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A NOVEL SYNTHESIS OF HETEROCYCLIC COMPOUNDS DERIVED FROM α-KETOKETENE S,S-ACETAL

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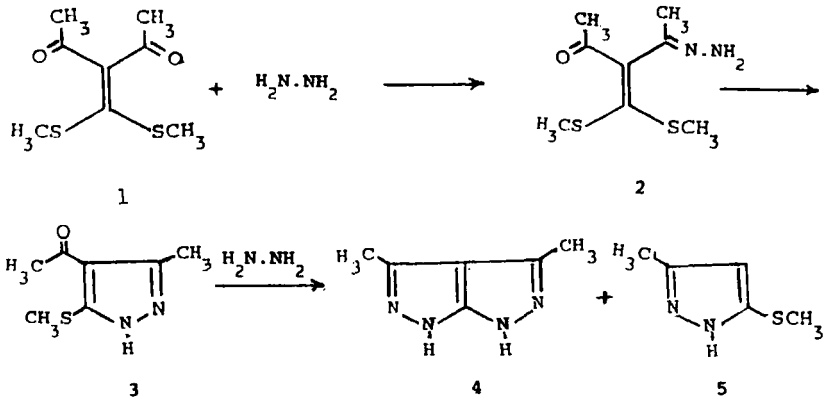
Novel heterocyclic compounds were prepared by the reaction of 2-acetyl-2-oxopropylidene S,S-acetal with different amino compounds namely, hydrazine hydrate, phenylhydrazine, guanidine hydrochloride, thiosemicarbazide, o-phenylenediamine, o-aminophenol or o-amino-thiophenol in different molar ratios.

The synthesis of ketoketene S,S-acetals[1-5] has attracted a considerable attention as versatile starting materials for the synthesis of a wide variety of fused heterocycles.

In an extension of our recent studies[6-8] in the application of ketoketene S,S-acetal in heterocyclic synthesis, we report here, the reaction of 2-acetyl-2-oxopropylidene S,S-acetal **1** with different bidentates to give the described compounds. The reaction of compound **1** which prepared by using PTC technique[9] with hydrazine hydrate in acetonitrile in 1:2.5 molar ratio affords different compounds according to the reaction conditions. Stirring of compound **1** with hydrazine hydrate in acetonitrile for 30 minutes at room temperature gave the corresponding mono hydrazone **2** but on continuous stirring

for 48 hours, the corresponding pyrazole derivative 3 was obtained. When the reaction was carried out under refluxing condition we obtained pyrazolo[3,4-c]pyrazole derivative 4 in 50% yield and methylthio-1H-pyrazole derivative 5 in 30% yield.



1 2

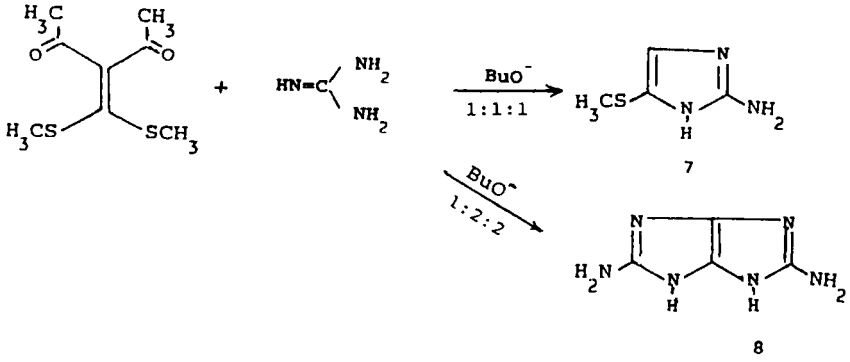
3 4 5

3-Methyl-5-methylthio-1-phenylpyrazole 6 was separated when compound 1 was reacted with phenylhydrazine in 1:1 or 1:2 molar ratios in refluxing acetonitrile.

6

Treatment of compound 1 with guanidine hydrochloride and triethylamine in 1:1:1 or 1:2:2 molar ratios in acetonitrile afforded the starting materials. But when compound 1 was allowed to react

with guanidine hydrochloride and sodium butoxide in 1:1:1 or 1:2:2 molar ratios in refluxing butanol, 2-amino-4-methylthio-1H-imidazole 7 or imidazolo[4,5-d]imidazole derivative 8 were separated.



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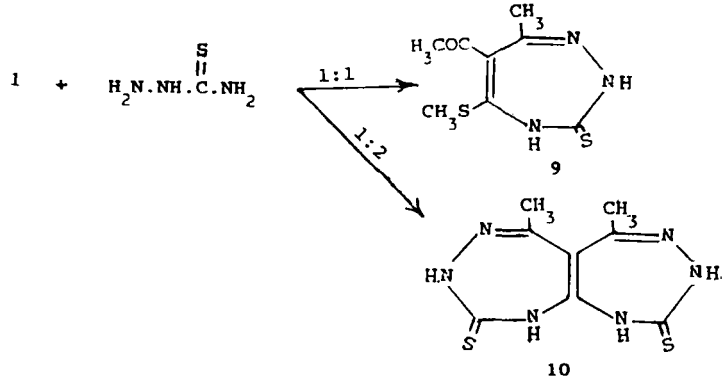
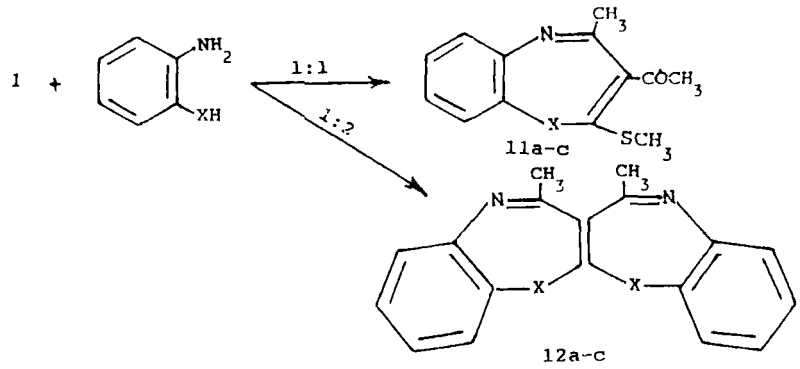
In case of reaction of compound 1 with thiosemicarbazide in 1:1 or 1:2 molar ratios in refluxing acetonitrile, triazebene derivative 9 or triazebeno[5,6-e]triazebene derivative 10 were obtained, respectively.



9

10

Reaction of compound 1 with o-phenylenediamine, o-aminophenol, or o-aminothiophenol in refluxing ethanol was reported[10] to give benzimidazole, benzoxazole or benzthiazole derivatives respectively. We report here, when compound 1 treated with the same reagents in 1:1 or 1:2 molar ratios in refluxing acetonitrile gave benzdiazebene, benzoxazebene, benzthiazebene derivatives 11a-c, as well as benzdiazebeno[5,6-e]-benzdiazebene, benzoxazebeno[5,6-e]-benzoxazebene and benzthiazebeno[5,6-e]benzthiazebene derivatives 12a-c respectively.



a: X = NH; b: X = O; c: X = S

EXPERIMENTAL

Synthesis of compounds 2 and 3

To a solution of compound 1 (0.005 mol) in acetonitrile (50 mL) hydrazine hydrate (0.0125 mol) was added. The reaction mixture was stirred at 20°C for 30 minutes or 48 hours. The reaction mixture was evaporated in vacuo. The residue was washed with water, triturated

with pet. ether 40-60°C and recrystallized from the proper solvent to afford compounds 2 or 3 respectively (cf Table I).

Synthesis of pyrazolo[3,4-c]pyrazole 4 and methylthio-1H-pyrazole derivative 5

A mixture of compound 1 (0.01 mol), hydrazine hydrate (0.025 mol) and acetonitrile (50 mL) was refluxed for 27 hours. The reaction mixture was cooled and shaked with 100 mL of water. The precipitated solid was collected by filteration and recrystallized to afford compound 5 An additional 50 mL of water was added to the mother liquor and left overnight. The precipitant was filtered off and recrystallized to give compound 4 (cf Table I).

Synthesis of 3-methyl-5-methylthio-1-phenylpyazole 6

An equimolar amounts (0.005 mol) of compound 1 and phenyl-hydrazine was refluxed in acetonitrile (50 mL) for 29 hours. The reaction mixture was evaporated in vacuo. The residue was washed with water, triturated with pet. ether 40-60°C and recrystallized (cf Table I).

Synthesis of 2-Amino-4-methylthio-1H-imidazole 7

A mixture of equimolar amounts (0.005 mol) of compound 1, guanidine hydrochloride, sodium butoxide and 30 mL butanol was refluxed for 7 hours. The reaction mixture was evaporated in vacuo. The solid residue was washed with water, triturated with pet. ether 40-60°C and recrystallized (cf Table I).

Synthesis of imidazolo[4,5-d]imidazole derivative 8

A mixture of compound 1 (0.005 mol), sodium butoxide (0.01

Table 1: Analytical and Spectral data of the prepared compounds

Product No.	Reaction time(h) Reaction Temp.(°C)	M.P.[a] (Cryst.Solv.)	Yield[b] (%) crude / crys.	Mol.Form. (Mol.Wt.)	Analytical Data[c] Cal./Found C	H	N
2	0.5/20	55	93	$C_8H_{14}N_2OS_2$	44.01	6.46	12.83
	stirring	(acetonitrile)	91	(218.34)	44.18	6.31	12.94
3	48/20	108-111	89	$C_7H_{10}N_2OS$	49.39	5.92	16.45
	stirring	(acetonitrile)	85	(170.23)	49.14	5.87	16.28
4	27/reflux	136	56	$C_6H_8N_4$	52.93	5.92	41.15
		(acetonitrile)	50	(136.16)	53.10	5.70	40.91
5	27/reflux	120	32	$C_5H_8N_2S$	46.85	6.29	21.85
		(acetonitrile)	30	(128.20)	47.08	6.13	21.63
6	29/reflux	144-145	61	$C_{11}H_{12}N_2S$	64.67	5.89	13.71
		(acetonitrile)	60	(204.30)	64.81	6.03	13.90
7	7/reflux	>320	73	$C_4H_7N_3S$	37.19	5.46	32.53
		(ethanol)	71	(129.18)	37.32	5.61	32.38
8	3/reflux	220	75	$C_4H_6N_6$	34.78	4.38	63.01
		(aq. ethanol)	73	(138.13)	34.62	4.56	63.27
9	17/reflux	315-317	78	$C_8H_{11}N_3OS_2$	41.90	4.84	18.32
		(dioxane)	75	(229.32)	41.76	4.69	18.18
10	8/reflux	281-283	67	$C_8H_{10}N_6S_2$	37.78	3.96	33.04
		(acetonitrile)	66	(254.34)	37.95	3.82	33.21
11a	27/reflux	119	65	$C_{13}H_{14}N_2OS$	63.39	5.73	11.37
		(pet.ether-benzene)	63	(164.33)	63.27	5.91	11.56
11b	38/reflux	177-179	68	$C_{18}H_{16}N_4$	74.98	5.60	19.43
		(benzene)	66	(288.36)	74.83	5.74	19.61
11c	26/reflux	204	59	$C_{13}H_{13}NO_2S$	63.13	5.30	5.66
		(benzene)	56	(247.33)	63.47	5.47	5.81
12a	38/reflux	140	57	$C_{18}H_{14}N_2O_2$	74.47	4.86	11.02
		(benzene)	53	(290.32)	74.65	4.71	11.18
12b	33/reflux	148	49	$C_{13}H_{13}NOS_2$	59.29	4.98	5.32
		(n-hexane)	48	(263.38)	59.41	4.82	5.48
12c	43/reflux	114	47	$C_{18}H_{14}N_2S_2$	67.05	4.38	8.69
		(n-hexane)	45	(322.45)	67.19	4.19	8.52

[a]) Uncorrected [b]) With respect to reaction molarity.

[c]) Satisfactory microanalysis obtained C; ∓0.35 % H; ∓0.20 %, N; ∓0.20 %

Table I (continued)

Product No.	IR (KBr)[d] $\nu(Cm^{-1})$	H-NMR(DMSO-d_6)[e] δ(ppm)
2	3297, 3388(NH_2); 1702(C=O); 1445(C-SCH_3).	7.14(s,2H,NH_2); 3.45(s,6H,2CH_3); 3.10(s,6H,2SCH_3).
3	3149(NH); 1705(C=O); 1435 (C-SCH_3).	10.35(s,1H,NH); 2.65(s,3H,CH_3); 2.20(s,6H,CH_3+SCH_3).
4	3224, 3189(2NH).	10.56(br,2H,2NH); 2.60(s,6H,2CH_3)
5	3167(NH); 1437(C-SCH_3).	10.75(s,1H,NH); 2.80(s,3H,CH_3); 2.60(s,3H,SCH_3).
6	1439(C-SCH_3).	7.55(s,5H,arom.); 6.50(s,1H,CH); 2.85(s,3H,CH_3); 2.70(s,3H,SCH_3).
7	3375, 3280, 3201(NH,NH_2); 1442(C-SCH_3).	10.62(s,1H,NH); 6.65(s,1H,CH); 4.45 (br,2H,NH_2); 2.80(s,3H,CH_3).
8	3312, 3292, 3210, 3199, 3179, 3125(2NH,2NH_2).	7.14(s,2H,NH_2); 3.45(s,6H,2CH_3); 3.10(s,6H,2SCH_3).
9	3236, 3224(2NH); 1701(C=O); 1440(C-SCH_3).	11.35(s,1H,NH); 10.95(s,1H,NH); 2.95 (s,6H,2CH_3+$COCH_3$); 2.75(s,3H,SCH_3).
10	3232, 3209, 3197, 3105(4NH)	11.45(br,2H,2NH); 11.25(br,2H,2NH); 2.90(s,6H,2CH_3).
11a	3198(NH); 1702(C=O); 1438 (C-SCH_3).	10.25(s,1H,NH); 7.70,7.10(m,4H, arom.); 2.85(s,6H,CH_3+$COCH_3$); 2.75 (s,3H,SCH_3).
11b	3264, 3189(2NH); 1439 (C-SCH_3)>	10.35(br,2H,2NH); 7.75-6.95(m,8H, arom.); 2.60(s,6H,2CH_3).
11c	1702(C=O); 1443(C-SCH_3).	7.80-7.10(m,4H,arom.); 2.45(br,6H, CH_3+$COCH_3$); 2.25(S,3H,SCH_3).
12a		8.10-7.20(m,8H,arom.); 2.55(s,6H, 2CH_3).
12b	1705(C=O).	7.65-7.05(m,4H,arom.); 2.95(br,6H, CH_3+$COCH_3$); 2.20(S,3H,SCH_3).
12c		8.15-7.15(m,8H,arom.); 2.85(br,6H, 2CH_3).

[d]) Measured on Nicolet 710 FT-IR spectrophotometer

[e]) Measured with a varian EM 360 L using TMS as internal standard

mol),guanidine hydrochloride (0.01 mol) and butanol (40 mL) was refluxed for 3 hours. The reaction mixture was evaporated in vacuo. The separated solid was washed with water, triturated with pet. ether 40-60°C and recrystallized (cf Table I).

Synthesis of triazebene and triazebeno[5,6-e]triazebene derivatives 9 and 10

To a solution of compound 1 (0.005 mol) in acetonitrile (50 mL), thiosemicarbazide (0.005 mol) or (0.01 mol) was added. The reaction mixture was refluxed for 17 or 8 hours.The reaction mixture was evaporated in vacuo and the residue was washed with water, triturated with pet. ether 40-60°C and recrystallized to give compounds 9 or 10 respectively (cf Table I).

Synthesis of benzdiazebene, benzoxazebene, benzthiazebene derivatives 11a-c

A mixture of an equimolar amounts (0.005 mol) of compound 1 and o-phenylenediamine, o-aminophenol or o-aminothiophenol was dissolved in acetonitrile (50 mL). The reaction mixture was refluxed for a period of time 26-38 hours. The reaction mixture was evaporated in vacuo and the residue was washed with water, triturated with pet. ether 40-60°C and recrystallized (cf Table I).

Synthesis of benzdiazebene[5,6-e]-benzdiazebene, benzoxazebeno-[5,6-e]benzoxazebene and benzthiazebeno[5,6-e]benzthiazebene derivatives 12a-c

To a solution of compound 1 (0.005 mol) in acetonitrile (50 mL) o-phenylenediamine, o-aminophenol or o-aminothiophenol (0.01 mol)

was added. The reaction mixture was refluxed for a period of time 33-48 hours. The reaction mixture was evaporated in vacuo. The residue was washed with water, triturated with pet. ether 40-60°C and recrystallized (cf Table I).

REFERENCES

1- A. Thuillier and J. Vialle, Bull. Chim. Soc. Fr., 2194 (1962).

2- I. Shahak and Y. Sasson, Tetrahedron Lett., 4207(1973).

3- R. Gompper R. R. Schmidt and E. Kutter, Ann., **684**, 37 (1965).

4- L. Jensen, L. Dalgaard and S. O. Lawesson, Tetrahedron, **30**, 2413 (1974).

5- N. Svenstrup and J. Becher, Synthesis, 215 (1995).

6- A. M. M. El-Saghier, Bull, Chem. Soc. Jpn., **66**, 2011-2015 (1993).

7- A. K. El-Shafei, A. H. Abdel-Ghany, A. Sultan and A. M. M. El-Saghier, Phosphorus, sulfur and Silicon, 73, 15-25 (1992).

8- A. K. El-Shafei, A. M. El-Sayed and A. M. M. El-Saghier, Phosphorus, Sulfur and Silicon 90, 213-218 (1994).

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

10- J. Sandstrom and I. Wennarbeck, Acta. Chem. Scand., **24**, 1191 (1970).

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