Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis of some new Spiro(Pyran-4,2′- Oxazolidine) and Pyridoxazolidine Derivatives

A. M. Soliman [a]

[a] Chemistry department, Faculty of Science, Sohag, Egypt

Version of record first published: 04 Dec 2007.

To cite this article: A. M. Soliman (2000): Synthesis of some new Spiro(Pyran-4,2′-Oxazolidine) and Pyridoxazolidine Derivatives, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 30:7, 1269-1279

To link to this article: http://dx.doi.org/10.1080/00397910008087148

SYNTHETIC COMMUNICATIONS, 30(7), 1269–1279 (2000)

SYNTHESIS OF SOME NEW SPIRO(PYRAN-4,2'- OXAZOLIDINE) AND PYRIDOXAZOLIDINE DERIVATIVES

A.M.Soliman

Chemistry department, Faculty of Science, Sohag, Egypt.

Abstract: Ketene S,S-acetal 2 reacts with aminoethanol to afford 2-(1-acetal -2-oxo propylidine)oxazolidine 3 which was allowed to react with some active methylene compounds having an α– cyano or α–keto group to give spiro(pyran -4,2'-oxazolidine) derivatives 5-11. Compound 3 reacted with some α, β -unsaturated nitriles to afford the corresponding pyridoxazolidine derivatives 12a-h through a nucleophilic addition and cyclization.

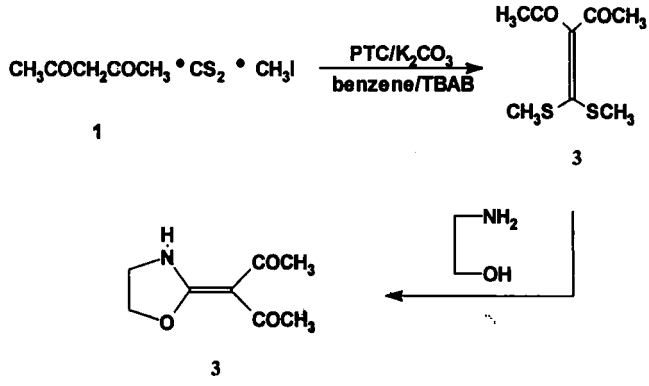
Introduction

Heterocyclic ketene N,N-[1-7] or N,S-acetals[3,8-12] are versatile starting materials for the senthesis of a wide variety of fused heterocycles. In an extention of our recent studies[13-20] on the application of cyano ketene or ketoketene S,S-acetals in heterocyclic synthesis using phase transfer catalysis conditions, we report here the synthesis of some new spiro heterocycles starting with heterocyclic ketene N,O- acetal[21-23] 3.

Results and discussion

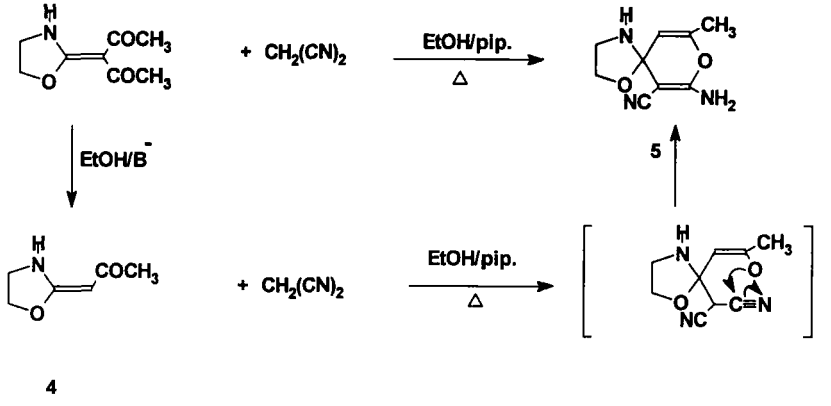
Compound 3 was prepared starting with 2-[di(methylthio)methylene] pentan- 2,4-dione 2[15] which was obtained via reaction of acetylacetone, CS_2 and two moles of methyl iodide in a one-pot reaction using PTC [K_2CO_3/benzene/ tetrabutylammonium bromide TBAB] in almost 100% yield.

Compound 2 then reacted with 2-aminoethanol in refluxing absolute ethanol for about 24 h to give compound 3 in a good yield(75%). This reaction was assumed to go through a nucleophilic attack of both -OH and $-NH_2$ groups at the ethylenic bond with loss of two moles of methyl mercaptan.



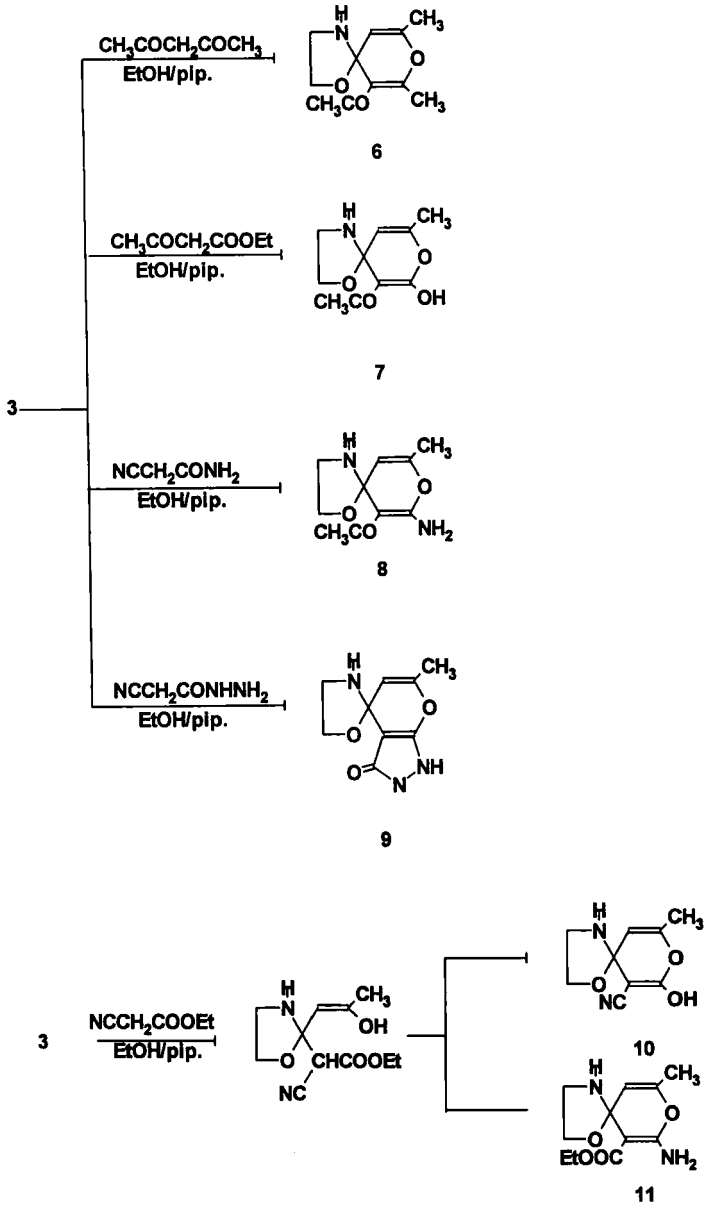
2-(1-Acetyl-2-oxopropylidine)oxazolidine 3 was then allowed to reacted with malononitrile in refluxing ethanol in presence of a piperidine base where spiro (2-amino-3-cyano-6-methylpyran-4,2'-oxazolidine) 5 was precipitated after heating for about 3 h. The proposed mechanism involves a hydrolysis

of one of the two acetyl groups followed by a nucleophilic addition of malononitrile at the ethylenic bond and cyclyzation. A proof of this mechanism was established via a two-step reaction procedure where compound 3 was hydrolysed in boiling ethanol in presence of piperidine or sodium methoxide into the intermediate product 2-(2-oxopropylidine) oxazolidine 4 which was refluxed in boiling ethanol with malononitrile in presence of a catalytic amount of piperidine to afford compound 5.



Scheme 1

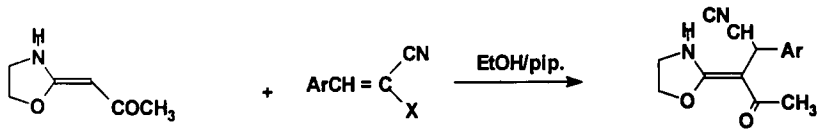
Compound 3 was then treated with a variety of active methylene reagents including acetylacetone, ethylacetoacetate, cyanoacetamide and Cyano-acetohydrazide in refluxing ethanol containing piperidine as a catalyst where in each case the reaction follows the same mechanism described for reaction with malononitrile. The expected spiro heterocycles, namely : spiro (3-acetyl-2,6-dimethylpyran-4,2'-oxazolidine) 6, spiro(3-acetyl-2 hydroxy ,6-methylpyran-4,2'-oxazolidine) 7 ,spiro(2-amino-3-carboxamido-6-



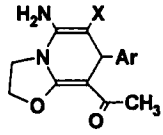
Scheme 2

methylpyran-4,2'-oxazolidine 8 and spiro[6-methyl pyrazolo(3,4-b)pyran-4,2'-oxazolidin- 3(1H,2H)-one] 9, respectively. The reaction of compound 3 with ethylcyanoacetate under the same experimental conditions gave two compounds. The major product, namely, spiro(3-cyano-2-hydroxy-6-methylpyran-4,2'-oxazolidine) 10, (yield 63%) was separated after cooling of the reaction mixture where the minor one spiro(2-amino-3-ethoxycarbonyl-6-methylpyran-4,2'-oxazolidine) 11, (yield 24%) was separated after concentration of the mother liquor. The reaction pathway is thus assumed to involve an intra-molecular nucleophilic attack of the -OH group in the intermediate compound at either the ethoxycarbonyl or the cyano groups to give compounds 10 or 11, respectively.

Compound 3 was also allowed to react with a variety of α , β– unsaturated nitriles including arylidenemalononitriles and arylidene ethyl cyanoacetate



a, Ar = Ph , X = CN
b, = Ph , = COOEt
c, = P.$NO_2C_6H_4$ = CN
d, = P.$NO_2C_6H_4$ = COOEt
e, = P.ClC_6H_4 = CN
f, = P.ClC_6H_4 =COOEt
g, = P.$N(CH_3)_2C_6H_4$ = CN
h, = P.$N(CH_3)_2C_6H_4$ = COOEt



12a-h

Scheme 3

in refluxing ethanol containing piperidine base where the ethylenic -CH hydrogen atom in the formed intermediate 4 was added at the arylidene double bond and cyclization into the corresponding 3H-pyrido(2,1-b)(1,3)oxazolidine derivatives 12a-h.

Experimental

All m.p.s. are uncorrected, IR spectra were obtained (KBr discs) on a Nicolet 710 FT-IR spectrometer. 1H-NMR spectra were optained on a Varian EM 360A at 60 MHz using TMS as an internal standard. The elemental analyses were carried out on an elemental analyzer model 240c.

2-(1-Acetyl-2-oxopropylidine)oxazolidine 3 :

An equimolar mixture of compound 2 and 2-aminoethanol (0.01 mol) was refluxed in 50 mL absolute ethanol for 24 h. On cooling, the precipitate was filtered off and recrystallized from ethanol in colourless needles.

2-(2-Oxopropylidine)oxazolidine 4 :

A mixture of compound 3 (0.01 mol) and piperidine (1 mL) in 50 ml absolute ethanol was refluxed for 1 h, the mixture was concentrated. On cooling, the precipitate was filtered off and recrystallized from ethanol.

Spiro(pyran-4,2'-oxazolidine) 5-11 and 3H-pyrido(2,1-b)(1,3)oxazolidine 12-a-h General Procedure:

Compound 3 (0.01 mol) and piperidine (1 mL) were added to a stirred suspention of the appropriate active methylene reagent (0.01 mol) or the α , β– unsaturated nitrile reagent (0.01 mol) in 50 mL ethanol . The reaction mixture was refluxed for different periods of time (cf,Tables 1) and then allowed to cool .

Table (1) Physical and Analytical Data of The Reported New Compounds.

Prod. No	T hr.	Yield %	M.P. (°C)[a]	Mol.Form. (M.Wt.)[b]	Analysis (Calc./ Found) C%	H%	N%	Cl%
3	24	75	127	$C_8H_{11}O_3N$	56.79	6.55	8.28	
				(169.18)	56.48	6.63	8.55	
4	4	84	92	$C_6H_9O_2N$	56.68	7.14	11.02	
				(127.14)	56.90	7.01	11.37	
5	2	80	168	$C_9H_{11}O_2N_3$	55.95	5.74	21.75	
				(193.20)	55.65	5.60	21.95	
6	3	79	162	$C_{11}H_{15}O_3N$	63.14	7.23	6.69	
				(209.24)	63.35	7.11	6.31	
7	3	73	175	$C_{10}H_{13}O_4N$	56.86	6.20	6.63	
				(211.21)	56.61	6.32	6.87	
8	3	76	191	$C_9H_{13}O_3N_3$	51.18	6.20	19.90	
				(211.21)	51.35	6.30	19.32	
9	4	74	210	$C_9H_{11}O_3N_3$	51.67	5.30	20.08	
				(209.20)	51.55	5.16	20.37	
10	3	61	177	$C_9H_{10}O_3N_2$	55.66	5.19	14.43	
				(194.18)	55.82	5.35	14.01	
11	3	24	158	$C_{11}H_{16}O_4N_2$	54.99	6.71	11.66	
				(240.25)	54.75	6.58	11.91	
12a	3	72	189	$C_{16}H_{16}O_2N_3$	68.31	5.38	14.94	
				(281.30)	68.51	5.25	15.17	
12b	4	69	156	$C_{18}H_{20}O_4N_2$	65.84	6.14	8.53	
				(328.35)	65.60	6.20	8.20	
12c	3	71	205	$C_{16}H_{14}O_4N_4$	58.89	4.32	17.17	
				(326.30)	58.65	4.20	17.40	
12d	4	70	193	$C_{18}H_{19}O_6N_3$	57.90	5.13	11.26	
				(373.35)	58.20	5.01	10.94	
12e	3	66	199	$C_{16}H_{14}O_2N_3Cl$	60.86	4.47	13.31	11.23
				(315.74)	60.61	4.54	13.48	11.51
12f	3	65	178	$C_{18}H_{19}O_4N_2Cl$	59.59	5.28	7.72	9.77
				(362.80)	59.76	5.15	7.99	9.49
12g	4	67	221	$C_{18}H_{20}O_2N_4$	66.65	6.22	17.27	
				(324.37)	66.52	6.09	17.53	
12h	3	63	190	$C_{20}H_{25}O_4N_3$	64.67	6.78	11.31	
				(371.42)	64.92	6.65	11.53	

(continued)

Table (1) IR and 1H-NMR Spectra of The Reported New Compounds. Continued

Prod. No	I.R.(KBr) (Cm^{-1})	^{1}H- NMR (DMSO-d^6)^d
3	3152(NH), 1610,1590, (2C=O), 1515 (C=C).	11.50 (s,1H,NH), 3.10, 3.90, (t,2H each,CH_2CH_2), 2.40(s,6H,CH_3).
4	3155(NH), 1595(C=O), 1520(C=C).	10.50(s,1H,NH), 5.30(s,1H, =CH), 3.80,3.20 (t,2H,each, CH_2CH_2,2.10(s,3H,CH_3).
5	3320,3210,3100(NH, NH_2),2975(CH,aliph.)	9.70(s,1H,NH),6.85-6.70(br,2H,NH_2),5.85(s,1H,=CH), 3.85,3.30(t,2H,each, CH_2 CH_2),2.30(s,3H,CH_3).
6	3160(NH),2970,CH, aliph.), 1640(C=O).	10.10(s,1H,NH),5.95(s,1H,=CH),3.80,3.25(t,2H,each, CH_2CH_2),2.50(s,3H,$COCH_3$), 2.25(s,6H,2CH_3).
7	3450(OH),3150(NH), 2970(CH,aliph.),1630, (C=O),1525(C=C)	10.20(s,1H,NH),9.45(s,1H, OH),6.00(s,1H,=CH), 3.80,3.30 (t,2H each,CH_2CH_2) , 2.55(s,3H,COCH3), 2.20 (s,3H,CH_3).
8	3420,3350,3220(2NH_2) 3160(NH),2975(CH, aliph.), 1670(C=O), 1520(C=C).	10.5(s,1H,NH),6.80-6.65(br, 2H,NH_2),6.10 (s,1H,=CH), 5.90-5.70(br,2H,$CONH_2$), 3.85,3.25 (t,2H,each,CH_2 CH_2), 2.25(s,3H,CH_3).
9	3390,3310,3150(3NH), 2970(CH,aliph.),1680, (C=O),1530(C=C).	10.20(s,1H,NH),8.80(d,2H, 2NH),6.10(s,1H,=CH), 3.80,3.20(t,2H each, CH_2CH_2), 2.20(s,3H,CH_3).
10	3450(OH),3160(NH), 2975 (CH,aliph.),2210(CN), 1535(C=C).	10.25(s,1H,NH),8.75(s,1H, OH),6.10(s,1H,=CH), 3.85,3.30(t,2H each,CH_2CH_2),2.40(s,3H,CH_3).
11	3390,3280,3150(NH, NH_2),2970(CH,aliph.) 1710(C=O),1535(C=C).	9.95(s,1H,NH),6.85(s,2H, NH_2),6.15(s,1H,=CH), 3.85, 3.20(t,2H,each,CH_2CH_2), 3.55-3.35(q,2H,CH_2), 2.35 (s,3H,CH_3),1.30-1.00(t,3H, CH_3 ester).
12a	3385,3270(NH_2),2970 (CH,aliph.),2210(CN), 1620(C=O),1530(C=C).	7.80-7.30(m,4H,arom.),6.40-6.25(br,2H,NH_2),5.80 (s,1H, CH),3.80,3.30(t,2H,each, CH_2CH_2),2.55 (s,3H,$COCH_3$).

Table (1). Continued

12b	3390,3280(NH_2),2975 CH,aliph.),1630,1710 (2C=O).	7.90-7.40((m,4H,arom.),6.40-6.30(br,2H,NH_2),5.90 (s,1H, CH),3.85,3.35((t,2H,each, CH_2CH_2),3.60-3.35 (q.2H, CH_2),2.45(s,3H,$COCH_3$),1.30-1.05 (t,3H,CH_3,ester).
12c	3395,3290(NH_2),2970 (CH,aliph),2208(CN), 1625(C=O).	8.20-8.00(q,2H,β,β',arom.), 7.90-7.70(q,2H, α,α',arom.) 6.70-6.55(br,2H,NH_2),6.10(s, 1H,CH), 3.85,3.35(t,2H,each, CH_2CH_2),2.60(s,3H,$COCH_3$).
12d	3390,3280(NH_2),2975 (CH,aliph),1620,1710 (2C=O)	8.20-8.00(q,2H,β,β',arom.), 7.90-7.70(q,2H,α,α', arom.) 6.50-6.35(br,2H,NH_2),6.05(s, 1H,CH), 3.80,3.30(t,2H,each, CH_2CH_2),3.55-3.35(q,2H,CH_2), 2.40(s,3H,$COCH_3$),1.35-1.10(t,3H,CH_3 ester).
12e	3380,3275(NH2),2970 (CH,aliph),2210(CN), 1625(C=O).	8.05-7.80(q,2H,β,β',arom.), 7.70-7.50(q,2H,α,α', arom.) 6.60-6.45(br,2H,NH_2),5.95(s, 1H,CH), 3.80,3.30(t,2H,each,CH_2CH_2),2.50(s,3H,$COCH_3$).
12f	3375,3270(NH_2),2975 (CH,aliph),1625,1710 (2C=O).	8.00-7.75(q,2H,β,β',arom.), 7.70-7.55(q,2H,α,α', arom.) 6.55-6.40(br,2H,NH_2),6.00(s, 1H,CH), 3.85,3.35(t,2H,each, CH_2CH_2),3.60-3.40(q,2H,CH_2) 2.45(s,3H,$COCH_3$),1.30-1.15(t,3H,CH_3 ester).
12g	3370,3260(NH2),2970 (CH,aliph),2205(CN), 1620(C=O).	7.90-7.80(q,2H,β,β',arom.), 7.70-7.60(q,2H,α,α', arom.) 6.45-6.35(br,2H,NH_2),5.75(s, 1H,CH), 3.80,3.35(t,2H,each,CH_2CH_2),3.60(s,6H,$N(CH_3)_2$, 2.40 (s,3H,$COCH_3$).
12h	3370,3255(NH_2),2970 (CH,aliph),1620,1710 2(C=O).	7.95-7.80(q,2H,β,β',arom.), 7.75-7.60(q,2H,α,α', arom.)6.40-6.30(br,2H,NH2)5.70(s, 1H,CH),3.80, 3.30(t,2H,each, CH_2CH_2),3.60(s,6H,$N(CH_3)_2$, 3.50- 3.40(q,2H,CH_2),2.40(s,3H, $COCH_3$),1.35-1.20 (t,3H,CH_3 ester).

a) Not corrected b) Satisfactory microanalyses obtained: C; + 0.40%,H; + 0.2, N; + 0.44%, Cl; + 0.23% c) Measured with Nicolet 710 FT-IR Spectrometer
d) Measured with a Varian EM 360A at 60 MHz using TMS as an internal standard.

The precipitated solid was collected by filtration and recrystallized from the proper solvent. In case of the reaction of compound 3 with ethylcyanoacetate,the major product 10 was precipitated after cooling, where the minor product 11 was obtained by concentration of the mother liquor.

References

1- R. Gompper and H. Schaefer, Chem. Ber., 100, 591 (1967).

2- S. Rajappa, R. Sreenivasan, B.G.Advani, R.H. Summerville and R. Hoffmann, Indian J. Chem. Sec. B., 15, 297 (1977); Chem. Abstr.,92, 76546 (1978).

3- M. Augustin and W. Doelling, J. Prakt. Chem., 324, 3 (1982).

4- M.D. Nair, S. Rajappa and J.A. Dessai, Indian J. Chem. Sec. B.,21,1 (1982) ; Chem. Abstr.,96, 217794d.

5- M.D. Nair and J.A. Dessai Indian J. Chem. Sec. B.,21,4 (1982). ; Chem. Abstr., 97, 6250f (1982).

6- S. Rajappa, M.D. Nair, R. Sreenivasan and B.G.Advani, Tetrahedron, 36, 1673 (1982).

7- Z.-T. Huang and Z.-R. Liu, Synthesis, 357 (1987).

8- R. Gompper and W. Toepfl,, Chem. Ber., 95, 2861 (1962).

9- K. Hirai, H. Matsuda and Y. Kishda, Z. Chem. Pharm. Bull., 20, 97 (1971).

10- N.B. mansour,W.-D. Rudorf and M.Z. Augustin, Chem., 21, 69 (1981).

11- S. Rajappa and B.G. Advani, Proc. Indian.Acad.Sci. (Chem Sci), 91, 463(1982) ; Chem. Abstr.,88, 226834(1982).

12- Z.-T. Huang and Xian Shi, Synthesis, 162 (1990).

13- A.K.El-Shafei, A.M.M. El-Saghier, A. Sultan and A.M. Soliman, Phosphorous,Sulphur and Silicon, 72, 73 (1992).

14- A.K.El-Shafei, H.A. Abdel-Ghany, A. Sultan and A.M.M. El-Saghier, Phosphorous,Sulphur and Silicon, 73,15 (1992).

15- A.K.El-Shafei, A.M.M. El-Saghier and E.A. Ahmed, Synthesis, 152 (1994).

16- A.K.El-Shafei, A.M. El-Sayed and A.M.M. El-Saghier, Phosphorous, Sulphur and Silicon, 90,213-218 (1994).

17- A.K.El-Shafei, A.M. Soliman, A.A. Sultan and A.M.M. El-Saghier, Gazz. Chem. Ital.,125, (1995).

18 - A.M. Soliman, Phosphorous,Sulphur and Silicon, 97,1 (1994).

19- A.M.M. El-Saghier, Bull.Chem.Soc.Jap., 66, 2011 (1993).

20- A.M. Soliman, A.A. Sultan and A.K.El-Shafei,Monatshefte fur Chem.,1995,126 , 615.

21- J. Sansstrom and Wennarbeck, Acta Chem. Scand., 24, 1191 (1970).

22- R.K. Dieter, Tetrahedron, 42 No. 12, 3029 (1986).
23- H. Junjappa, H. Ila and C.V. Asokan, Tetrahedron, (1990), 46, 5423.

(Received in the USA 09 August 1999)