

2-(*E*)-苯亚甲基-5-(*N*-取代胺甲基)环戊酮的合成及抗炎作用

董金华 徐莉英 秦 华 陈思维 计志忠* 王敏伟

(沈阳药科大学, 沈阳 110015)

摘要 本文报道 19 个 2-(*E*)-苯亚甲基环戊酮 Mannich 碱类化合物的合成。所有产物结构经元素分析、核磁共振氢谱和红外光谱证实。初步药理试验表明部分化合物有较强的抗炎活性。其中 1 个化合物对二甲苯致小鼠耳廓肿胀、角叉菜胶致大鼠足爪肿胀和乙酸致小鼠腹腔毛细血管通透性增加均有显著的抑制作用,抑制能力与布洛芬、阿斯匹林相近。

关键词 抗炎药物; 环戊酮 Mannich 碱; 胺交换反应

2-取代亚甲基-5-(*N*-取代胺烷基)环戊酮是一类新型结构的具有抗癌、抗炎活性的化合物^[1],近几年,已有一些关于这类化合物的合成设计和生物活性的报道^[2~10]。过去的研究发现,某些 2-(*E*)-芳亚甲基-5-(*N*-取代胺甲基)环戊酮具有显著的抗炎活性^[2,3]。为进一

步揭示这类化合物的构效关系,发现新的抗炎药物,最近我们合成了一系列 2-(*E*)-苯亚甲基环戊酮 Mannich 碱类化合物,并试验了部分化合物的抗炎活性。目标化合物合成路线见图 1,其结构经元素分析和波谱数据(IR, ¹HNMR)确证见表 1 及表 2。

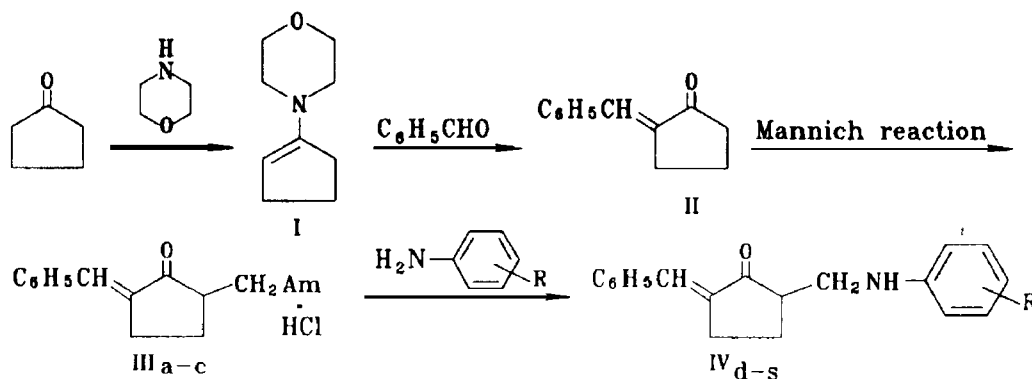


Fig 1 Route of synthesis.

胺交换反应的影响因素

实验发现,取代苯胺的碱性强弱和反应温度对胺交换反应有显著的影响。当取代基为供电子基团,取代苯胺的碱性较强时,室温下反应立即发生;当取代基为中性基团或弱的吸电子基团,取代苯胺的碱性较弱时,室温下反应也能进

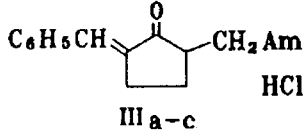
行;取代基为强的吸电子基团,室温下反应难以发生,IV_k-IV_s 必须在加热或回流的反应条件下才能得到。根据反应情况,我们推测 III_a 与取代苯胺的胺交换主要是通过取代反应进行的,和文献^[10]中报道的反应机制有所区别。化合物的抗炎作用

我们对目标化合物进行了初步的抗炎活性筛选,发现部分化合物有抗炎活性,其中, J₁₈ 有显著的抗炎活性。

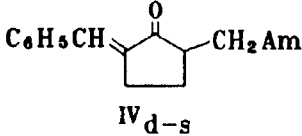
本文于 1997 年 11 月 10 日收到。

* 联系人




















Tab 1 Structures, the data of experiment and elemental analysis



III a-c



IV d-s

Compd	Am	MP (°C)	Yield (%)	Elemental analysis (%)					
				Calcd			Found		
				C	H	N	C	H	N
IIIa		150~152	68.2	66.33	7.20	4.55	66.12	7.20	4.25
IIIb		153~156	53.2	70.68	7.91	4.58	70.88	7.81	4.48
IIIc		135~137	34.3	69.97	7.60	4.80	69.84	7.73	4.83
IVd		147~150	92.9	82.27	6.90	5.05	82.11	6.97	5.01
IVe		160~162	54.8	82.44	7.26	4.81	82.67	7.36	4.62
IVf		122~124	50.4	82.44	7.26	4.81	81.82	7.26	4.58
IVg		156~159	67.1	78.14	6.89	4.56	78.13	6.83	4.66
IVh		158~160	48.1	78.47	7.21	4.36	78.40	7.19	4.44
IVi		173~175	57.8	73.19	5.82	4.49	73.37	5.89	4.50
IVj		175~177	63.3	64.05	5.09	3.93	64.15	5.04	3.87
IVk		177~179	64.5	78.97	6.63	4.39	78.75	6.80	4.29
IVl		114~116	69.9	78.97	6.63	4.39	78.79	6.75	4.36
IVm		169~172	63.9	70.79	5.63	8.69	70.96	5.41	8.63
IVn		121~123	52.0	70.79	5.63	8.69	71.23	5.46	8.38
IVo		145~148	70.3	69.19	5.20	4.25	69.14	5.10	4.17
IVp		183~186	56.1	74.74	5.96	4.36	74.82	5.84	4.44
IVq		154~157	64.2	74.74	5.96	4.36	75.08	5.81	4.38
IVr		158~161	30.4	74.74	5.96	4.36	75.29	5.83	4.24
IVs		188~190	66.2	64.02	5.66	7.86	63.83	5.68	7.80

从表 3~5 可以看出, J_{18} 对二甲苯致小鼠耳廓肿胀、角叉菜胶致大鼠足跖肿胀和乙酸致小鼠腹腔毛细血管通透性增加均有明显的抑制作用, 并且都呈剂量依赖性。用简化机率单位法求得 J_{18} 对 3 种实验模型的 ED_{50} 依次为 67.8 , 25.3 和 $41.8 \text{ mg} \cdot \text{kg}^{-1}$, 阳性对照药消炎痛、布洛芬和阿斯匹林的 ED_{50} 分别为 2.6 ,

21.0 和 $29.1 \text{ mg} \cdot \text{kg}^{-1}$, J_{18} 的抗炎活性约和布洛芬、阿斯匹林相当。

2-(E)-苯亚甲基-5-(N-取代胺甲基)环戊酮类化合物有抗炎活性, 也进一步证实 2-(E)-芳亚甲基是环戊酮 Mannich 碱类化合物有生物活性的重要基团。目前, 我们正在对这类化合物的作用特点和抗炎机理进行研究。

Tab 2 Spectral data of the compounds

Compd	¹ HNMR(δ ppm)	IR(cm ⁻¹)
IIIa	1.48~1.63(m, 1H), 2.30~2.50(m, 1H), 2.70~3.10(m, 3H), 3.10~3.60(m, 6H), 3.70~4.20(br, 4H), 7.30(s, 1H), 7.40~7.60(m, 5H)	3417, 2864, 2523, 1712, 1625, 1445, 1248, 1174, 1125, 1098, 992, 900, 863, 770, 690
IIIb	1.30~1.50(m, 2H), 1.60~1.90(m, 5H), 2.20~2.40(m, 1H), 2.45~2.70(m, 2H), 2.70~3.00(m, 4H), 3.20~3.26(m, 1H), 3.37(d, 2H), 7.09(s, 1H), 7.38(s, 5H)	3414, 2937, 2862, 2615, 2511, 1714, 1625, 1443, 1282, 1230, 1171, 1137, 1082, 1018, 937, 756, 688
IIIc	1.30~1.55(m, 1H), 1.90~2.20(br, 4H), 2.20~2.40(m, 1H), 2.60~3.10(m, 6H), 3.36(dd, 1H), 3.45~3.70(br, 2H), 7.19(s, 1H), 7.30~7.50(m, 5H)	3410, 2956, 2555, 2444, 1708, 1625, 1448, 1234, 1190, 1164, 1075, 1016, 939, 758, 690
IVd	1.65~1.85(m, 1H), 2.30~2.45(m, 1H), 2.65~2.95(m, 2H), 3.00~3.15(m, 1H), 3.36(dd, 1H), 3.47(dd, 1H), 6.60~6.80(m, 3H), 7.20(t, 2H), 7.30~7.60(m, 6H)	3380, 3035, 2832, 1700, 1621, 1505, 1439, 1369, 1318, 1268, 1159, 1115, 1024, 924, 868, 748, 692
IVe	1.60~1.85(m, 1H), 2.30~2.45(m, 1H), 2.65~3.20(m, 3H), 3.44(dd, 1H), 3.49(dd, 1H), 6.65(d, 2H), 7.03(d, 2H), 7.35~7.60(m, 6H)	3374, 2906, 2811, 1700, 1623, 1519, 1449, 1365, 1317, 1264, 1028, 950, 815, 750, 692
IVf	1.65~1.85(m, 1H), 2.30(s, 3H), 2.33~2.50(m, 1H), 2.70~3.20(m, 3H), 3.35(dd, 1H), 3.50(dd, 1H), 6.50~6.60(m, 3H), 7.10(dt, 1H), 7.35~7.60(m, 6H)	3388, 3033, 2904, 1701, 1622, 1513, 1442, 1269, 1241, 1161, 1027, 925, 845, 776, 691
IVg	1.60~1.85(m, 1H), 2.20~2.50(m, 1H), 2.65~3.15(m, 3H), 3.25(dd, 1H), 3.42(dd, 1H), 6.69(d, 2H), 6.81(d, 2H), 7.35~7.60(m, 6H)	3367, 2900, 2816, 1700, 1622, 1513, 1449, 1364, 1292, 1257, 1232, 1159, 1123, 1047, 950, 823, 753, 694
IVh	1.38(t, 3H), 1.65~1.82(m, 1H), 2.25~2.45(m, 1H), 2.65~3.15(m, 3H), 3.31(dd, 1H), 3.42(dd, 1H), 3.97(q, 2H), 6.68(d, 2H), 6.80(d, 2H), 7.30~7.60(m, 6H)	3368, 2970, 2901, 2810, 1700, 1621, 1513, 1446, 1396, 1231, 1158, 1120, 1054, 924, 822, 749, 692
IVi	1.60~1.80(m, 1H), 2.30~2.50(m, 1H), 2.60~3.20(m, 3H), 3.30~3.50(m, 2H), 6.63(d, 2H), 7.15(d, 2H), 7.30~7.60(m, 6H)	3372, 2902, 2813, 1696, 1619, 1500, 1447, 1339, 1317, 1288, 1263, 1240, 1160, 1122, 950, 925, 823, 751, 692
IVj	1.60~1.80(m, 1H), 2.30~2.45(m, 1H), 2.60~3.20(m, 3H), 3.30~3.50(m, 2H), 6.62(d, 2H), 7.30(d, 2H), 7.35~7.60(m, 6H)	3371, 2811, 1695, 1618, 1498, 1446, 1396, 1260, 1159, 945, 819, 750, 691
IVk	1.65~1.80(m, 1H), 2.35~2.45(m, 1H), 2.51(s, 3H), 2.70~3.15(m, 3H), 3.49(d, 2H), 6.70(d, 2H), 7.40~7.56(m, 6H), 7.85(d, 2H)	3378, 2903, 2818, 1696, 1670, 1617, 1518, 1489, 1449, 1414, 1358, 1327, 1266, 1161, 952, 828, 754, 693
IVl	1.65~1.80(m, 1H), 2.30~2.45(m, 1H), 2.57(s, 3H), 2.60~3.11(m, 3H), 3.44(d, 2H), 6.88(d, 1H), 7.20~7.31(m, 3H), 7.35~7.45(m, 4H), 7.54(d, 2H)	3385, 3057, 2880, 1710, 1679, 1624, 1594, 1519, 1484, 1423, 1359, 1327, 1270, 1229, 1155, 946, 762, 689
IVm	1.65~1.80(m, 1H), 2.30~2.45(m, 1H), 2.60~3.20(m, 3H), 3.40~3.60(m, 2H), 6.59(d, 2H), 7.41~7.57(m, 6H), 8.09(d, 2H)	3392, 1699, 1598, 1534, 1500, 1471, 1366, 1314, 1185, 1157, 1106, 950, 921, 831, 756, 686
IVn	1.65~1.85(m, 1H), 2.30~2.50(m, 1H), 2.60~3.20(m, 3H), 3.40~3.50(m, 2H), 6.96(d, 1H), 7.30(d, 1H), 7.35~7.50(m, 5H), 7.55(d, 3H)	3413, 2947, 1706, 1623, 1525, 1451, 1346, 1158, 1115, 1021, 951, 839, 756, 691
IVo	1.65~1.76(m, 1H), 2.25~2.45(m, 1H), 2.60~3.15(m, 3H), 3.20~3.40(m, 2H), 6.51(dt, 1H), 6.67(dd, 1H), 6.96(t, 1H), 7.30~7.60(m, 6H)	3379, 2893, 1701, 1618, 1512, 1398, 1287, 1222, 1160, 1104, 1048, 953, 923, 814, 761, 689
IVp	1.65~1.76(m, 1H), 2.20~2.35(m, 1H), 2.60~3.10(m, 3H), 3.10~3.25(m, 1H), 3.35~3.50(m, 1H), 6.61(dd, 2H), 7.28(s, 1H), 7.40~7.70(m, 7H)	3380, 2900, 1694, 1604, 1526, 1488, 1423, 1320, 1268, 1171, 1121, 950, 838, 772, 693

Continued

Compd	¹ HNMR(δ ppm)	IR(cm ⁻¹)
IVq	1.65~1.85(m, 1H), 2.35~2.45(m, 1H), 2.65~3.15(m, 3H), 3.46(d, 2H), 6.91(d, 1H), 7.27~7.30(m, 1H), 7.35~7.50(m, 6H), 7.56(d, 2H)	3399, 2831, 1691, 1614, 1516, 1443, 1305, 1160, 948, 865, 754, 686
IVr	1.65~1.76(m, 1H), 2.15~2.35(m, 1H), 2.70~3.05(m, 3H), 3.32(dd, 1H), 3.54(dd, 1H), 6.56(t, 1H), 6.79(d, 1H), 7.20~7.50(m, 5H), 7.63(d, 2H), 7.78(d, 1H)	3370, 2943, 1705, 1662, 1620, 1578, 1517, 1448, 1441, 1331, 1254, 1161, 924, 749, 689
IVs	1.60~1.75(m, 1H), 2.20~2.35(m, 1H), 2.60~3.05(m, 3H), 3.18(dd, 1H), 3.46(dd, 1H), 6.66(d, 2H), 7.28(s, 1H), 7.35~7.52(m, 5H), 7.62(d, 2H)	3390, 3331, 3235, 1698, 1601, 1521, 1452, 1317, 1235, 1149, 1100, 899, 822, 756, 690

实验部分

Yanaco 显微熔点测定仪, 温度未校正, Shimadzu IR-27G 红外分光光谱仪(KBr 压片), Bruker ARX-300 核磁共振仪, MOD 1106 元素自动分析仪。

1 I, II 的合成

按 Stork 等给出的方法合成^[11]。

2 IIIa-c 的合成

将杂环胺 10 mmol 和无水乙醇 20 ml 置于 100 ml 烧瓶中, 滴加浓盐酸调溶液 pH 3~4, 加入 II 10 mmol 和多聚甲醛 15 mmol, 回流 2 h 后, 续加多聚甲醛 10 mmol, 回流 2 h, 趁热过滤, 浓缩滤液, 冷却后析出白色固体, 用甲醇—氯化氢重结晶。

3 IVd 的合成

将盐酸苯胺 6 mmol 和 50% 乙醇水溶液 25 ml 置于 100 ml 烧瓶中, 用 5% 碳酸钠水溶液调 pH 至 8, 加入 IIIa 5 mmol, 很快有白色固体生成, 室温搅拌 2 h, 抽滤, 用 50% 乙醇水溶液洗涤。所得粗品用苯—乙醇重结晶。

4 IVe-j 的合成

将 IIIa 5 mmol、取代苯胺 6 mmol、50% 乙醇水溶液 25 ml 置于 100 ml 烧瓶中, 室温搅拌 2~6 h, 得黄色固体, 用苯—乙醇重结晶。

5 IVk-o 的合成

将 IIIa 5 mmol、取代苯胺 6 mmol、50% 乙醇水溶液 25 ml 置于 100 ml 烧瓶中, 于 40℃ 搅

拌 20 h, 得黄色固体, 用苯—乙醇重结晶。

6 IVp-s 的合成

将 IIIa 5 mmol、取代苯胺 6 mmol、50% 乙醇水溶液 25 ml 置于 100 ml 烧瓶中, 回流 2~4 h, 得黄色固体。IVp-r 用苯—乙醇重结晶, IVs 用三氯甲烷重结晶。

7 化合物的抗炎试验

对小鼠二甲苯性耳廓肿胀的影响: 小鼠 70 只, 雌雄兼用, 体重 20 ± 2 g, 随机分成 7 组, ig 给药, 45 min 后用二甲苯 0.03 ml 致炎, 致炎 15 min 后处死动物, 用直径 8 mm 打孔器在双耳对称处打下耳片称重, 左右耳片重量差为肿胀度, 结果见表 3。

Tab 3 Effect of J₁₈ on xylene-induced mice ear swelling

	Dose (mg•kg ⁻¹)	Weight increase of earflap (mg, $\bar{x} \pm s$)	Inhibition (%)
1% CMC	—	7.18 ± 2.41	
Indomethacin	1.5	4.15 ± 0.78***	42.2
	4.5	3.10 ± 0.84***	56.8
	13.5	1.53 ± 0.55***	78.7
J ₁₈	40	4.40 ± 1.00***	38.7
	92	3.17 ± 0.67***	55.8
	210	1.91 ± 0.72***	73.4

n = 10, *** P < 0.01 vs control.

对大鼠角叉菜胶性足爪肿胀的影响: 大鼠 64 只, 雌雄兼用, 体重 135 ± 15 g, 随机分成 8 组, ig 给药, 1 h 后于一侧足跖 sc 1% 角叉菜胶

0.1 ml 致炎, 分别测定致炎后 1, 2, 3, 4, 5 和 6 h 各时间点肿胀度, 求出肿胀率, 结果见表 4。

Tab 4 Effect of J₁₈ on carrageenin induced rats paw edema

	Dose (mg•kg ⁻¹)	Edema rate at different time(%) ($\bar{x} \pm s$)					
		1 h	2 h	3 h	4 h	5 h	6 h
1% CMC	—	40.5 ± 8.7	56.5 ± 14.4	78.2 ± 13.4	82.8 ± 13.4	76.3 ± 10.7	72.6 ± 16.6
Ibuprofen	12.5	35.7 ± 15.0 (12.0)	43.0 ± 12.0 (23.9)	54.6 ± 9.2 ^{**} (25.0)	61.0 ± 10.6 ^{**} (26.3)	53.4 ± 18.0 ^{**} (30.0)	54.0 ± 15.2 [*] (25.6)
	25	30.7 ± 14.7 (24.2)	32.3 ± 13.0 ^{**} (42.8)	36.3 ± 16.5 ^{***} (50.0)	34.5 ± 17.0 ^{***} (58.3)	28.5 ± 17.5 ^{***} (62.6)	34.9 ± 16.7 ^{***} (52.0)
	50	30.7 ± 15.0 (24.2)	27.5 ± 12.6 ^{***} (51.3)	23.5 ± 9.8 ^{***} (68.0)	23.4 ± 9.2 ^{***} (71.7)	18.4 ± 8.4 ^{***} (75.9)	18.4 ± 9.6 ^{***} (74.7)
J ₁₈	100	30.3 ± 9.8 [*] (25.1)	24.8 ± 12.9 ^{***} (56.1)	22.1 ± 11.2 ^{***} (70.0)	24.7 ± 7.1 ^{***} (70.2)	15.0 ± 6.2 ^{***} (80.3)	17.4 ± 12.0 ^{***} (76.0)
	25	36.5 ± 10.2 (14.7)	37.3 ± 7.8 ^{**} (34.0)	47.1 ± 12.1 ^{**} (35.3)	45.7 ± 12.1 ^{***} (44.8)	42.3 ± 13.0 ^{***} (44.6)	40.7 ± 11.3 ^{***} (43.9)
	50	28.5 ± 14.4 (29.6)	28.1 ± 12.5 ^{***} (50.0)	27.4 ± 15.6 ^{***} (62.4)	20.3 ± 11.8 ^{***} (75.5)	19.0 ± 12.0 ^{***} (75.0)	25.2 ± 14.3 ^{***} (65.0)
	100	27.0 ± 13.5 [*] (33.3)	26.2 ± 12.7 ^{***} (54.0)	24.8 ± 13.5 ^{***} (66.0)	18.2 ± 6.5 ^{***} (78.0)	22.5 ± 10.0 ^{***} (70.5)	21.6 ± 10.5 ^{***} (70.2)

n = 8, * P < 0.05, ** P < 0.01, *** P < 0.01 vs control, () Inhibition.

对小鼠腹腔毛细血管通透性的影响: 小鼠 70 只, 雌雄各半, 体重 20 ± 2 g, 随机分成 7 组, ig 给药, 40 min 后, iv 0.5% Evans 蓝(0.05 ml • 10 g⁻¹), 5 min 后, ip 0.7% 乙酸(0.1 ml • 10 g⁻¹), 30 min 后处死动物, 剖腹, 用蒸馏水多次冲洗腹腔, 合并冲洗液, 用蒸馏水稀释至 10 ml, 加 0.1 mol • L⁻¹ 氢氧化钠 0.1 ml 混匀, 离心后, 于 590 nm 处测吸光度。测得的吸光度按预作的 Evans 蓝标准曲线求出渗出量, 结果见表 5。

Tab 5 Effect of J₁₈ on increased capillary permeability induced with acetic acid in mice

	Dose (mg•kg ⁻¹)	Evans blue ($\mu\text{g} \cdot \text{ml}^{-1}, \bar{x} \pm s$)	Inhibition (%)
1% CMC	—	2.400 ± 0.640	
Aspirin	25	1.314 ± 0.172 ^{***}	45.3
	50	0.498 ± 0.283 ^{***}	79.2
	100	0.093 ± 0.055 ^{***}	96.2
J ₁₈	40	1.226 ± 0.353 ^{***}	48.9
	92	0.538 ± 0.280 ^{***}	77.6
	210	0.255 ± 0.059 ^{***}	89.4

n = 10, *** P < 0.001 vs control.

参 考 文 献

- 1 周淑兰, 计志忠. 环戊酮衍生物的合成及其抗癌、抗炎活性. 中国药物化学杂志, 1990, 1:26
- 2 陈海涛, 景永奎, 计志忠, 等. 2-(E)取代苯亚甲基环戊酮及其 Mannich 碱盐酸盐类化合物的合成和抗炎、抗癌活性研究. 药理学报, 1991, 26: 183
- 3 吴华璞, 葛敏, 於传斌, 等. MB-2 的抗炎作用及胃肠道刺激性. 蚌埠医学院学报, 1991, 16:234
- 4 Chen HT, Ji ZZ, Wong LK, et al. Synthesis and anti-cancer activity of 2-alkylaminomethyl-5-(E)-alkylidene cyclopentanone hydrochlorides. *Bioorg Med Chem*, 1994, 2:1091
- 5 Chen HT, Ji ZZ, Wong LK, et al. Synthesis and cytotoxic activities of the amine-exchange products of 2-dimethylaminomethyl-5-(E)-substituted arylidene cyclopentanones with anilines: 2-Arylaminoethyl-5-(E)-arylidene cyclopentanones. *Drug Design Discov*, 1996, 14:43
- 6 Chen HT, Ji ZZ, Wong LK, et al. Synthesis, anti-inflammatory, and cytotoxic activities of 2-alkyl and 2-benzyl-2-dimethylaminomethyl-5-(E)-arylidene cyclopentanone hydrochlorides. *Pharm Res*, 1996, 13:1482
- 7 Qi CM, Ji ZZ. Synthesis and potential antineoplastic activity of α -(1-cyclopentenyl) cyclopentanone

- derivatives—A new family of anticancer agents. *Chin Chem Lett*, 1995, **6**:847
- 8 齐传民, 计志忠, 李玉兰, 等. 2-烷基环戊-2-烯酮衍生物的合成及抗炎活性研究. 高等学校化学学报, 1996, **17**:258
- 9 李玉兰, 康影, 计志忠. 2-(N-芳胺甲基)-5-(E)-戊亚基环戊酮衍生物的合成及其抗炎活性研究. 中国药物化学杂志, 1996, **6**:85
- 10 康影, 李玉兰, 计志忠, 等. 2-对甲氧基苯亚甲基-5-取代胺甲基环戊酮衍生物的合成及其抗炎活性. 中国药物化学杂志, 1996, **6**:249
- 11 Stork G, Brizzolara A, Landensman H, *et al.* The enamine alkylation and acylation of carbonyl compounds. *J Am Chem Soc*, 1963, **85**:207

SYNTHESIS AND ANTIINFLAMMATORY ACTIVITY OF 2-(E)-BENZYLIDENE-5-(N-SUBSTITUTED AMINOMETHYL) CYCLOPENTANONES

Dong Jinhua(Dong JH), Xu Liying(Xu LY), Qin Hua(Qin H), Chen Siwei(Chen SW),
Ji Zhizhong(Ji ZZ) and Wang Minwei(Wang MW)

(*Shenyang Pharmaceutical University, Shenyang 110015*)

ABSTRACT Nineteen kinds of 2-(E)-benzylidene-5-(N-substituted aminomethyl) cyclopentanones were synthesized via Mannich reaction or amine exchange reaction and identified spectrometrically. One compound exhibited significant antiinflammatory activity, showing obvious inhibitory effect on xylene-induced mice ear swelling, carrageenin-induced rats paw edema and increased capillary permeability induced with acetic acid in mice. Its ED₅₀ values in these inflammatory models were calculated to be 67.8 mg•kg⁻¹, 25.3 mg•kg⁻¹ and 41.8 mg•kg⁻¹ respectively, nearly equal to those of ibuprofen and aspirin.

KEY WORDS Antiinflammatory agent; Cyclopentanone Mannich base; Amine exchange reaction