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3-(4-苯基-1,3-二硫戊环-2-亚甲基)-2,4-戊二酮的合成及其与芳醛的缩合反应

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摘要: 以碳酸钾为碱,以 N,N-二甲基甲酰胺为溶剂,乙酰丙酮与二硫化碳及 1,2-二溴苯乙烷反应,以中等产率(47%)合成了 3-(4-苯基-1,3-二硫戊环-2-亚甲基)-2,4-戊二酮 2. 碱性条件下,化合物 2 比较稳定,通过对碱的选择和芳醛量的控制,化合物 2 与芳醛缩合可分别以较高的产率合成单面和双面缩合产物 1d 和 1e.

关键词: 3-(4-苯基-1,3-二硫戊环-2-亚甲基)-2,4-戊二酮; 芳醛; 缩合反应
中图分类号: O626 **文献标识码**: A

Study of synthesis of 3-(4-phenyl-1,3-dithiolan-2-ylidene) pentane-2,4-dione and its condensation reaction with arylaldehydes

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Abstract: 3-(4-Phenyl-1,3-dithiolan-2-ylidene) pentane-2,4-dione (2) was prepared in moderate (47%) yield by the reaction of acetylacetone with carbon disulfide and 1-(1,2-dibromoethyl) benzene using potassium carbonate as base. Under the optimized conditions, the condensation of compound 2 with arylaldehydes led to the corresponding products α-acetyl-α′ cinnamoyl ketene dithioacetals 1d and α,α′-dicinnamoyl ketene dithioacetals 1e, respectively, in high to excellent yields.

Key words: 3-(4-phenyl-1,3-dithiolan-2-ylidene) pentane-2,4-dione; arylaldehydes; condensation reaction

0 引 言

由 α-乙酰基二硫缩烯酮与芳醛缩合所得的 α-肉桂酰基二硫缩烯酮(1)(见图 1)是一类

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重要有机合成中间体,可用于合成多种具有重要意义的化合物.烷硫基的多样性赋予了这类化合物反应的多样性,即烷硫基结构的不同反应结果也不同.例如,烷硫基为环状结构的 α-肉桂酰基二硫缩烯酮(1a)可合成 2,3-二氢-4*H*-硫代吡喃-4-酮[3]、双环[3.2.0]庚烷-2,4-二酮[4]和特窗酸衍生物[5];烷硫基为开链结构的 α-肉桂酰基二硫缩烯酮(1b)经[5+1]环合可构建多取代酚[6]及含氮[7,8]、硫[9]等六员杂环化合物;烷硫基为环烯结构的 α-肉桂酰基二硫缩烯酮(1c)与二胺双亲核体发生多米诺类型反应,合成多杂环化合物[10].

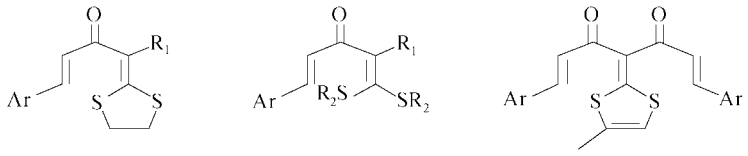


图 1 化合物 1 的结构

Fig. 1 Structure of compounds 1

为进一步拓展 α-肉桂酰基二硫缩烯酮类化合物在有机合成中的应用,本文进行了 3-(4-苯基-1,3-二硫戊环-2-亚甲基)-2,4-戊二酮 2 的合成及其与芳醛的缩合反应研究.已有研究工作表明,碱性条件下烷硫基为环状结构的 α,α′-二乙酰基二硫缩烯酮与芳醛缩合常得到双面缩合产物[4,11,12];烷硫基为开链结构的 α,α′-二乙酰基二苄硫缩烯酮与芳醛反应则易得到单面缩合脱乙酰基的产物[13].然而,实验表明,化合物 2 是容易制备的,碱性条件下它比较稳定,不易脱去乙酰基,通过控制碱和芳醛的量,与芳醛缩合可分别以较高的产率合成单面和双面缩合产物 1d 和 1e.本文详细报道此研究结果,反应式如图 2 所示.

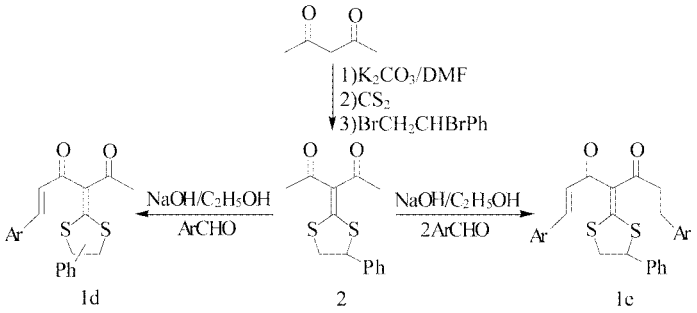


图 2 合成路线

Fig. 2 Synthesis route

注:1da Ar = 4-N(CH$_3$)$_2$C$_6$H$_4$; 1db Ar = CH$_2$O$_2$C$_6$H$_3$; 1dc Ar = C$_6$H$_5$; 1dd Ar = 4-CH$_3$OC$_6$H$_4$; 1de Ar = 4-ClC$_6$H$_4$; 1ea Ar = 4-N(CH$_3$)$_2$C$_6$H$_4$; 1eb Ar = CH$_2$O$_2$C$_6$H$_3$; 1ec Ar = C$_6$H$_5$; 1ed Ar = 4-CH$_3$OC$_6$H$_4$; 1ee Ar = 3-CH$_3$OC$_6$H$_4$; 1ef Ar = 4-CH$_3$C$_6$H$_4$; 1eg Ar = 4-FC$_6$H$_4$; 1eh Ar = 3-NO$_2$C$_6$H$_4$; 1ei Ar = Furyl

1 实验部分

1.1 仪器与试剂

Magna-560 显微红外光谱仪(KBr 压片法);Unity-400 核磁共振仪($CDCl_3$ 溶剂,TMS 为内标);PE-2400 自动元素分析仪;熔点用微量法测定(温度计未经校正);所用试剂均为市售分析纯.

1.2 3-(4-苯基-1,3-二硫戊环-2-亚甲基)-2,4-戊二酮(2)的合成[14]

向盛有 DMF(20.0 mL)的 50 mL 三颈瓶中加入无水碳酸钾(5.5 g,40.0 mmol)、乙酰丙酮(2.1 mL,20.0 mmol)后，常温下搅拌0.5 h. 冰水浴冷却下一次性加入 CS_2 1.33 mL (22.0 mmol)后继续搅拌 1 h. 然后向三颈瓶中滴加 1,2-二溴苯乙烷(5.8 g,22.0 mmol)的 DMF 溶液. 常温搅拌 14 h，TLC 监测至底物消失. 将反应液倒入盛有冰水的烧杯中，搅拌至析出黄色沉淀，抽滤，用乙醇洗涤滤饼，晾干后得纯净的化合物(2)2.6 g，产率 47%.

1.3　化合物 2 与芳醛的缩合反应

以化合物 1eb 的合成为例. 在 50 mL 三颈瓶中加入底物(2)(556.0 mg,2.0 mmol)，胡椒醛(600.5 mg,4.0 mmol)和 25 mL95%的乙醇，搅拌使其溶解，0.5 h 后，冰水浴冷却下滴加 EtONa 的乙醇溶液4.0 mL (c = 1 mol · L^{-1}). 常温搅拌，TLC 监测至底物消失(约 6 h). 将反应液倾入水中、搅拌，析出黄色固体. 抽滤、用乙醇洗涤滤饼，晾干后得黄色固体(1eb)0.9 g，产率 83%. 在制备化合物 1d 时，加入等摩尔的醛，用 NaOH 作碱，其它方法同上. 化合物 1d、1e 和 2 的实验结果及波谱数据分别如表 1 和表 2 所示.

表 1　化合物 1d、1e 和 2 的实验结果

Tab. 1　Experimental results of compound 1d, 1e and 2

Compd.	appearance	m. p/℃	yield/%	elemental analysis/%
2	Yellow crystal	79-80	47	C 60.27 (60.40), H 5.14 (5.07)
1da	Yellow crystal	188-190	76	C 67.33 (67.45), H 5.70 (5.66)
1db	Yellow crystal	134-136	84	C 64.47 (64.37), H 4.39 (4.42)
1dc	Yellow crystal	118-120	80	C 68.90 (68.82), H 4.90 (4.95)
1dd	Yellow crystal	91-93	78	C 66.53 (66.64), H 5.03 (5.08)
1de	Yellow crystal	142-144	86	C 63.00 (62.91), H 4.22 (4.27)
1ca	Yellowish crystal	165-167	83	C 70.97 (71.08), H 5.88 (5.96)
1cb	Yellowish crystal	200-202	83	C 66.51 (66.40), H 4.05 (4.09)
1cc	Yellow crystal	212-214	70	C 74.05 (73.98), H 4.82 (4.88)
1cd	Yellow crystal	215-217	90	C 70.15 (70.01), H 5.01 (5.09)
1ce	Yellow crystal	146-148	73	C 69.89 (70.01), H 5.14 (5.09)
1cf	Yellow crystal	178-179	83	C 74.53 (74.65), H 5.52 (5.43)
1cg	Yellowish crystal	206-208	81	C 68.45 (68.55), H 4.15 (4.11)
1ch	Yellowish crystal	154-156	54	C 61.85 (61.75), H 3.65 (3.70)
1ei	Yellow crystal	188-200	90	C 66.49 (66.34), H 4.09 (4.18)

注：括号内为理论值.

表 2　化合物 1d、1e 和 2 的波谱数据

Tab. 2　^{1}H NMR and IR data for compound 1d, 1c and 2

Compd.	υ(IR)/cm^{-1}	^{1}H NMR: δ, J
2	1 647, 1 607, 1 490, 1 442, 1 383, 1 229, 971, 880	2.44 (3H, s, CH_3), 2.46 (3H, s, CH_3), 3.52 (2H, m, SCH_2), 4.92 (1H, m, SCH), 7.35 - 7.46 (5H, m, ArH)
1da	1 582, 1 524, 1 450, 1 369, 1 267, 1 058, 983, 813	2.31 (1.5H, s, CH_3), 2.32 (1.5H, s, CH_3), 3.05 (3H, s, NCH_3), 3.07 (3H, s, NCH_3), 3.49 - 3.51 (2H, m, SCH_2), 4.93 - 4.95 (1H, m, SCH), 6.66 - 6.69 (2H, m, ArH), 6.74 (1H, m, = - H), 7.35 - 7.37 (2H, m, ArH), 7.42 - 7.49 (5H, m, ArH), 7.55 (1H, m, = - H)
1db	1 623, 1 583, 1 524, 1 449, 1 369, 974, 776, 712	2.33 (1.5H, s, CH_3), 2.34 (1.5H, s, CH_3), 3.55 - 3.57 (2H, m, SCH_2), 4.94 - 4.95 (1H, m, SCH), 6.02 (1H, s, OCH_2O), 6.03 (1H, s, OCH_2O), 6.80 (1H, m, = - H), 6.82 - 6.84 (1H, m, ArH), 7.04 - 7.09 (2H, m, ArH), 7.33 - 7.46 (5H, m, ArH), 7.51 (1H, m, = - H)

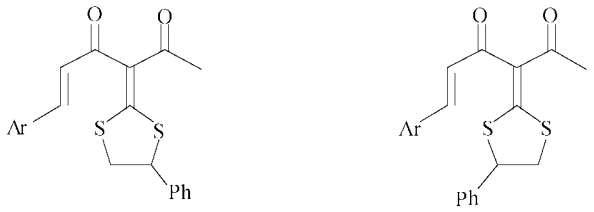
续表 2

Compd.	ν(IR)/cm^{-1}	^{1}H NMR:δ,J
1dc	1 627, 1 566,1 516, 1 497,1 449,1 333,1 276, 975, 769,690	2.45 (1.5H, s, CH_3), 2.46 (1.5H, s, CH_3), 3.52 - 3.61 (2H, m, SCH_2), 4.91 - 5.02 (1H, m, SCH), 7.02 - 7.06 (1H, m, = - H), 7.35 - 7.42 (5H, m, ArH), 7.46 - 7.52 (5H, m, ArH), 7.70 - 7.76 (1H, m, = - H)
1dd	1 706, 1 645,1 578, 1 563, 1 539,1 395, 1 248, 1 030,814	2.32 (1.5H, s, CH_3), 2.33 (1.5H, s, CH_3), 3.47 - 3.59 (2H, m, SCH_2), 3.81 (1.5H, s, CH_3), 3.83 (1.5H, s, CH_3), 4.92 - 4.98 (1H, m, SCH), 6.80 - 6.86 (1H, m, = - H), 6.91 - 6.95 (2H, m, ArH), 7.33 - 7.39 (3H, m, ArH), 7.43 - 7.45(1H, m, ArH), 7.52 - 7.53 (1H, m, = - H), 7.54 - 7.59 (3H, m, ArH)
1dc	1 628,1 563,1 513,1 454,1 331, 1 275, 1 090,822,697	2.44 (1.5H, s, CH_3), 2.45 (1.5H, s, CH_3), 3.48 - 3.56 (2H, m, SCH_2), 4.90 - 5.00 (1H, m, SCH), 6.95 - 7.00 (1H, m, = - H), 7.35 - 7.51 (9H, m, ArH), 7.55 - 7.65 (1H, m, = - H)
1ca	1 608, 1 568, 1 523, 1 456,1 369, 1 261, 980,816	2.99 (6H, s, NCH_3), 3.00 (6H, s, NCH_3), 3.55 (2H, m, SCH_2), 4.95 (1H, m, SCH), 6.60 (2H, d, J = 8.8, ArH), 6.61 (2H, d, J = 8.8, ArH), 6.82 (1H, d, J = 15.6, = - H), 6.83 (1H, d, J = 15.6, = - H), 7.36 (2H, d, J = 8.8 Hz, ArH), 7.41 (2H, d, J = 8.8, ArH), 7.41 - 7.48 (5H, m, ArH), 7.67 (1H, d, J = 15.6, = - H),7.91 (1H, d, J = 15.6, = - H)
1eb	1 628, 1 580, 1 489, 1 446, 1 247, 1 037, 977, 929, 812	3.57 (2H, m, SCH_2), 4.98 (1H, m, SCH), 5.97 (2H, s, OCH_2O), 5.98 (2H, s, OCH_2O), 6.78 (1H, d, J = 8.0, ArH), 6.79(1H, d, J = 8.0, ArH), 6.82(1H, d, J = 15.6, = - H), 6.83 (1H, d, J = 15.6, = - H), 7.00 - 7.04 (4H,m,J = 8.0,ArH),7.35 - 7.48(5H, m, ArH), 7.61(1H, d, J = 15.6, = - H), 7.63(1H, d, J = 15.6, = - H)
1ec	1 631, 1 592, 1 449, 1 412, 976, 773, 716	3.60 (2H, m, SCH_2), 4.99 (1H, m, SCH), 7.03 (1H, d, J = 15.6, = - H),7.04 (1H, d, J = 15.6, = - H), 7.32 - 7.52 (15 H, m, ArH), 7.71 (1H,d,J = 15.6, = - H),7.73(1H, d,J = 15.6, = - H)
1cd	1 629, 1 588, 1 510, 1 423, 1 256, 1 172, 981, 829, 772, 699	3.57 (2H, m, SCH_2), 3.80 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 4.97 (1H, m, SCH), 6.85 (2H, d, J = 8.8, ArH), 6.86 (2H, d, J = 8.8, ArH), 6.90(1H, d,J = 15.6, = - H),6.92(1H, d, J = 15.6, = - H), 7.35 - 7.48 (5H, m, ArH), 7.45 - 7.47 (4H, d, J = 8.8, ArH), 7.68 (1H, d, J = 15.6, = - H), 7.70 (1H, d, J = 15.6, = - H)
1cc	1 632, 1 580, 1 452, 1 258, 1 046, 978, 718, 785	3.60 (2H, m, SCH_2), 3.70 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 4.99 (1H, m, SCH), 6.89 (2H, d, J = 8.0, ArH), 6.99 (2H, s, ArH), 7.00 (1H,d,J = 15.6, = - H),7.04 (1H, d, J = 15.6, = - H), 7.10 (1H, d,J = 6.4 Hz,ArH),7.11(1H, d, J = 6.4, ArH), 7.23 (1H, d, J = 8.0, ArH), 7.24 (1H, d, J = 8.0, ArH),7.35 - 7.49(5H,m,ArH),7.67(1H,d,J = 15.6, = - H),7.68 (1H, d, J = 15.6, = - H)
1ef	3 025, 1 631, 1 589, 1 451, 1 328, 1 298, 980, 813	2.34 (3H, s, CH_3), 2.35 (3H, s, CH_3), 3.58 (2H, m, SCH_2), 4.98 (1H, m, SCH), 6.99 (1H, d, J = 15.6, = - H), 7.00 (1H, d, J = 15.6, = - H), 7.13 (2H, d, J = 7.6, ArH), 7.14 (2H, d, J = 7.6, ArH), 7.36 (2H, d, J = 7.6, ArH), 7.41 (2H, d, J = 7.6, ArH), 7.39 - 7.49 (5H, m, ArH), 7.69(1H, d, J = 15.6, = - H), 7.71 (1H, d, J = 15.6, = - H)
1eg	1 630, 1 586, 1 508, 1 415, 1 231, 1 159, 979, 831, 729, 784	3.60 (2H, m, SCH_2), 4.99 (1H, m, SCH), 6.92 (1H, d,J = 15.6, = - H),6.95 (1H,d, J = 15.6, = - H), 7.02 (2H, t, J = 8.4, ArH), 7.03(2H,t,J = 8.4, ArH), 7.36 - 7.52 (5H, m, ArH), 7.48 (2H, d, J = 8.4, ArH), 7.49 (2H, d, J = 8.4, ArH), 7.67 (1H, d, J = 15.6, = - H), 7.68 (1H, d, J = 15.6, = - H)
1eh	1 636, 1 595, 1 452, 1 242, 1 122, 881	3.64 (2H, m, SCH_2), 5.03 (1H, m, SCH),7.12 (1H, d, J = 15.6, = - H),7.15 (1H, d,J = 15.6, = - H),7.38 - 7.50 (5H, m, ArH), 7.54 (1H, t, J = 8.0, ArH), 7.56 (1H, t, J = 8.0, ArH), 7.74 (1H, d, J = 15.6, = - H), 7.75(1H, d, J = 15.6, = - H), 7.80 (1H, d, J = 8.0, ArH), 7.81 (1H, d, J = 8.0, ArH), 8.19 (2H, d, J = 8.0, ArH), 8.32 (1H, s, ArH), 8.34 (1H, s, ArH)
1ei	1 633, 1 589, 1 455, 1 281, 1 017, 969, 748, 699	3.57 (2H, m, SCH_2),4.98 (1H, m, SCH), 6.46 (1H, t, J = 1.6, J = 3.6, Furanyl - H), 6.47 (1H, t, J = 1.6, J = 3.6, Furanyl - H), 6.66 (1H, d, J = 3.6, Furanyl - H) , 6.67 (1H, d, J = 3.6, Furanyl - H), 6.86 (1H, d, J = 15.6, = - H), 6.89 (1H, d, J = 15.6, = - H), 7.35 - 7.49 (5H, m, ArH), 7.46(1H, d, J = 15.6, = - H), 7.47 (1H ,d, J = 15.6, = - H), 7.48 (1H, d, J = 1.6, Furanyl - H),7.49 (1H, d, J = 1.6, Furanyl - H)

2　结果与讨论

3-(4-苯基-1，3-二硫戊环-2-亚甲基)-2，4-戊二酮(2)的烷硫基为环状结构且具有苄硫基的结构特征[14]，在碱性条件下与芳醛的缩合反应中，未发现脱乙酰基的产物及单面缩合脱乙酰基的产物生成[12-14]，这充分表明化合物 2 主要体现出了烷硫基为环状结构的 α,α'-二乙酰基二硫缩烯酮的性质，碱性条件下比较稳定. 在实验中，通过对所用碱的选择和反应物量的控制，分别成功地实现单面缩合产物 1d 和双面缩合产物 1e 的合成. 当用 NaOH 作碱，化合物 2、芳醛和碱的摩尔比等于 1∶1∶2 时，高产率得到的单面缩合产物 1d，通过 TLC 检测，没观察到有双面缩合产物 1e 生成；当用 EtONa 作碱，化合物 2、芳醛和碱的摩尔比等于 1∶2∶4 时，高产率生成双面缩合的产物 1e.

另外，1d 的 ^{1}H NMR 谱图上显示，乙酰基中-CH_3 的三个 H 在相应的 δ(ppm)出现的是面积几乎相等的两个单峰，这说明 1d 是顺反异构体 1d′和 1d″的混合物(见图 3)，摩尔比大约是 1∶1. 它们的极性几乎一致，用柱层析法很难分离. 有关化合物 1d 和 1e 在合成中的应用研究正在进行中，结果将另文发表.



1d′　　1d″

图 3　化合物 1d′和 1d″的结构式

Fig. 3　Structural formula of 1d′ and 1d″

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