COMMUNICATIONS

DE LA FACULTÉ DES SCIENCES
DE L'UNIVERSITÉ D'ANKARA

Série B : Chimie

TOME : 31 ANNÉE : 1985

STUDIES ON β-LACTAMS AND THIAZOLIDINONES PART I. SYNTHESIS AND BIOLGICAL ACTIVITY OF SOME NEW TRIAZOLYLAZETIN-2-ONES AND THIAZOLIDIN-4-ONES.

by

A. DEEB, B.E. BAYOUMY and M. EL-MOBAYED

Faculté des Sciences de l'Université d'Ankara
Ankara, Turquie

Communications dé la Faculté dés Sciéncés dé l'Univérsité d'Ankara

Comite de Redaction de la Serie B
T. Gündüz. C. Tüzün. M. Alpbaz.
Secretaire de Publication
Ö. Çakar

La Revue "Communications de la Fac ulté des Sciences de l'Universite d'Ankara" est un organe de publication englobant toutes les diciplines scientifiques représentées à la Faculté des Sciences de l'Université d'Ankara.

La Revue, jusqu'à 1975 a l'exception des tomes, I, II, III etait composée de trois séries

Série A : Mathématiques, Physique et Astronomie,
Série B : Chimie,
Série C : Sciences Naturelles.

A partir de 1975 la Revue comprend sept séries:

Série A_1 : Mathématiques,
Série A_2 Physique,
Série A_3 : Astronomie,
Série B : Chimie,
Série C_1 : Géologie,
Série C_2 : Botanique,
Série C_3 : Zoologie.

A partir de 1983 les séries de C_2 Botanique et C_3 Zoologie ont été réunies sous la seule série Biologie C et les numéros de Tome commencerons par le numéro 1.

En principe, la Revue est réservée aux mémoires originaux des membres de la Faculté des Sciences de l'Université d'Ankara. Elle accepte cependant, dans la mesure de la place disponible les communications des auteurs étrangers. Les langues Allemende, Anglaise et Française seront acceptées indifféremment. Tout article doit être accompagné d'un resumé.

Les articles soumis pour publications doivent être remis en trois exemplaires dactylographiés et ne pas dépasser 25 pages des Communications, les dessins et figures portés sur les feuilles séparées devant pouvoir être reproduits sans modifications.

Les auteurs reçoivent 25 extraits sans couverture.

l'Adresse : Dergi Yayın Sekreteri
Ankara Üniversitesi,
Fen Fakültesi,
Beşevler-Ankara
TURQUIE

STUDIES ON β-LACTAMS AND THIAZOLIDINONES PART I. SYNTHESIS AND BIOLOGICAL ACTIVITY OF SOME NEW TRIAZOLYL-AZETIDIN-2-ONES AND THIAZOLIDIN-4-ONES.

A. DEEP, B.E. BAYOUMY and M. EL-MOBAYAD.

Chemistry Department, Faculty of Science Zagazig, Zagazig, Egypt.

Arylidene-3-amino-1,2,4-triazoles (1) were prepared by condensation of 3-amino-1,2,4-triazole with aromatic aldehydes. Cyclocondensation of chloroacetylchloride, phthaloyl gylcyl chloride and mercaptoacetic acid on (1) giving the corresponding azetidin-ones (2 and 3) and 4-thiazolidinones (4) respectively, in good yield.

INTRODUCTION

In view of the fact that the antibiotic activity of penicillin and cephalosporin-C is mainly due to the substituted β-Lactam ring structure[1], and that 4-thiazolidinones are of important interest as local anesthetic agents[2], it was of interest to incorporate this molecule into the well known antimicrobial triazole[3] to evaluate these for the pharmacological activity.

RESULTS AND DISCUSSION

In this communication, the basic synthetic approach to the hitherto unreported heterocyclic compound was established by the following routes (i) Preparation of the key intermediates arylidene-3- amino -1,2,4-triazoles (1); (ii) Cycloaddition of the key intermediates on chloroacetylchloride (or phtalyl glycyl chloride) (2 and 3) and (iii) Cycloaddition of key intermediates on mercaptoacetic acid (4).

Thus arylidene -3- amino- 1,2,4- triazoles (1) were prepared by the condensation of 3-amino-1, 2, 4- triazole with aromatic aldehydes in ethanol in the presence of piperidine as a catalyst or by heating the reactant to about 200°C for a period of 5-10 min.

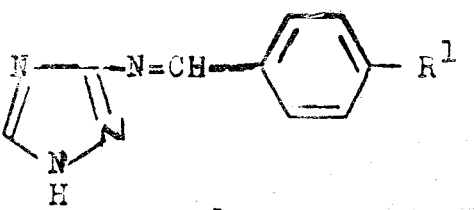
The structure of compounds (1) was confirmed from elemental analysis and the IR spectra which showed absorption band at 1660–1640 cm^{-1} ($\nu C{=}N$)[4].

The β-Lactams were prepared by the reaction between an acid chloride and anils in the presence of a base[5]. Thus, the cyclo condensation reaction of chloroacetylchloride and/or phthaloyl glycyl chloride

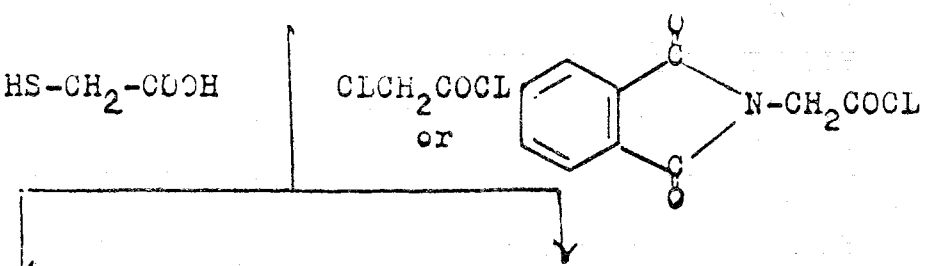
(1) was carried out in dry benzene in the presence of triethylamine as a catalyst, giving 1- (3-1, 2,4- triazolyl)-2-azetidinones 2 and 3 respectively.

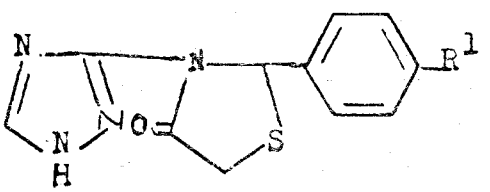
The structure of compounds 2 and 3 were identified from the microanalytical data and the IR spectra, which showed an absorption band at about 1750-1710 cm^{-1} for $\nu C{=}O$ (monocyclic B-Lactam)[6].

The cyclocondensation reaction of mercaptoacetic acid on (1) was carried out in dry benzene using Deanstark trap. The compounds obtained from this reaction were 3-(3-1, 2, 4- triazolyl)-4- thiazolidinones (4) which is in agreement with data given by Surrey[2]. Substituted 4-thiazolidinones (4) were identified by a combination of spectral and elemental analysis. The IR spectra of compounds 4 are characterized by an absorption band in the region of 1700–1690 cm^{-1}, $\nu C{=}O$ group.

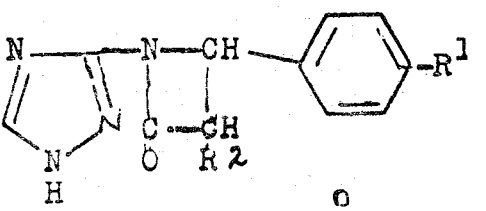


1



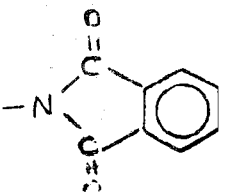


4



2: R^2 = Cl

3: R^2 =



ANTIMICROBIAL ACTIVITY:

Compounds 2, 3 and 4 penicillin Gprocain (reference sample) were tested in vitro for the biological activity against a variety such as Salmonella Sp., Proteus Sp., Staphylococcus Albus and Bacillus Subtilis[6,7]. The activity of the tested compounds was compared with that of Penicillin G procaine at a concentration of 0.2 g / L. The most potent compounds against Salmonella Sp. are 2b, and 4e and against B. subtilis are 3a and 3c.

EXPERIMENTAL

All melting points were uncorrected. The IR spectra were recorded on a Pye Unicam SP 200 G spectrophotometer using KBr discs. The purity of the compounds prepared were checked by TLC.

ARYLIDINE-3-AMINO-1,2,4-TRIAZOLES (1):

A mixture of equimolecular amounts of 3-amino-1, 2, 3- triazojle and the appropriate aldehyde was heated at about 200°C for 5-10 min. The product was cooled, washed with ether and recrystallized from dioxane with 60–85 % yield. The results are given in table 1.

Table 1. Physical date of Arylidene-3-amino-1, 2, 4- Triazoles (1)

Compound	R^1	M.P. C°	Molecular formula	Analysis (calc / found)			
				C	H	N	Cl
a	H	193	$C_9H_8N_4$	62.79 62.78	4.65 4.66	32.55 32.53	—
b	Cl	213	$C_9H_7N_4Cl$	52.30 52.40	3.38 3.39	27.12 27.14	17.19 17.21
c	OCH_3	195	$C_{10}H_{10}ON_4$	59.40 59.42	4.95 4.95	27.72 27.70	—
d	$N(CH_3)_2$	292	$C_{11}H_{13}N_5$	61.39 61.36	6.05 6.07	32.56 32.58	—
e	NO_2	254	$C_9H_7O_2N_6$	49.77 49.78	3.22 3.23	32.26 32.28	—

SUBSTITUDE 3-(1-3, 2, 4-TRIAZOLYL) AZETIDIN -2-ONES (2 AND 3).

To a well stirred solution of anils 1 (0.01 mol) and triethylamine (0.02 mol) in dry benzene (50 ml) was added monoochloroacetylchloride or phthalolyl glycyl chloride (0.01 mol) at room temperature. The mixture was stirred for about 10 hours and left at room temperature for 7 days. The precipitated $N(C_2H_2)_3$. HCL was filtered of and washed tho-

roughly with dioxane. The filtrate was evaporated under reduced pressure, and the residue obtained was washed with dil. HCl then with H_2O. It was then dried and recrystallized from dioxan with 40–60 % yield. The results are listed in table 2.

Table 2. Physical Data of Substituted 1-(3-1, 2, 4-triazolyl) azetidin-2-ones (2 and 3)

Compound	R^1	M.P °C	Molecular formula	Analysis (Calc. found)			
				C	H	N	Cl
2a	H	302	$C_{11}H_9ON_4Cl$	53.12	3.62	22.53	14.11
				53.11	3.60	22.51	14.03
2b	Cl	310	$C_{11}H_8ON_4Cl_2$	46.64	3.18	19.79	25.08
				46.66	3.19	19.76	25.06
2c	OCH_3	320	$C_{12}H_{11}O_2N_4Cl$	51.70	3.95	20.11	12.59
				51.73	3.94	20.13	12.56
2d	$N(CH_3)_2$	359	$C_{13}H_{14}ON_5Cl$	53.52	4.80	24.01	12.02
				53.55	4.83	24.03	12.01
2e	NO_2	297	$C_{11}H_8O_3N_3Cl$	44.97	2.72	23.85	12.09
				44.99	2.74	23.88	12.01
3a	H	297	$C_{19}H_{13}O_3N_5$	63.51	3.62	19.49	—
				63.52	3.63	19.50	—
3b	Cl	305	$C_{19}H_{12}O_3B_5Cl$	57.94	3.04	17.78	8.90
				57.91	3.06	17.77	8.92
3c	OCH_3	350	$C_{20}H_{15}O_4N_5$	61.69	3.85	17.99	—
				61.68	3.82	17.96	—
3d	$N(CH_3)_2$	332	$C_{21}H_{18}O_3N_6$	62.68	4.48	20.89	—
				62.66	4.45	20.86	—
3e	No_2	350	$C_{19}H_{12}O_5N_6$	56.43	2.97	20.79	—
				56.41	2.99	20.77	—

SUBSTITUTED 4-THIAZOLIDINONES (4):

A mixture of anils 1 (0.02 mol) and metcaptoacetic acid (0.02 mol) in dry benzene (50 ml) was refluxed using water separator until the theoretical amount of water was collected. When most of the benzene had been removed the residue was dissolved in ether and seeded. The results are listed in Table 3.

Table 3. Physical Data of Substituted 3-(3-1, 2, 4-Triazolyl) Thiazolidin-4-ones (4)

Compound	R^1	M.P. °C	Molecular formula	Analysis (Calc. found)				
				C	H	N	S	Cl
4a	H	150	$C_{11}H_{10}N_4OS$	53.66	4.06	22.76	13.0	—
				53.62	4.05	22.72	13.1	—
4b	Cl	170	$C_{11}H_9ON_4SCl$	47.06	3.21	19.96	11.41	12.5
				47.08	3.22	19.97	11.44	12.6
4c	OCH_3	147	$C_{12}H_{12}O_2N_4S$	52.17	4.34	20.29	11.59	
				52.19	4.35	20.26	11.56	
4d	$N(CH_3)_2$	163	$C_{13}H_{15}ON_5S$	53.98	5.19	24.22	11.07	
				53.99	5.18	24.23	11.09	
4e	NO_2	85	$C_{11}H_9O_3N_5S$	45.36	3.09	24.05	10.99	
				45.37	3.06	24.08	10.90	

REFERENCES

1. CLARKE, H.T., JOHNSON, J.R. AND ROBINSON, R., The Chemistry of Penicillin (Princeton University Press, Princeton, NJ, USA (1949).
2. SURREY, A.R., J. Am. Chem. Soc. 71, 3354 (1949); 69, 2911 (1947).
3. PATHAK, R.B.; JAHAN, B. and BAHEL, S.C. (Chem. Dep. Gorakhpur Univ., Garakhpur, India). Bakin Bobai 8 (4) 149.53 (1980); Through C.A. 94, 30660 (1981).
4. BELLAMY, L.J. The Infrared spectra of Complex Molecules 2nd ed. Methuen and Co. Ltd., London (1958).
5. BOSE, A.K., Y.H. Chiang and M.S. Manhas, Tetrahedron Letters London, 4091 (1972).
6. IRVING, G.W., J. Bacteriol, 52, 101 (1946).
7. VINCENT, J.G., and H.W. VINCENT, Prac. exp. Biol. Med. 55, 162 (1944).