云南大学学报(自然科学版),2018,40(1):125~131 DOI:10.7540/j.ynu.20170361
Journal of Yunnan University

茚并[1,2-*b*]吡咯-4(1*H*)-酮类化合物的合成*

罗大云, 杨昌龙, 资全兴, 林　军, 严胜骄
(云南大学 教育部自然资源药物化学重点实验室,化学科学与工程学院,云南 昆明　650091)

摘要:以 N,N′-二烷基-2-硝基乙烯-1,1-二胺(1)和水合茚三酮(2)为原料,在乙醇介质中,50 ℃条件下反应并以优异的产率(92%~98%)合成了茚并[1,2-*b*]吡咯-4(1*H*)-酮类化合物 3a~3k.该反应具有操作简便、条件温和和产率高等特点.

关键词:茚并[1,2-*b*]吡咯-4(1*H*)-酮;茚三酮;烯二胺;合成
中图分类号:O 626.1　　**文献标志码**:A　　**文章编号**:0258-7971(2018)01-0125-07

吡咯类化合物具有优良的抗肿瘤[1-2]、抗病毒[3]、抗细菌[4]、抗真菌[5]、降低胆固醇[6]等活性和作用.多年来备受药物、化学家们广泛关注,到目前为止已有大量的文献报道其合成方法[1-7].

茚或茚酮骨架结构广泛存在于天然产物及各种生物活性分子中,多年来备受关注[8-13].茚/茚酮化合物具有广谱而优良的生物活性,如抗菌[8-9]、抗肿瘤[10]、抗病毒[11]、杀虫(图 1,A)[12]等活性[13],致使其在医药、农药中都有广泛的应用.

1,1-烯二胺包括环状 1,1-烯二胺(cyclic 1,1-enediamines),又称杂环烯酮缩胺(heterocyclic ketene aminals (HKAs))和链状 1,1-烯二胺(EDAMs).杂环烯酮缩胺作为多功能合成砌块,广泛用于合成结构多样的杂环化合物[14-17]如喹啉、喹啉亚胺、吲哚、吲哚酮、异香豆素、吡啶、吡咯类化合物,这些化合物具有抗肿瘤、除草、杀虫、抗焦虑、抗菌等生物活性[17].链状 1,1-烯二胺(EDAMs)[18]也用于合成吡啶、1,4-二氢吡啶、吡啶-2-酮、吲哚、异喹啉等类杂环化合物,所合成的化合物具有十分优异的生物活性.

因而将吡咯结构和茚/茚酮结构进行杂合的分子[19-20],预测将具有潜在的更为广谱的生物活性,

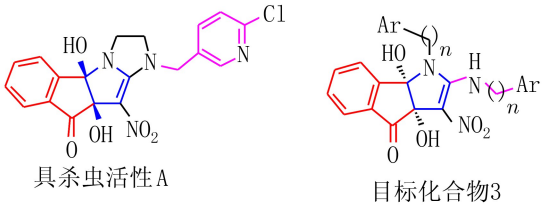

图 1　具有杀虫活性的化合物及目标化合物

Fig. 1 Insecticidal activity of compounds and the target compounds

为今后进行生物活性筛选打下基础.我们从链状 1,1-烯二胺出发,合成具有吡咯和茚/酮结构的杂合化合物 3,为后续进行杀虫活性测试奠定基础.

1　实　验

1.1　仪器和试剂　熔点用 XT-4A 型显微熔点测定仪,温度未校正;IR 用 Thermo Nicolet Avatar 360 型傅立叶红外光谱仪测定,KBr 压片;HRMS 用 Agllent LC/Msd TOF 质谱仪测定;NMR 用 Bruker DRX500 或 Bruker DRX600 型核磁共振仪测定.所用试剂均购于国药集团且均为化学纯或分析纯.

1.2　合成方法

1.2.1　合成茚并[1,2-*b*]吡咯-4(1*H*)-酮类化合

* **收稿日期**:2017-06-11
基金项目:国家自然科学基金(21362042,21662042,U1202221,21262042);云南省自然科学基金(2017FA003);云南省中青年学术和技术带头人及后备人才(2012HB001);云南大学东陆学者,云南大学青年英才计划项目.
作者简介:罗大云(1991-),男,云南人,硕士,主要从事抗肿瘤药物合成.E-mail:986189022@qq.com.
通信作者:林　军(1960-),男,云南人,博士,教授,主要从事有机合成.
严胜骄(1973-),男,云南人,博士,教授,主要从事抗肿瘤药物的设计合成.E-mail:yansj@ynu.edu.cn.

物 3 在 50 mL 圆底烧瓶中加入 N,N′-二烷基-2-硝基乙烯-1,1-二胺 1(1.0 mmol)和水合茚三酮 2(1.0 mmol),再加入 20 mL 乙醇,将反应液搅拌并加热至 50 ℃左右,反应约 1 h,TLC 监测反应.待反应完全后,停止加热,冷却(部分加入少量石油醚),析出大量固体,抽滤,滤液经减压蒸馏浓缩至少量液体时,再加入少量石油醚析出固体,接着抽滤.合并 2 次抽滤得到的固体,采用丙酮或乙酸乙酯进行重结晶 1~2 次,便可得到白色固体 3a~3k,产率达 92%~98%,反应式见图 2,产率见表 1.

1.2.2 代表化合物单晶结构 化合物 3d 的单晶结构图见图 3.从单晶结构图中可以看出,化合物 3d 结构中 2 个羟基处于同侧,2 个手性碳构型为(*S*,*S*).由于环结构的作用导致反应的非对映选择性很高,反应中没有监测到 2 个手性碳构型为(*R*,*S*)或(*S*,*R*)的产物.化合物 3d 单晶 cif 文件寄存于剑桥晶体数据中心(CCDC 号为 1555282).

2 实验数据

(3a*S*,8b*S*)-1-(4-氟苄基)-2-((4-氟苄基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮(3a) 白色固体,m.p. 190.6~192.6 ℃;IR(KBr)ν:3 420,3 082,1 724,1 641,1 604,1 557,1 511,1 434,1 352,1 290,1 224,1 197,1 158,1 089,1 035,986,941,925,840,807,785,758,714,646 cm^{-1};^1H NMR(600 MHz,DMSO-d_6)δ:4.35~4.39(m,2H,CH_2),4.83~5.36(m,2H,CH_2),6.61(br,1H,OH),6.95(d,J=7.2 Hz,4H,ArH),7.22(t,J=8.7 Hz,2H,ArH),7.43~7.46(m,2H,ArH),7.53(d,J=7.6Hz,1H,ArH),

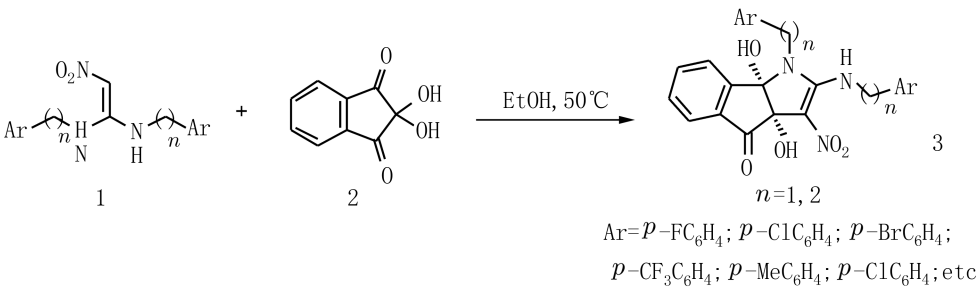

图 2 合成茚并[1,2-*b*]吡咯-4(1*H*)-酮类化合物 3

Fig.2 Synthesis of indeno[1,2-*b*]pyrrol-4(1*H*)-one compounds 3

表 1 合成化合物 3 的反应时间和产率

Tab.1 Synthesis reaction time and yields of compounds 3

序号	*n*	Ar	1	2	反应时间/h	产物	产率[a]/%
1	1	*p*-FC_6H_4	1a	2a	1	3a	96
2	1	*p*-ClC_6H_4	1b	2b	1	3b	98
3	1	*p*-BrC_6H_4	1c	2c	1	3c	94
4	1	*p*-$CF_3C_6H_4$	1d	2d	1	3d	94
5	1	2,4-difluorophenyl	1e	2e	1	3e	92
6	1	2,4-dichlorophenyl	1f	2f	1	3f	96
7	1	furan-2-yl	1g	2g	1	3g	94
8	2	C_6H_5	1h	2h	1	3h	96
9	2	*p*-MeC_6H_4	1i	2i	1	3i	97
10	2	*p*-FC_6H_4	1j	2j	1	3j	93
11	2	*m*-ClC_6H_4	1k	2k	1	3k	96

[a] 柱色谱分离产率

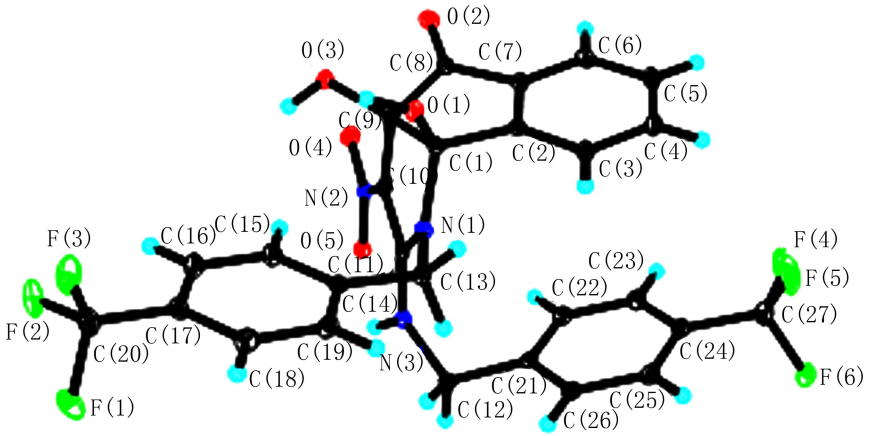

图 3　化合物 3d 的单晶结构图

Fig.3 X-ray crystal structures of compound 3d

7.56~7.61 (m,2H,ArH+OH),7.65 (t,*J*=7.3 Hz,1H,ArH),7.73 (t,*J*=7.4 Hz,1H,ArH),9.84 (br,1H,NH);^{13}C NMR (150 MHz,DMSO-d_6) δ:45.2,45.9,81.0,93.6,109.2,115.9 (d,*J*=21.0 Hz),123.6,124.6,128.7~128.8 (m),131.1,134.1~134.3 (m),135.9,148.1,154.2,161.1 (d,*J*=18.0 Hz),162.7 (d,*J*=16.5 Hz),195.7;HRMS (TOF ES$^+$) *m/z*: $C_{25}H_{19}F_2N_3NaO_5$ [M+Na]$^+$,计算值 502.118 5,实测值 502.118 7.

(3a*S*,8b*S*)-1-(4-氯苄基)-2-((4-氯苄基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3b)　白色固体,m.p. 205.5~207.5 ℃;IR (KBr) ν:3 419,3 067,1 721,1 643,1 557,1 493,1 426,1 407,1 366,1 289,1 232,1 198,1 158,1 093,1 035,1 012,987,946,925,835,798,757,714,644 cm^{-1};^{1}H NMR (600 MHz,DMSO-d_6) δ:4.31~4.43 (m,2H,CH_2),4.77~5.35 (m,2H,CH_2),6.60 (br,1H,OH),6.92 (d,*J*=8.3 Hz,2H,ArH),7.15 (d,*J*=8.4 Hz,2H,ArH),7.40~7.43 (m,4H,ArH),7.49 (d,*J*=7.4 Hz,1H,ArH),7.59~7.65 (m,3H,ArH+OH),7.73 (d,*J*=7.3 Hz,1H,ArH),9.85 (br,1H,NH);^{13}C NMR (150 MHz,DMSO-d_6) δ:45.2,45.9,81.0,93.6,109.3,123.6,124.5,128.4,128.7,129.0,129.0,131.0,132.5,134.1,135.9,136.9,137.2,148.0,154.3,195.7;HRMS (TOF ES$^+$) *m/z*: $C_{25}H_{19}Cl_2N_3NaO_5$ [M+Na]$^+$,计算值 534.059 4,实测值 534.059 4.

(3a*S*,8b*S*)-1-(4-溴苄基)-2-((4-溴苄基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3c)　白色固体,m.p. 209.8~211.8 ℃;IR (KBr) ν:3 063,1 722,1 643,1 603,1 557,1 489,1 427,1 403,1 365,1 289,1 228,1 198,1 180,1 157,1 091,1 072,1 035,1 008,986,925,837,796,757 cm^{-1};^{1}H NMR (600 MHz,DMSO-d_6) δ:4.28~4.42 (m,2H,CH_2),4.74~5.32 (m,2H,CH_2),6.59 (br,1H,OH),6.86 (d,*J*=8.2 Hz,2H,ArH),7.28 (d,*J*=8.3 Hz,2H,ArH),7.34 (d,*J*=8.2 Hz,2H,ArH),7.48 (d,*J*=7.5 Hz,1H,ArH),7.54~7.65 (m,5H,ArH+OH),7.73 (d,*J*=7.3 Hz,1H,ArH),9.84 (br,1H,NH);^{13}C NMR (150 MHz,DMSO-d_6) δ:45.3,46.0,81.0,93.6,109.3,121.0,121.1,123.6,124.5,128.7,129.0,131.0,131.7,131,9,131.9,134.1,135.9,137.3,137.7,148.0,154.3,195.7;HRMS (TOF ES$^+$) *m/z*: $C_{25}H_{19}Br_2N_3NaO_5$[M+Na]$^+$,计算值 621.958 4,实测值 621.958 4.

(3a*S*,8b*S*)-1-(4-(三氟甲基)苄基)-2-((4-(三氟甲基)苄基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3d)　白色固体,m.p.205.5~207.5 ℃;IR (KBr) ν:3 426,3 079,1 728,1 637,1 620,1 553,1 468,1 419,1 326,1 291,1 236,1 161,1 118,1 067,1 036,1 016,985,929,831,816,783,760,637 cm^{-1};^{1}H NMR (500 MHz,DMSO-d6) δ:=4.42~4.63 (m,2H,CH_2),4.91~5.47 (m,2H,CH_2),6.63 (br,1H,OH),7.10 (d,*J*=7.5 Hz,2H,ArH),7.42 (d,*J*=8.0

Hz,2H,ArH),7.54~7.67 (m,8H,ArH+OH),7.74~7.75 (m,1H,ArH),9.97 (br,1H,NH);^{13}C NMR (125 MHz,DMSO-d_6) δ:45.6,46.1,81.1,93.6,109.4,121.4 (d,J=20.0 Hz),123.4,123.6,124.5,125.6~125.8 (m),127.0,127.6,127.8~128.7 (m),131.1,134.1,135.8,142.5,143.1,148.0,154.4;HRMS (TOF ES$^+$) m/z:$C_{27}H_{19}F_6N_3NaO_5$[M+Na]$^+$,计算值602.112 1,实测值602.112 2.

(3a*S*,8b*S*)-1-(2,4-二氟苄基)-2-((2,4-二氟苄基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3e) 白色固体,m.p.197.9~199.9 ℃;IR (KBr) ν:3 420,3 092,1 726,1 638,1 604,1 556,1 506,1 423,1 356,1 274,1 231,1 194,1 158,1 141,1 101,1 035,968,920,873,848,835,787,755 cm^{-1};^{1}H NMR (500 MHz,DMSO-d_6) δ:4.46~4.49 (m,2H,CH_2),5.06~5.27 (m,2H,CH_2),6.61 (br,1H,OH),6.79~6.83 (m,1H,ArH),6.88~6.93 (m,1H,ArH),7.05~7.09 (m,1H,ArH),7.16~7.37 (m,3H,ArH),7.58~7.75 (m,5H,ArH+OH),9.94 (br,1H,NH);^{13}C NMR (125 MHz,DMSO-d_6) δ:40.1,40.2,81.1,93.9,104.2~104.7 (m),109.1,112.0~112.2 (m),121.0 (d,J=13.8 Hz),123.6,124.9,129.8~130.0 (m),131.2,134.3,136.0,147.9,154.2,158.8 (dd,J=61.3,12.5 Hz),160.8 (dd,J=62.5,12.5 Hz),161.1~161.3 (m),163.1~163.2 (m),195.6;HRMS (TOF ES$^+$) m/z:$C_{25}H_{17}F_4N_3NaO_5$[M+Na]$^+$,计算值538.099 7,实测值538.099 7.

(3a*S*,8b*S*)-1-(2,4-二氯苄基)-2-((2,4-二氯苄基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3f) 白色固体,m.p.192.1~194.1 ℃;IR (KBr) ν:3 435,3 058,2 970,1 734,1 619,1 562,1 469,1 449,1 407,1 387,1 344,1 307,1 258,1 221,1 175,1 110,1 045,970,932,866,828,771,724 cm^{-1};^{1}H NMR (600 MHz,DMSO-d_6) δ:4.36~4.46 (m,2H,CH_2),5.00~5.13 (m,2H,CH_2),6.65 (br,1H,OH),6.85 (d,J=8.3 Hz,1H,ArH),7.14 (d,J=8.2 Hz,1H,ArH),7.23 (d,J=8.0 Hz,1H,ArH),7.35 (d,J=8.3 Hz,1H,ArH),7.55~7.60 (m,2H,ArH),7.63~7.66 (m,2H,ArH),7.71~7.79 (m,3H,ArH+OH),10.06 (br,1H,NH);^{13}C NMR (150 MHz,DMSO-d_6) δ:43.6,44.0,81.1,94.1,108.8,123.8,125.0,127.9,128.0,129.3,129.3,129.4,129.8,131.4,132.0,132.5,133.4,133.4,134.0,134.2,134.4,136.1,147.7,154.4,195.5;HRMS (TOF ES$^+$) m/z:$C_{25}H_{17}Cl_4N_3NaO_5$[M+Na]$^+$,计算值601.981 5,实测值601.981 5.

(3a*S*,8b*S*)-1-(呋喃-2-基甲基)-2-((呋喃-2-基甲基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3g) 白色固体,m.p.197.3~199.3 ℃;IR (KBr) ν:3 415,3 126,1 719,1 618,1 544,1 500,1 427,1 338,1 289,1 246,1 209,1 149,1 089,1 030,1 010,990,937,925,830,788,760,746 cm^{-1};^{1}H NMR (600 MHz,DMSO-d_6) δ:4.69~4.77 (m,2H,CH_2),5.11~5.24 (m,2H,CH_2),6.25 (d,J=3.1 Hz,1H,ArH),6.36~6.37 (m,1H,ArH),6.51 (d,J=3.0 Hz,1H,ArH),6.55 (t,J=4.9 Hz,1H,ArH),6.59 (br,1H,OH),7.25 (d,J=7.7 Hz,1H,ArH),7.41 (br,1H,OH),7.54 (d,J=0.9 Hz,1H,ArH),7.58 (t,J=7.4 Hz,1H,ArH),7.66~7.71 (m,2H,ArH),7.74 (d,J=0.7 Hz,1H,ArH),9.89 (br,1H,NH);^{13}C NMR (150 MHz,DMSO-d_6) δ:40.3,40.4,81.3,94.1,108.5,109.1,109.3,111.1,111.5,123.5,125.1,131.2,134.3,136.0,143.5,143.7,147.9,150.4,150.5,154.8,195.6;HRMS (TOF ES$^+$) m/z:$C_{21}H_{17}N_3NaO_7$[M+Na]$^+$,计算值449.095 9,实测值449.096 0.

(3a*S*,8b*S*)-1-苯乙基-2-(苯乙基氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3h) 白色固体,m.p.195.6~197.6 ℃;IR (KBr) ν:3 425,3 200,1 724,1 621,1 569,1 478,1 407,1 344,1 289,1 237,1 211,1 182,1 146,1 090,1 030,973,875,844,784,766,745,703 cm^{-1};^{1}H NMR (600 MHz,DMSO-d_6) δ:2.73~2.85 (m,2H,CH_2),2.88~3.14 (m,2H,CH_2),3.73~3.82 (m,2H,CH_2),3.89~4.22 (m,2H,CH_2),6.54 (br,1H,OH),7.05 (d,J=6.8 Hz,2H,ArH),7.12~7.18 (m,3H,ArH),7.27~7.30 (m,1H,ArH),7.34~7.38 (m,5H,ArH+OH),7.62 (t,J=7.4 Hz,1H,ArH),7.73 (d,J=7.6 Hz,1H,ArH),7.79 (t,J=7.5 Hz,1H,ArH),7.88 (d,J=7.8 Hz,1H,ArH),9.57 (br,1H,NH);^{13}C NMR (150 MHz,DMSO-d_6) δ:35.7,36.2,44.4,45.0,81.1,94.0,108.7,123.6,

124.9, 127.0, 127.2, 128.8, 129.1, 129.1, 129.3, 131.2, 134.3, 136.3, 138.1, 138.4, 148.4, 154.1, 195.8; HRMS (TOF ES$^+$) *m/z*: $C_{27}H_{25}N_3NaO_5$ [M+Na]$^+$,计算值 494.168 6,实测值 494.169 0.

(3a*S*,8b*S*)-1-(4-甲基苯乙基)-2-((4-甲基苯乙基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3i) 白色固体, m.p. 184.1 ~ 186.1 ℃; IR (KBr) ν: 3 524, 3 423, 1 739, 1 625, 1 555, 1 514, 1 437, 1 398, 1 369, 1 347, 1 263, 1 201, 1 176, 1 158, 1 129, 1 096, 996, 958, 887, 852, 810, 774, 641 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.21 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 2.68 ~ 2.79 (m, 2H, CH_2), 2.83 ~ 3.08 (m, 2H, CH_2), 3.70 ~ 3.77 (m, 2H, CH_2), 3.86 ~ 4.18 (m, 2H, CH_2), 6.54 (br, 1H, OH), 6.93 (d, *J* = 7.9 Hz, 2H, ArH), 6.98 (d, *J* = 7.9 Hz, 2H, ArH), 7.17 (d, *J* = 7.8 Hz, 2H, ArH), 7.23 (d, *J* = 7.9 Hz, 2H, ArH), 7.35 (br, 1H, OH), 7.62 (t, *J* = 7.4 Hz, 1H, ArH), 7.73 (d, *J* = 7.6 Hz, 1H, ArH), 7.78 (t, *J* = 7.5 Hz, 1H, ArH), 7.88 (d, *J* = 7.8 Hz, 1H, ArH), 9.56 (br, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 21.1, 21.2, 35.3, 35.9, 44.5, 45.1, 81.1, 94.0, 108.7, 123.6, 124.8, 129.0, 129.1, 129.3, 129.4, 129.7, 131.1, 134.3, 134.9, 135.2, 136.0, 136.2, 148.4, 154.2, 195.8; HRMS (TOF ES$^+$) *m/z*: $C_{29}H_{29}N_3NaO_5$ [M+Na]$^+$,计算值 522.199 9,实测值 522.200 1.

(3a*S*,8b*S*)-1-(4-氟苯乙基)-2-((4-氟苯乙基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3j) 白色固体, m.p. 147.2 ~ 149.2 ℃; IR (KBr) ν: 3 388, 1 731, 1 608, 1 549, 1 509, 1 402, 1 363, 1 283, 1 220, 1 184, 1 156, 1 108, 985, 967, 928, 880, 832, 765, 642 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.72 ~ 2.83 (m, 2H, CH_2), 2.90 ~ 3.11 (m, 2H, CH_2), 3.74 ~ 3.77 (m, 2H, CH_2), 3.88 ~ 4.18 (m, 2H, CH_2), 6.57 (br, 1H, OH), 6.94 ~ 6.95 (m, 2H, ArH), 7.04 ~ 7.05 (m, 2H, ArH), 7.19 ~ 7.20 (m, 2H, ArH), 7.35 ~ 7.40 (m, 3H, ArH+OH), 7.62 ~ 7.63 (m, 1H, ArH), 7.71 ~ 7.79 (m, 2H, ArH), 7.87 ~ 7.88 (m, 1H, ArH), 9.52 (br, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 34.8, 35.2, 44.4, 44.9, 81.1, 94.0, 108.7, 115.5 (d, *J* = 21.0 Hz), 115.8 (d, *J* = 21.0 Hz), 123.6, 124.8, 130.9 (d, *J* = 7.5 Hz), 131.2 (d, *J* = 7.5 Hz), 134.2 (d, *J* = 12.0 Hz), 134.5, 136.2, 148.3, 154.2, 160.7 (d, *J* = 33.0 Hz), 162.3 (d, *J* = 33.0 Hz), 195.8; HRMS (TOF ES$^+$) *m/z*: $C_{27}H_{23}F_2N_3NaO_5$ [M+Na]$^+$,计算值 530.149 8,实测值530.149 9.

(3a*S*,8b*S*)-1-(3-氯苯乙基)-2-((3-氯苯乙基)氨基)-3a,8b-二羟基-3-硝基-3a,8b-二氢茚并[1,2-*b*]吡咯-4-(1*H*)-酮 (3k) 白色固体, m.p.164.8 ~ 166.8 ℃; IR (KBr) ν: 3 422, 1 728, 1 627, 1 598, 1 569, 1 505, 1 476, 1 428, 1 393, 1 362, 1 317, 1 280, 1 244, 1 224, 1 153, 1 087, 1 034, 987, 869, 842, 777, 765 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ: 2.73 ~ 2.87 (m, 2H, CH_2), 2.92 ~ 3.12 (m, 2H, CH_2), 3.73 ~ 3.81 (m, 2H, CH_2), 3.91 ~ 4.23 (m, 2H, CH_2), 6.55 (br, 1H, OH), 6.96 (d, *J* = 7.0 Hz, 1H, ArH), 7.13 ~ 7.17 (m, 3H, ArH), 7.33 ~ 7.40 (m, 4H, ArH+OH), 7.46 (s, 1H, ArH), 7.62 (t, *J* = 7.4 Hz, 1H, ArH), 7.72 (d, *J* = 7.6 Hz, 1H, ArH), 7.78 (t, *J* = 7.4 Hz, 1H, ArH), 7.89 (d, *J* = 7.8 Hz, 1H, ArH), 9.51 (br, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6) δ: 35.2, 35.6, 44.0, 44.7, 81.2, 94.0, 108.8, 123.6, 124.8, 127.0, 127.2, 127.8, 128.1, 129.0, 129.1, 130.5, 130.9, 131.2, 133.5, 133.7, 134.3, 136.2, 140.7, 140.9, 148.3, 154.1, 195.7; HRMS (TOF ES$^+$) *m/z*: $C_{27}H_{23}Cl_2N_3NaO_5$ [M+Na]$^+$,计算值 562.090 7,实测值 562.090 8.

参考文献:

[1] 李衍忠,赵萍,詹晓平,等.新型吡咯类氨基酸缀合物的合成与抗肿瘤活性测定[J].有机化学,2015,35(1):167-174.
LI Y Z, ZHAO P, ZHAN X P, et al. Synthesis and cytotoxic activities of novel amino acid-conjugates of pyrrole derivatives [J]. Chinese Journal of Organic Chemistry, 2015, 35(1): 167-174.

[2] 赵凯,王帅,詹晓平,等.4-(甲氧基噻吩基)-3-(取代苯甲酰基)-吡咯类化合物的合成与抗肿瘤活性研究[[J].有机化学,2017,37(4):943-953.
ZHAO K, WANG S, ZHAN X P, et al. Synthesis and anti-tumor activity of 4-(Methoxyl thienyl)-3-(substituted benzoyl) pyrroles [J]. Chinese Journal of Organic Chemistry, 2017, 37(4): 943-953.

[3] REGUEIRO-REN A, XUE Q M, SWIDORSKI J J, et al. Inhibitors of human immunodeficiency virus type 1 (HIV

-1) attachment.12.Structure-activity relationships associated with 4-fluoro-6-azaindole derivatives leading to the identification of 1-(4-benzoylpiperazin-1-yl)-2-(4-fluoro-7-[1,2,3]triazol-1-yl-1h-py[J].Journal of Medicinal Chemistry,2013,56(4):1 656-1 669.

[4] EL-GABY M S A,GABER A M,ATALLA A A,et al. Novel synthesis and antifungal activity of pyrrole and pyrrolo[2,3-d]pyrimidine derivatives containing sulfonamido moieties[J].Il Farmaco,2002,57(8):613-617.

[5] TRZOSS M,BENSEN D C,LI X,et al.Pyrrolopyrimidine inhibitors of DNA gyrase B (GyrB) and topoisomerase IV (ParE),Part II:development of inhibitors with broad spectrum, Gram - negative antibacterial activity [J]. Bioorganic & Medicinal Chemistry Letters, 2013, 23 (5):1 537-1 543.

[6] ESTEVEZ V,VILLACAMPA M,MENENDEZ J C.Multicomponent reactions for the synthesis of pyrroles[J]. Chemical Society Reviews,2010,39(11):4 402-4 421.

[7] 郑品官,朱洪友,杨宗璐,等.α-(2,5-二甲基-3,4-二乙酰基吡咯基)萘的合成和晶体结构[J].云南大学学报:自然科学版,2002,24(5):370-374.
ZHENG P,ZHU H Y,YANG Z L,et al.Synthesis and crystal structure of α-(2,5-dimethyl -3,4-diacetyl -pyrry l) naphthaline[J].Journal of Yunnan University: Natural Sciences Edition,2002,24(5):370-374.

[8] MOHIL R,KUMAR D,MOR S.Synthesis and antimicrobial activity of some 1,3-Disubstituted Indeno[1,2c]pyrazoles[J].Journal of Heterocyclic Chemistry,2014, 51(1):203-211.

[9] 陈兴,夏沙,王少杰,等.新型二氢化茚-咪唑衍生物的合成及生物活性研究 [J].云南大学学报:自然科学版,2015,37(3):422-428.
CHEN X,XIA S,WANG S J,et al.Synthesis and biological activities of novel indane-imidazole derivatives[J]. Journal of Yunnan University:Natural Sciences Edition, 2015,37(3):422-428.

[10] LOBO G,MONASTERIOS M,RODRIGUES J,et al. Synthesis,crystal structure and effect of indeno[1,2-*b*] indole derivatives on prostate cancer in vitro.Potential effect against MMP-9[J]. European Journal of Medicinal Chemistry,2015,96:281-295.

[11] FINKIELSZTEIN L M,CASTRO E F,FABIAN L E,et al.New 1-indanone thiosemicarbazone derivatives active against BVDV[J]. European Journal of Medicinal Chemistry,2008,43(8):1 767-1773.

[12] CHEN N,MENG X,ZHU F,et al. Tetrahydroindeno [1′,2′:4,5] pyrrolo [1,2-a] imidazol-5(1*H*)-ones as novel neonicotinoid insecticides:Reaction selectivity and substituent effects on the activity level [J]. Journal of Agricultural and Food Chemistry, 2015,63(5):1 360-1 369.

[13] 段义杰,刘建利,王翠玲,等.茚酮类化合物的研究进展[J].有机化学,2010,30(7):988-996.
DUAN Y J,LIU J L,WANG C L,et al.Progress in the studies of indanones[J]. Chinese Journal of Organic Chemistry,2010,30(7):988-996.

[14] 郝晓盼,姜秀阳,林军,等.1,3-二氮杂环并[1,2-c]-1,2,3-三唑的简便合成[J].云南大学学报:自然科学版,2015,37(5):766-769.
HAO X P,JIANG X Y,LIN J,et al.convenient synthesis of 5,6-dihydro-4H-imidazo[1,2-c]-[1,2,3] triazoles[J].Journal of Yunnan University:Natural Sciences Edition,2015,37(5):766-769.

[15] 孔令斌,杨瑞霞,杜璇璇,等.双环吡咯酮类化合物的简便合成[J].有机化学,2016,36(10):2437-2441.
KONG L B,YANG R X,DU X X,et al.Simple synthesis of bicyclic pyrrole ketone compounds[J]. Chinese Journal of Organic Chemistry,2016,36(10):2 437-2 441.

[16] 陈亮,王保取,赵宇澄,等.一锅法合成多取代色酮并双环吡啶类化合物[J].有机化学,2017,37(6):1433-1442.
CHRN L,WANG B Q,ZHAO Y C,et al.One-pot synthesis of multisubstituted chromone-fused bicyclic pyridine compounds[J].Chinese Journal of Organic Chemistry,2017,37(6):1 433-1 442.

[17] YU F C,LIN X R,LIU Z C,et al.Beyond the antagonism: self-labeled xanthone inhibitors as modeled "Two-in-One" drugs in cancer therapy[J].ACS Omega,2017,2(3):873-889.

[18] 赵宇澄,肖强,王保取,等.亚胺基吡咯酮类化合物的合成[J].有机化学,2017,37(10):2 690-2 696.DOI:10.6023/cjoc201705004.
ZHAO Y C,XIAO Q,WANG B Q,et al.Synthesis of iminopyrrolone compounds[J].Chinese Journal of Organic Chemistry,2017,37(10):2 690-2 696.DOI:10.6023/cjoc201705004.

[19] LIU X M,LIN X R,YAN S J,et al.Environmentally friendly approach to convergent synthesis of highly functionalized indanone fused multicyclic pyrrolines [J].Tetrahedron,2016,72:5 314-5 322.

[20] FAN Y,LIU S,CHEN N,et al.Oxidation strategy for the synthesis of regioisomeric spiroisobenzofuranopyrroles:facile entries to spiro[isobenzofuran-1,2′-pyrrole] and spiro[isobenzofuran-1,3′-pyrrole] derivatives[J].Synlett,2015,26:393-403.

Synthesis of indeno[1,2-*b*]pyrrol-4(1*H*)-one compounds

LUO Da-yun, YANG Chang-long, ZI Quan-xing, LIN Jun, YAN Sheng-jiao
(Key Laboratory of Medicinal Chemistry for Natural Resource (Ministry of Education),
School of Chemical Science and Technology, Yunnan University, Kunming, 650091, China)

Abstract: An efficient synthetic protocol for indeno[1,2-*b*]pyrrol-4(1*H*)-one (3) had been developed. The methods used N,N′-dialkyl-2-nitroethene-1,1-diamines (1) and ninhydrin hydrate (2) as raw materials, which was heated at 50 ℃ in ethanol medium and gave the target compounds 3a—3k with excellent yields (92%—98%). This protocol possessed some advantages including simple operation, mild reaction conditions and excellent yields and so on.

Key words: indeno[1,2-*b*]pyrrol-4(1*H*)-one; ninhydrin; 1,1-enediamines; synthesis