 55, 2583-2590.

[165] Pink, J. J.; Wu, S. Q.; Wolf, D. M.; Bilimoria, M. M.; Jordan, V. C.: A novel 80 kDa human estrogen receptor containing a duplication of exons 6 and 7. *Nucleic Acids Res.*, **1996**, 24, 962-969.

[166] Wood, K. V.: The chemistry of bioluminescent reporter assays. *Promega Notes*, **1998**, 65, 14-20.

[167] de Wet, R. J.; Wood, K. V.; de Luca, M.; Helinsky, D. R.; Subramani, S.: Firefly luciferase gene: structure and expression in mammalian cells. *Mol. Cell. Biol.*, **1987**, 7, 725-737.

[168] Promega Co.: Luciferase Assay System Technical Bulletin No. 281.

[169] Hafner, F.; Holler, E.; von Angerer, E.: Effect of growth factors on estrogen receptor mediated gene expression. *J. Steroid Biochem. Molec. Biol.*, **1996**, 58, 385-393.

[170] von Angerer, E.; Biberger, C.: 1-Benzyl-2-phenylindole- and 1,2-diphenylindole-based antiestrogens. Estimation of agonist and antagonist activities in transfection assays. *J. Steroid Biochem. Molec. Biol.*, **1998**, 64, 277-285.

[171] Bradford, M. M.: A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal. Biochem.*, **1976**, 72, 248-254.

[172] Basly, J. P.; Marre-Fournier, F.; Le Bail, J. C.; Habrioux, G.; Chulia, A. J. : Estrogenic/ antiestrogenic and scavenging properties of (E)- and (Z)-resveratrol. *Life Sci.*, **2000**, 66, 769-777

[173] Gehm, B. D.; McAndrews, J. M.; Chien, P. Y.; Jameson, J. L.: Resveratrol, a polyphenolic compound found in grapes and wine, is an agonist for the estrogen receptor. *Proc. Natl. Acad. Sci. USA*, **1997**, 94, 14138-14143.

[174] Gust, R.; Keilitz, R.; Schmidt, K.: Investigations of new lead structures for the design of selective estrogen receptor modulators. *J. Med. Chem.*, **2001**, 44, 1963-1970.

[175] Gust, R.; Keilitz, R.; Schmidt, K.: Synthesis, structural evaluation, and estrogen receptor interaction of 2,3-diarylpiperazines. *J. Med. Chem.*, **2002**, 45, 2325-2337.

[176] von Rauch, M.; Schlenk, M.; Gust, R.: Effects of C2-alkylation, N-alkylation, and N,N'-dialkylation on the stability and estrogen receptor interaction of (4R,5S)/(4S,5R)-4,5-bis(4-hydroxyphenyl)-2-imidazolines. *J. Med. Chem.*, **2004**, 47, 915-927.

[177] Hay, R. J.: The seed stock concept and quality control for cell lines. *Anal. Biochem.*, **1988**, 171, 225-237.

[178] Gillies, R. J.; Didier, N.; Denton, M.: Determination of cell number in monolayer cultures. *Anal. Biochem.*, **1986**, 159, 109-113.

[179] Kueng, W.; Silber, E.; Eppenberger, U.: Quantification of cells cultured on 96-well plates. *Anal. Biochem.*, **1989**, 182, 16-19.