1-{2-[(取代苯基)甲氧基]-2-(取代苯基)乙基}-1H-三唑和苯并三唑类化合物的合成及抗真菌活性*

李 科 张万年 杨济秋 吕加国 吴秋业

(第二军医大学药学院，上海 200433)

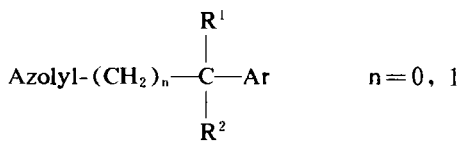
摘要 报道了39个新的1-{2-[(取代苯基)甲氧基]-2-(取代苯基)乙基}-1H-三唑和苯并三唑类化合物的合成与体外抑菌试验，结果表明，化合物**6**，**13**的抗真菌活性为益康唑的4～10倍，化合物**10**，**12**，**14**，**15**，**20**，**22**，**23**，**28**，**30**和**31**等对大部分真菌活性也优于或相当于益康唑及克霉唑，化合物**23**和**31**抗裴氏着色菌活性为益康唑、克霉唑的30倍以上，化合物**22**抗白念珠菌活性为益康唑的8倍，克霉唑的4倍。

关键词 三唑类；苯并三唑类；抗真菌活性

由于临床上广谱抗菌素、皮质激素和抗肿瘤药物的广泛使用，导致真菌感染率大为提高，特别是深部真菌感染已成为癌症病人、爱滋病人及免疫丧失病人死亡的因素之一。临床迫切需要高效低毒、广谱、选择性好的抗真菌尤其抗深部真菌的药物。

自60年代末，克霉唑(clotrimazole)[1]、咪康唑(miconazole)[2]和益康唑(econazole)[3]等相继出现后，氮唑类抗真菌药物的发展最为引人注目。近几年，由于三唑类化合物对深部真菌作用较好被日益重视，相继开发了如氟康唑(fluconazole)[4]、伊曲康唑(itriaconazole)[5]和terconazole[6]等抗深部真菌药物，有的已在多个国家上市。

构效关系研究表明，绝大多数有抗真菌活性的氮唑类化合物有如下基本结构：

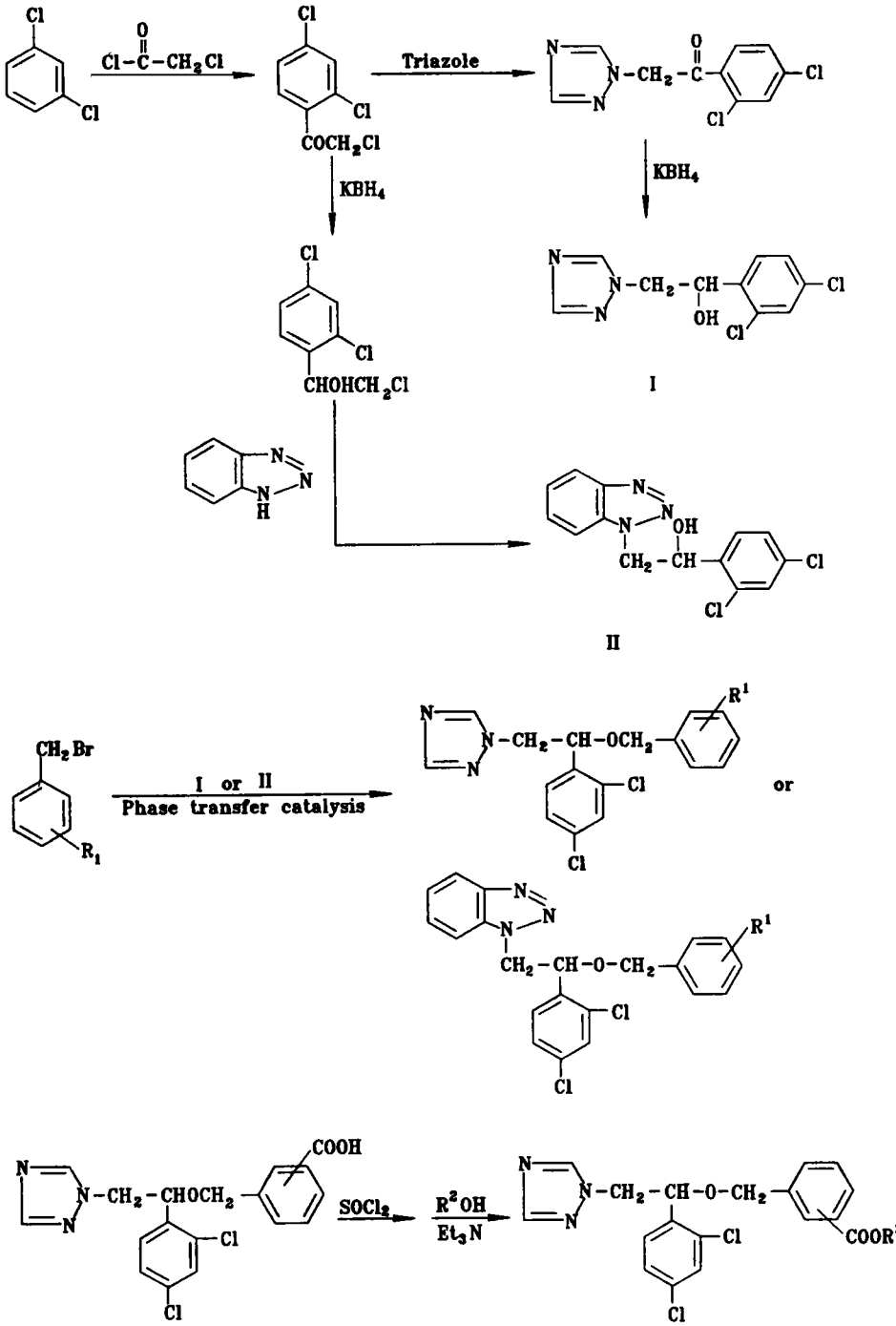


分子中咪唑环或三唑环是必需的，而且1位氮原子必须与分子中央的碳原子相连接，改变其它基团则影响理化性质，从而影响其抗真菌活性。

根据氮唑类抗真菌药物的构效关系及作用机理[7]，我们以益康唑为先导化合物，用三唑或苯并三唑(可看作三唑取代物)替换咪唑基团，同时变换分子中芳环上取代基，设计合成了39个1-{2-[(取代苯基)甲氧基]-2-(取代苯基)乙基}-1H-三唑和苯并三唑类化合物(见图1及表1)。用二倍稀释法测定了它们对13种常见真菌的体外抑菌活性，并与益康唑、克霉唑对照(见表2)。

本文于1994年6月23日收到。

*总后卫生科研基金资助课题，编号C－10。

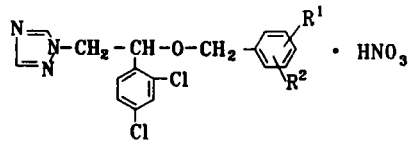


R^1=H, CH_3, CH_3O, Cl, F, CN, NO_2, COOH, etc.

R^2=H, CH_3, C_2H_5, C_3H_7, $CH_2CH=CH_2$, $CH_2C_6H_5$, etc.

Fig 1 Route of synthesis of the title compounds.

Tab 1 Structure and physical properties of the compounds

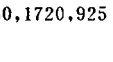


Compd[a]	R^1	R^2	MP ℃	Yield %	IR(KBr) cm^{-1}	^{1}HNMR(δppm, DMSO-d_6)
1	H	H	159～160	50.24	860,830,790,752	7.30(m,5H,Ph-H)
2	*p*-CH_3	H	174～175	53.46	870,858,830,815	2.30(s,3H,Ph-CH_3)
3	*p*-OCH_3	H	162～163	13.61	1210,850,824,810	
4	b		133～135	63.24	1040,860,820	
5	c		160～161	56.81	875,860,815,790	
6	d		128～129	56.81	3120,925,835,640	8.96(s,1H, ), 8.33(s,1H, ), 7.66 (d,1H, J=2.12 Hz, 7.49 dd,1H, J_1=2.1 Hz, J_2=11.8 Hz, 7.40 d,1H, J=11.8 Hz)  5.64(m,1H,Ph-CH-CH_2-O), 5.17(m,2H,=CH_2), 5.05(m,1H,-CH=), 4.17(m,2H,Ph-CH(O)-CH_2-N), 3.72(m,2H,O-CH_2-)
7	*o*-Cl	H	159～161	53.81	860,825,635	7.70～7.25(m,7H,Ph-H), 5.22 (dd,J_1=3.66 Hz,J_2=8.14 Hz,1H, Ar-CH(O)-CH_2)
8	*m*-Cl	H	149～150	58.30	865,730,635	7.75～7.02(m,7H,Ph-H), 5.14 (dd,J_1=3.58 Hz,J_2=8.24 Hz,1H, Ar-CH(O)-CH_2)
9	*p*-Cl	H	165～166	40.27	845,823,828	
10	2-Cl	4-Cl	168～170	52.25	860,840,828	
11	*o*-F	H	164～166	52.84	870,828,780,763	
12	*m*-F	H	158～160	78.80	860,740,630	7.68～6.86(m,7H,Ph-H), 4.57 (m,2H,-CH_2-N)
13	*p*-F	H	160～162	69.93	845,830,635	7.67～7.12(m,7H,Ph-H), 5.13 (dd,J_1=3.64 Hz, J_2=8.14 Hz, 1H,Ph-CH(O)-CH_2N), 4.55(m,2H,-CH(O)-CH_2-N), 4.38(m,2H,O-CH_2-C_6H_4F)

Continued

Compd[a]	R^1	R^2	MP C	Yield %	IR(KBr) cm^{-1}	^{1}HNMR(δppm, DMSO-d_6)
14	*o*-NO_3	H	131～133	43.86	1525,1380,860,720	5.27(dd, J_1=3.64 Hz, J_2=7.48 Hz, 1H, Ph-CH(O)-CH_2)
15	*p*-NO_3	H	168～169	51.40	890,860,830	
16	*p*-CN	H	173～174	74.39	2160,870,828,780	
17	H	*o*-$COOC_2H_5$	150～153	32.26	1715,865,830	
18[c]	H	*m*-COOH	163～166	68.00	2520,1950,1690,740	
19	H	*m*-$COOCH_3$	145～147	57.69	1720,820,755	8.00～7.35(m, 7H, Ph-H), 3.84(s, 3H, $COOCH_3$)
20	H	*m*-$COOC_2H_5$	151～152	32.52	1720,825,750,635	4.29(q, J=9.1 Hz, 2H, $COOCH_2$-CH_3), 1.31(t, J=9.1 Hz, 3H, $COOCH_2$-CH_3)
21	H	*m*-$COOC_3H_7$	139～140	72.73	1720,750,735,640	4.20(t, J=6.57 Hz, 2H, $COOCH_2$-CH_2CH_3), 1.73(m, J=7.53 Hz, 2H, $COOCH_2$-CH_2-CH_3), 0.97(t, J=7.53 Hz, 3H, $COOCH_2CH_2$-CH_3)
22	H	*m*-$COOCH_2CH=CH_2$	132～134	55.56	3110,1710,920,750	6.07(m, 1H, -CH=CH_2), 5.37(m, 2H, -$COOCH_2CH=CH_2$), 4.81(m, 2H, CH_2-$CH=CH_2$)
23	H	*m*-$COOCH(CH_3)_2$	150～152	46.05	1715,730,640	5.10[m, J=6.25 Hz, 1H, $COOCH(CH_3)_2$], 1.31[d, J=6.25 Hz, 6H, $COOCH(CH_3)_2$]
24	H	*m*-$COOCH_2CH(CH_3)_2$	138～139	76.92	1720,1220,740,635	4.06(d, J=6.44 Hz, 2H, $COOCH_2$-CH-), 2.03(m, J_1=12.3 Hz, J_2=6.44 Hz, 1H, $-CH_2-CH-$), 0.98[d, J=12.3 Hz, 6H, $COOCH_2CH(CH_3)_2$]
25	H	*m*-$COOCH_2C_6H_5$	120～122	60.24	1725,745,740	5.35(s, 2H, $-OCH_2$-Ph)
26[c]	H	*p*-COOH	187～189	71.43	2500,1940,1690	12.9(s, 1H, -COOH), 7.87～7.19(m, 7H, Ph-H), 5.17(dd, J_1=3.7 Hz, J_2=8.0 Hz, 1H, Ar-CH(O)-CH_2-), 4.54(m, 2H, -CH(O)-CH_2-N), 4.38(m, 2H, O-CH_2-Ar)
27	H	*p*-$COOCH_3$	145～147	55.60	1720,830,640	5.16(dd, J_1=3.81 Hz, J_2=8.22 Hz, 1H, -CH(O)-CH_2)
28	H	*p*-$COOC_2H_5$	140～142	41.41	1725,875,830	1.35(t, J=7.0 Hz, 3H, $-OCH_2CH_3$)
29	H	*p*-$COOCH_2CH_2CH_3$	139～141	78.95	1720,836,645	4.20(t, J=6.54 Hz, 2H, -O-CH_2-CH_2-), 1.69(m, J_1=6.54 Hz, J_2=7.4 Hz, 2H, $-CH_2$-CH_2-CH_3), 0.95(t, J=7.44 Hz, 3H, $-CH_2-CH_2-CH_3$)

Continued

Compd[a]	R^1	R^2	MP C	Yield %	IR(KBr) cm^{-1}	^{1}HNMR(δppm, DMSO-d_6)
30	H	*p*-$COOCH_2CH=CH_2$	140～142	73.68	3130,1720,925	8.80(s,1H, ), 8.19(s, 1H,), 7.91～7.24(m, 7H,Ph-H), 5.18(dd,J_1=3.37 Hz, J_2=8.07 Hz, 1H, Ar-CH(O)-CH_2-), 6.07(m, 1H, $COOCH_2CH=CH_2$), 5.36(m, 2H, $COOCH_2CH=CH_2$), 4.81(m,2H,$COOCH_2$-CH=CH_2)
31	H	*p*-$COOCH(CH_3)_2$	154～155	52.61	1718,1380,835	7.82～7.18(m,7H,Ph-H)
32	H	*p*-$COOCH_2CH(CH_3)_2$	142～144	71.43	1725,830,650	4.39(m,2H,O-CH_2-Ph)
33	H	*p*-$COOCH_2C_6H_5$	125～127	48.19	1720,835,755	8.0～7.2(m,12H,Ph-H), 5.35(s, 2H,$COOCH_2$-Ph)
34	H	*p*-SO_3	258～260	65.42	2500,1350,1160	4.50(s,bra,1H,-SO_3H)
35[f]	H	H	184～186	16.11	860,830,740	
36[f]	2-Cl	4-Cl	110～111	33.1	860,840,830	
37[f]	*p*-CN	H	168～171	21.74	2230,815,730	
38[f]	H	g	145～147	44.21	3140,1715,820	
39[f]	H	*p*-COOH	185～188	38.30	2610,1940,1715	12.1(s,1H,-COOH), 8.02～7.37 (m,11H,Ph-H)

a. C, H, N analyses were within 0.5% of calculated values. b. Compd **4**: Phenyl group replaced by 1,2,3,4-tetrahydronaphthyl group. c. Compd **5**: Phenyl group replaced by 1-naphthyl group. d. Compd **6**: phenyl group replaced by allyl group. e. Compds **18,26,34,36,29**: Free bases. f. Compds **35**～**39**: Triazolyl group replaced by benztriazolyl group. g. Compd **38**: Phenyl group replaced by allyl group.

对1H-1,2,4-三唑烷基化文献报道在回流的乙酸乙酯中相转移催化反应[8],后处理困难,收率低。现改为在冰水浴下二氯甲烷中反应,适当延长反应时间,收率明显提高。

Williamson 反应制备目标化合物中,使用氢化钠,要求无水,条件苛刻,我们改为相转移催化醚化,反应条件温和,反应后在溶剂中直接加硝酸成盐,重结晶纯化,避开了层析,简化了操作。

体外抑菌试验初步表明,大多数目标化合物对所测的多种真菌均有不同程度的抗菌活性。化合物**6,13**对所测菌种活性最高,为先导化合物益康唑的4～10倍,化合物**10,12,14,15,20,22,23,28,30**和**31**等对大部分真菌的活性也优于或相当于益康唑及克霉唑。引人注目的是部分化合物对深部真菌有较好的活性,化合物**14**除了新型隐球菌和熏烟色曲菌外,对其它真菌均优于克霉唑,化合物**23**和**31**抗裴氏着色菌活性为益康唑及克霉唑的30倍以上,化合物**22**抗白念珠菌活性为益康唑的8倍,克霉唑的4倍。

Tab 2 Antifungal activities of the compounds

	MIC* (μg·ml⁻¹)												
Compd	*Trichophyton gypseum*	*T. violaceum*	*T. rubrum*	*Microsporum gypseum*	*M. canis*	*M. ferrugineum*	*Epidermophyton floccosum*	*Sporotrichum schenckii*	*Cladosporium carrionii*	*Candida albicans*	*Cryptococcus neoformans*	*Fonseaea pedrosoi*	*Aspergillus fumigatus*
1	5	1.25	0.31	1.25	2.50	0.63	10	>40	>40	>40	>40	>40	>40
2	10	2.50	0.16	5	5	2.50	10	20	5	>40	>40	2.50	>40
3	10	2.50	2.50	>40	10	40	20	>40	40	>40	40	40	10
4	10	5	5	40	>10	5	10	10	20	40	>40	40	>10
5	10	10	1.25	40	40	20	10	>10	10	>40	>40	>40	>10
6	0.08	0.16	0.08	1.25	0.31	0.63	0.08	10	1.25	40	20	10	10
7	10	2.50	0.31	10	2.50	0.16	2.50	40	5	>40	>40	2.50	>40
8	20	5	1.25	40	5	1.25	5	40	5	>40	>40	5	>40
9	20	0.63	0.31	20	10	0.16	1.25	20	10	20	>40	20	>40
10	20	0.16	2.50	1.25	5	0.16	0.31	20	20	20	>40	40	>40
11	1.25	1.25	0.16	5	5	1.25	2.50	>40	1.25	>40	>40	>40	>40
12	2.50	0.31	0.16	5	2.50	5	0.63	20	40	>40	>40	2.50	>40
13	0.63	0.31	0.08	5	5	1.25	0.31	1.25	0.63	20	>40	5	20
14	2.50	2.50	2.50	20	20	10	5	5	5	10	5	5	>40
15	2.50	0.63	0.08	5	1.25	0.63	0.31	20	2.50	40	40	5	20
16	5	2.50	0.16	10	5	2.50	1.25	40	2.50	10	>40	5	>40
17	10	2.50	5	10	10	10	20	20	5	>40	>40	20	>40
18	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40
19	10	2.50	1.25	10	40	10	2.50	10	1.25	40	>40	10	40
20	10	0.31	0.16	2.50	20	20	5	10	2.50	40	40	10	40
21	20	0.08	1.25	40	40	0.31	5	40	2.50	40	>40	20	>40
22	20	10	5	20	20	2.50	5	5	2.50	5	40	10	>40
23	20	0.63	1.25	20	5	5	0.63	10	40	10	>40	1.25	>40
24	40	5	20	40	40	20	20	10	40	40	40	20	>40
25	40	40	20	40	>40	>40	40	>40	40	>40	>40	40	>40
26	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40
27	10	1.25	0.63	10	10	2.50	20	40	10	40	40	10	>40
28	10	0.63	0.16	1.25	10	20	5	20	2.50	>40	>40	10	>40
29	10	0.63	0.16	5	5	1.25	20	40	5	>40	>40	5	>40
30	5	20	5	20	10	1.25	20	5	2.50	20	20	10	>40
31	10	0.63	1.25	20	5	0.63	10	40	5	>40	>40	1.25	20
32	20	10	10	5	20	2.50	40	40	40	>40	>40	10	>40
33	40	20	40	40	>40	10	>40	20	40	>40	20	10	>40
34	40	20	>40	40	40	>40	>40	>40	>40	20	40	40	>40
35	40	2.50	1.25	5	>40	5	>40	40	40	>40	>40	>40	>40
36	>40	20	40	>40	>40	20	>40	>40	40	>40	>40	>40	>40
37	40	5	5	>40	40	2.50	>40	40	1.25	40	>40	>40	1.25
38	40	5	2.50	5	20	1.25	>40	10	>40	>40	>40	>40	>40
39	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40	>40
**	0.63	0.63	2.50	20	20	0.31	5	25	10	20	0.63	>40	2.50
***	0.63	0.63	0.31	20	>40	20	20	—	—	40	>40	>40	>40

*Drugs: All compounds were dissolved in DMSO and diluted with Sabourand's dextrose agar medium; incubation at 37 C for 2～7 d. **Clotrimazole was imported for Italy. ***Econazole was synthesized in our laboratory.

实 验 部 分

熔点用毛细管法测定，温度未校正；元素分析仪为 MOD-1106型；红外光谱仪为 Hitachi 270-50型，KBr 压片；核磁共振仪为 AC-300P 型，TMS 为内标，DMSO-d_6为溶剂。

1-(2,4-二氯苯基)-2-(1H-1,2,4-三唑基-1-)乙醇[9]

将三唑 13.6 g(0.2 mole) 悬浮于 CH_2Cl_2 70 ml 中，于冰水浴冷却下滴入 α-2,4-三氯苯乙酮20.1 g(0.09 mole)和 CH_2Cl_2 30 ml 混合液，滴毕于0～5℃搅拌反应6 h，放置过夜，减压回收溶剂，残物倾入300 ml 冰水中，过滤，水洗，干燥，溶于 CH_3OH 100 ml，冰浴冷却下分批加入 KBH_4 10 g，加毕搅拌1 h，加热回流4 h，回收溶剂，残物倾入冰水中，滤集，水洗，干燥，95%乙醇重结晶，得白色固体19.6 g，收率83%，mp 89～90℃(90℃)[9]。

4-{[2-(1H-1,2,4-三唑基-1-)-1-(2,4-二氯苯基)乙氧基]甲基}苯甲酸(26)

将 NaOH 0.5 g 溶于水2 ml 中，加入 THF 30 ml，正四丁基溴化铵0.1 g 和1-(2,4-二氯苯基)-2-(1H-1,2,4-三唑基-1-)乙醇1.30 g(5 mmole)，冰水浴冷却并搅拌下，滴入对溴甲基苯甲酸乙酯2.0 g 和 THF 15 ml 混合液，滴毕室温搅拌反应12 h，再加热回流7 h 后，加入10% NaOH 1 ml，再回流搅拌3 h，蒸出溶剂，向残物中加入水50 ml，乙酸乙酯提取，水相用醋酸酸化至 pH 4～5，乙酸乙酯提取，水洗，干燥，蒸去溶剂，异丙醇重结晶得白色固体1.40 g，收率71%，mp 187～189℃。元素分析 $C_{18}H_{15}Cl_2N_3O_3$，理论值%：C 55.12，H 3.85，N 10.72；实测值%：C 55.02，H 3.81，N 10.79。

化合物**18**和**39**合成方法同**26**。

4-{[2-(1H-1,2,4-三唑基-1-)-1-(2,4-二氯苯基)乙氧基]甲基}苯甲酸烯丙基酯(30)

将**26** 0.60 g(1.53 mmole)溶于 $CHCl_3$ 10 ml，滴入 $SOCl_2$ 3 ml，加热回流1 h，回收溶剂及多余氯化亚砜，加入烯丙醇10 ml 及吡啶0.5 ml，室温搅拌过夜，回收烯丙醇，向残留物中加水50 ml，调 pH 呈碱性，二氯甲烷提取，水洗，干燥，蒸去二氯甲烷，将残物溶于异丙醇，滴入浓硝酸成盐，乙醇重结晶，得0.56 g，收率73%，mp 140～142℃。

化合物**17**,**19**～**25**和**27**～**33**按此法合成。

1-{2-[(4-氯苯基)甲氧基]-2-(2,4-二氯苯基)乙基}-1H-1,2,4-三唑硝酸盐(13)

取2-(1H-1,2,4-三唑基-1-)-1-(2,4-二氯苯基)乙醇1.3 g(5 mmole)，加入50% NaOH 水溶液1.0 g，CH_2Cl_2 20 ml，四丁基溴化铵0.1 g，回流搅拌5 min，于室温滴加含对溴甲基氯苯1.0 g 的 CH_2Cl_2液10 ml，滴毕，室温搅拌1 h，再加热回流5 h，反应完毕水洗反应液，加硝酸成盐，冷却，过滤得粗品，用乙醇—丙酮(1:1)重结晶，得无色固体1.5 g，收率69%，mp 160～162℃。元素分析 $C_{17}H_{14}Cl_2N_3O\cdot HNO_3$，理论值%：C 47.57，H 3.52，N 13.06；实测值%：C 47.49，H 3.61，N 13.06。

化合物**1**～**16**,**35**～**38**均按此法合成。

4-{[2-(1H-1,2,4-三唑基-1-)-1-(2,4-二氯苯基)乙氧基]甲基}苯磺酸(34)

将 NaOH 0.5 g 溶于水2 ml 中，加入 THF 30 ml，正四丁基溴化铵0.1 g，1-(2,4-二氯苯基)-2-(1H-1,2,4-三唑基-1-)乙醇1.3 g(5 mmole)，冰浴冷却，搅拌下滴入对溴甲基苯磺酸乙酯2.0 g 和 THF 15 ml 混合液，滴毕室温搅拌反应60 h，加热回流5 h，蒸出溶剂，向残物中加入水50 ml，甲苯提取3次，水相用浓硝酸酸化，有片状结晶析出，异丙醇重结晶，得闪亮鳞片状结晶1.45 g，收率65%，mp 258～260℃。元素分析 $C_{17}H_{15}Cl_2N_3O_4S$，理论值%：C 47.67，H 3.53，N 9.81；实测值%：C 47.44，H 3.48，N 9.84。

致谢 抑菌活性由长征医院廖万清教授及徐红、赵谨同志代测。元素分析、红外光谱、核磁共振由本院精密仪器中心徐卫民、王勇和扬根金同志代测。

参 考 文 献

1 Buckel KH, Regel E, Plemple M. *N*-tritylimidazoles as antimycotics. *S African*, 68 05, 392; *CA*, 1969,**71**:91473m

2 Holt RJ. Laboratory and clinical studies on anti fungal drugs of the imidazole series. *Adv Antimicrob Antineoplast Chemother*, 1972,**1**:243

3 Thirnpont D, Van Cutsem J, Van Nueten JM *et al*. Biological and toxicological properties of econazole a broad-spectrum antimycotic. *Arzneimittel-forsch*, 1975,**25**:224

4 Richardson K, Brammer KW, Marriott MS *et al*. Activity of UK-49858, a bis-triazole derivative, against experimental infections with *Candida albicans* and *Trichophyton mentagrophytess*. *Antimicrob Agents Chemother*, 1985,**27**:832

5 Espinel-Ingroff A, Shadomy S, Gebnart RJ. *In vitro* studies with R-51211 (Itraconazole). *Antimicrob Agents Chemother*, 1984,**26**:5

6 Heeres J, Handrickx R, Van Cutsem J. Antimycotic azole 6. Synthesis and anti-fungal properties of terconazole, a novel triazole ketal. *J Med Chem*, 1983,**26**:611

7 Plempel M. Experience, recognitions and questions in azole antimycotics. *Jpn J Med Mycol*, 1982, **23**:17

8 张洪奎,廖联安,郭奇珍. 固液相转移催化1,2,4-三唑 *N*-烷基化的研究. 有机化学, 1986,**2**:108

9 Timmler H, Kraemer W, Buechel KH *et al*. Fungicidal and nematocidal 1-acyloxy-1-phenyl-2-triazolylethanes. *Ger Offen*, 2,628,419; *CA*,1978,**88**:152624m

SYNTHESIS AND ANTIFUNGAL ACTIVITIES OF 1-{2-[(SUBSTITUTED-PHENYL)METHOXY]-2-(SUBSTITUTED-PHENYL)ETHYL}-1H-TRIAZOLES AND BENZTRIAZOLES

K Li, WN Zhang, JQ Yang, JG Lu and QY Wu

(*Department of Medicinal Chemistry, College of Pharmacy, Second Military Medical University, Shanghai 200433*)

ABSTRACT Thirty-nine 1-{2-[(2,4-dichlorophenyl)methoxy]-2-(substituted-phenyl)ethyl}-1H-triazoles and benztriazoles were synthesized and all title compounds are reported for the first time.

Results of preliminary biological tests showed that the most active compounds **6** and **13** are 4～10 times more active than the lead compound econazole. The antifungal activities of compounds **10**, **12**, **14**, **15**, **20**, **22**, **23**, **28**, **30** and **31** are better than or comparable to the activities of econazole and clotrimazole against most fungi. Compounds **23** and **31** are 30 times more active than econazole and clotrimazole against *Fonseaea pedrosoi*. Compound **22** is 4 and 8 times more active than clotrimazole and econazole, respectively, against *Candide albicans*.

Key words Triazoles; Benztriazoles; Antifungal activity