Oxidation of Aldehyde Semicarbazones with Lead Dioxide: Application to the Syntheses of 2-Amino-1,3,4-oxadiazoles and 2,4-Dihydro-1,2,4-triazol-3-ones

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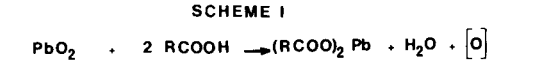
Received February 28, 1985

The oxidation of aldehyde semicarbazones with lead dioxide in acid media was effected. The 4,4-disubstituted semicarbazones of aromatic aldehydes afford 2-amino-1,3,4-oxadiazole derivatives. The 2,4-disubstituted semicarbazones give 2,4-dihydro-1,2,4-triazol-3-ones, often in higher yields than the known methods. The mechanisms for the formation of these compounds are proposed.

J. Heterocyclic Chem., **22**, 1383 (1985).

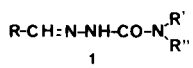
A number of studies on the oxidation of various functional groups such as alcohols, phenols, aldehydes, hydrazines, oximes,...with lead dioxide has been investigated. The activity of the oxidant is increased in polar solvents [1]. The use of pure organic aliphatic acids or their dilution in a solvent (dichloromethane) constitutes an interesting method of oxidation. Actually, the oxidizing efficiency of lead dioxide is enhanced by the strength of the acids as solvents. This may be explained by the increasing rate of the formation of lead(II) salts along with the acidity, which is accompanied by the release of active "oxygen" (Scheme I).

SCHEME I



Without an organic reducing agent, this reaction is very slow. Thus, lead(II) acetate is only obtained after several hours in refluxing acetic acid whereas, in the presence of a reducing agent, the reaction occurs between a few minutes and half an hour, depending on the nature of the agent used. As far as we know, no thorough study on the oxidation mechanism has yet been carried out.

Recently, by this route, we have reported that aroylhydrazone of aromatic aldehydes are easily oxidized into 1,3,4-oxadiazoles in excellent yields [2]. In continuation of our studies, the oxidation of structures **1** and **2** has been undertaken.



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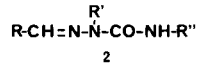


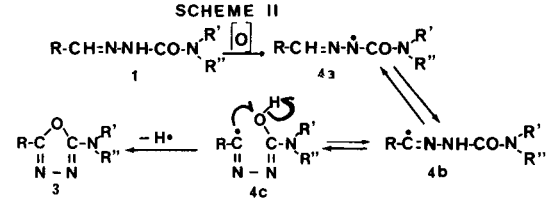
2

Previously, the oxidation of semicarbazones **1**, derivatives of 4,4-disubstituted semicarbazides, into 2-amino-1,3,4-oxadiazoles has been performed with bromine [3], sodium hypobromite [4] and lead tetraacetate [5].

When an equimolecular ratio of lead dioxide is added to a solution of semicarbazone **1** in pure formic acid at 25°, only one part of **1** is rapidly converted to 2-amino-1,3,4-oxadiazole **3**. Addition of more oxidant or heating does not allow completion but gives resinous material. The breakdown of the reaction may be due to the various possible configurations of the semicarbazones. Some of them may undergo facile cyclisation to heterocycles **3**, others may lead to polymerization. This remark is supported by the results with lead tetraacetate [6].

Previous studies on oxidations with lead dioxide indicated radical reaction mechanism [7]. Similarly, it is what we propose herein (Scheme II).

SCHEME II



The initial step of the reaction is the formation of a pseudo-allylic radical **4a**, in equilibrium with **4b** (amide form) and **4c** (iminoalcohol from). By the loss of an "hydrogen" radical, **4c** cyclises to 2-amino-1,3,4-oxadiazole **3**.

Compounds **3** prepared by this route are listed in Table I.

Table I

Compounds **3**

3	R	R'	R''	Yield %	Mp °C
a	C_6H_5	H	CH_3	50	153 [a,b]
b	C_6H_5	CH_3	CH_3	40	84 [c,d]
c	C_6H_5	C_6H_5	C_6H_5	20	156 [a,e]
d	4-CH_3O-C_6H_4	CH_3	CH_3	40	104 [c,f]
e	4-NO_2-C_6H_4	CH_3	CH_3	20	235 [g]

[a] Ethanol. [b] Lit [8] mp 154°. [c] Ethanol:hexane. [d] Lit [9] mp 84-85°. [e] Lit [5] mp 156°. [f] Lit [9] mp 104°. [g] Benzene.

Although this method is very rapid, it gives lower yields than the one using lead tetraacetate as an oxidant [5]. The replacement of formic acid by acetic acid or a mixture of

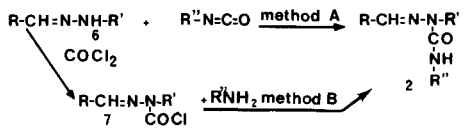
formic acid with dichloromethane are fruitless.

In a similar way, 2,4-disubstituted semicarbazones **2** are converted into the corresponding 2,4,5-trisubstituted 2,4-dihydro-1,2,4-triazol-3-ones **5** (Scheme IV) in good yields, with some exceptions.

Different modes of preparation of triazolones **5** have been reported. Some use the conversion of other ring systems like 1,2,4,5-tetrazoles [10] or 1,2,4-oxadiazolines [11]. Therefore those methods cannot easily be generalized. Another one results from the reaction of arylisocyanate with amidrazone [12]. Recently have been recorded the cycloaddition of α-chlorobenzaldehyde phenylhydrazone with aroyl azides [13], the cyclization of 1-acyl-2,4-diarylsemicarbazides in alkaline media [14] and the reaction between methyl (or ethyl) 1-alkoxy(or thioalkyl)alkylidene carbamate and arylhydrazine [14]. In recent years synthetic pathways of this class of compounds have been extensively investigated, owing to the discovery of Etoperidon (a very active antiparkinsonian agent) [15] and to the herbicide properties of some chlorinated derivatives [14].

Few semicarbazones **2** have been recorded in the literature. We describe herein their general synthetic routes (Scheme III).

SCHEME III



The first way (method A) consists of treating arylhydrazone of aromatic aldehyde **6** with arylisocyanate [16]. This procedure is slow and requires an excess of arylisocyanate. Under the same conditions alkylisocyanates do not react.

The second path (method B) includes two steps. First, treatment of **6** with phosgene to afford the corresponding 2-chloroformylhydrazones **7** in good yields. Secondly, the addition of **7** to an ethanolic solution of primary amines at 0° [17] which gives rise to quantitative semicarbazones **2**

Table II

Compounds **7** ($R' = C_6H_5$)

7	R	Yield %	Mp °C
a	C_6H_5	66	98 [a,b]
b	4-CH_3-C_6H_4	66	186 [a]
c	4-Cl-C_6H_4	83	[c]
d	5-NO_2-2-furyl	94	162 [d]
e	5-NO_2-2-thienyl	90	198 [d]
f	4-pyridyl	75	140 dec [d]

[a] Diethyl ether:petroleum ether 40-60. [b] Lit [16] mp 101-102°. [c] Undistillable oil. [d] Benzene.

Table III

Substituents (R, R' and R'') for Compounds **2a-ai** and **5e-ai**

Compound **2** and **5**	R	R'	R''
a	C_6H_5	C_6H_6	CH_3
b	C_6H_5	C_6H_5	C_2H_5
c	C_6H_5	C_6H_5	n-C_3H_7
d	C_6H_5	C_6H_5	n-C_4H_9
e	C_6H_5	C_6H_5	cyclohexyl
f	C_6H_5	C_6H_5	$C_6H_5CH_2$
g	C_6H_5	C_6H_5	C_6H_5
h	C_6H_5	C_6H_5	2-CH_3O-C_6H_4
i	C_6H_5	C_6H_5	3-CH_3O-C_6H_4
j	C_6H_5	C_6H_5	4-CH_3O-C_6H_4
k	C_6H_5	C_6H_5	4-EtOCO-C_6H_4
l	C_6H_5	C_6H_5	4-Br-C_6H_4
m	C_6H_5	C_6H_5	4-Cl-C_6H_4
n	C_6H_5	C_6H_5	3-NO_2-C_6H_4
o	C_6H_5	C_6H_5	4-NO_2-C_6H_4
p	C_6H_5	$C_6H_5CH_2$	C_6H_5
q	4-CH_3-C_6H_4	C_6H_5	C_6H_5
r	4-CH_3-C_6H_4	C_6H_5	4-Br-C_6H_4
s	4-CH_3-C_6H_4	C_6H_5	4-Cl-C_6H_4
t	4-CH_3O-C_6H_4	C_6H_5	C_6H_5
u	4-Cl-C_6H_4	C_6H_5	C_6H_5
v	4-Cl-C_6H_4	C_6H_5	4-Br-C_6H_4
w	4-Cl-C_6H_4	C_6H_5	4-NO_2-C_6H_4
x	4-NO_2-C_6H_4	$C_6H_5CH_2$	C_6H_5
y	4-NO_2-C_6H_4	C_6H_5	C_6H_5
z	4-pyridyl	C_6H_5	C_6H_5
aa	5-NO_2-2-furyl	C_6H_5	C_6H_5
ab	5-NO_2-2-furyl	C_6H_5	3-CH_3O-C_6H_4
ac	5-NO_2-2-furyl	C_6H_5	4-Br-C_6H_4
ad	5-NO_2-2-furyl	C_6H_5	4-ClC_6H_4
ae	5-NO_2-2-furyl	C_6H_5	4-NO_2-C_6H_4
af	5-NO_2-2-thienyl	C_6H_5	C_6H_5
ag	5-NO_2-2-thienyl	C_6H_5	3-CH_3O-C_6H_4
ah	5-NO_2-2-thienyl	C_6H_5	4-Br-C_6H_4
ai	5-NO_2-2-thienyl	C_6H_5	4-Cl-C_6H_4

within a few minutes. Arylhydrazones **6** in which the 2-position aryl group carried electron-withdrawing substituents do not undergo reaction with phosgene, therefore this application is relatively limited. Compounds **7** are summarized in Table II and compounds **2** in Tables III and IV.

The oxidation of some semicarbazones **2** has been undertaken either with an alcoholic solution of ferric chloride in sealed tubes for one hour at 125° [16] or with pentyl nitrite at reflux for several hours [20]. These conditions give triazolones **5** in low yields and often with tarry products (removal which requires chromatography). Before using lead dioxide, all our attempts to oxidize **2** with lead tetraacetate, potassium ferricyanide or bromine were unsuccessful (no reaction, mixtures containing several by-products or resinous material). With lead dioxide (in excess), the employed solvents are acetic acid or an appropriate mixture acetic acid (or formic acid):organic solvent. This implies previous attempts for the determination of the reaction mixture. Depending on the substituents, the

Table IV

Compounds **2**

2 [18]	Method	Yield %	Mp °C	Formula	Analyses Calcd. (Found) C	H	N	IR, ν cm^{-1} N-H C=O	^1H NMR [a] δ ppm
a	B	92	141 [b]	$C_{15}H_{15}N_3O$	71.12 (71.04)	5.97 (6.08)	16.59 (16.68)	3420 1670	2.8 (d, 3H), 6.9-7.8 (m, 12H)
b	B	95	107 [b]	$C_{16}H_{17}N_3O$	71.88 (71.96)	6.41 (6.38)	15.70 (15.72)	3420 1680	1.1 (t, 3H), 3.3 (m, 2H), 6.9-7.7 (m, 12H)
c	B	88	128 [b]	$C_{17}H_{19}N_3O$	72.57 (72.69)	6.81 (6.76)	14.94 (15.04)	3430 1680	0.95 (t, 3H), 1.3-1.9 (m, 2H), 3.1-3.5 (m, 2H), 7.1-8 (m, 12H)
d	B	93	132 [b]	$C_{18}H_{21}N_3O$	73.19 (73.11)	7.17 (7.22)	14.23 (14.25)	3430 1680	1 (t, 3H), 1.3-1.8 (m, 4H), 3.1-3.5 (m, 2H),7.1-8 (m, 12H)
e	B	90	162 [b]	$C_{20}H_{23}N_3O$	74.43 (74.48)	7.21 (7.18)	13.07 (13.11)	3410 1680	1.2-2.3 (m, 10H), 3.8 (broad, 1H, cyclohexyl), 7-7.8 (m, 12H)
f	B	97	168 [b]	$C_{21}H_{19}N_3O$	76.57 (76.64)	5.81 (5.82)	12.76 (12.67)	3420 1680	4.5 (d, 2H, CH_2), 7-8.3 (m, 17H)
g	A,B	70,80	173 [b,c]	$C_{20}H_{17}N_3O$				3380 1680	7.1-8 (m, 16H), 9.4 (s, 1H, NH)
h	B	95	195 [d]	$C_{21}H_{19}N_3O_2$	73.02 (72.91)	5.55 (5.59)	12.17 (12.12)	3360 1690	3.9 (s, 3H), 6.7-8.2 (m, 15H), 9.7 (broad, 1H, NH)
i	B	96	133 [d]	$C_{21}H_{19}N_3O_2$	73.02 (72.95)	5.55 (5.53)	12.17 (12.21)	3330 1670	3.9 (s, 3H), 6.7-8.1 (m, 15H), 9.5 (s, 1H, NH)
j	B	93	200 [d]	$C_{21}H_{19}N_3O_2$	73.02 (73.07)	5.55 (5.49)	12.17 (12.22)	3360 1690	3.8 (s, 3H), 6.9-8 (m, 15H), 9.3 (s, 1H, NH)
k	B	80	186 [e]	$C_{23}H_{21}N_3O_3$	71.30 (71.20)	5.46 (5.36)	10.85 (10.84)	3320 1680	1.35 (t, 3H), 4.3 (q, 2H, CH_2), 7.2-8.1 (m, 15H), 9.75 (s, 1H, NH)
l	B	90	223 [e]	$C_{20}H_{16}BrN_3O$	60.92 (61.13)	4.09 (4.16)	10.66 (10.78)	3370 1680	7.1-8 (m, 15H), 9.45 (broad, 1H, NH)
m	B	88	222 [e]	$C_{20}H_{16}ClN_3O$	68.67 (68.51)	4.61 (4.53)	12.01 (12.10)	3370 1680	7-8.1 (m, 15H), 9.5 (broad, 1H, NH)
n	B	74	171 [f]	$C_{20}H_{16}N_4O_3$	66.66 (66.47)	4.48 (4.47)	15.55 (15.68)	3330 1670	7.3-8.2 (m, 15H), 9.9 (s, 1H, NH)
o	A,B	60,70	260 [g:h]	$C_{20}H_{16}N_4O_3$	66.66 (66.52)	4.48 (4.55)	15.55 (15.66)	3320 1680	7.3-8.4 (m, 15H), 10.1 (s, 1H, NH)
p	A	62	151 [b:i]	$C_{21}H_{19}N_3O$	76.57 (76.67)	5.81 (5.77)	12.76 (12.86)	3370 1680	5.3 (s, 2H, CH_2), 7-8.1 (m, 16H), 9.3 (1H, NH)
q	A,B	57,94	160 [j]	$C_{21}H_{19}N_3O$	76.57 (76.49)	5.81 (5.89)	12.76 (12.81)	3380 1690	2.4 (s, 3H), 7.1-7.9 (m, 15H), 9.5 (s, 1H, NH)
r	B	89	176 [d]	$C_{21}H_{18}BrN_3O$	61.77 (61.74)	4.44 (4.38)	10.29 (10.35)	3370 1670	2.4 (s, 3H, 7.2-7.95 (m, 14H), 9.6 (s, 1H, NH)
s	B	96	188 [d:e]	$C_{21}H_{18}ClN_3O$	69.32 (69.36)	4.99 (4.97)	11.55 (11.50)	3370 1690	2.4 (s, 3H), 7.1-7.9 (m, 14H), 9.6 (s, 1H, NH)
t	A	85	192-194 [i]	$C_{21}H_{19}N_3O_2$	73.02 (73.12)	5.55 (5.50)	12.17 (12.21)	3370 1680	3.6 (s, 3H), 6.9-8.1 (m, 15H), 9.5 (s, 1H, NH)
u	A,B	87,95	178 [d]	$C_{20}H_{16}ClN_3O$	68.67 (68.57)	4.61 (4.67)	12.01 (12.03)	3390 1690	7-8 (m, 15H), 9.4 (s, 1H, NH)
v	B	77	188 [e]	$C_{20}H_{15}BrClN_3O$	56.03 (55.89)	3.53 (3.60)	9.80 (9.72)	3330 1670	7.3-8.15 (m, 14H), 9.7 (s, 1H, NH)
w	B	75	241 [d:e]	$C_{20}H_{15}ClN_4O_3$	60.84 (60.95)	3.83 (3.90)	14.19 (14.26)	3380 1700	7.2-8.4 (m, 14H), 10.5 (broad, 1H, NH)
x	A	67	194 [k]	$C_{21}H_{18}N_4O_3$	67.37 (67.25)	4.85 (4.91)	14.97 (14.93)	3390 1680	5.4 (s, 2H, CH_2), 7.2-8.3 (m, 15H), 9.6 (s, 1H, NH)
y	A	70	204 [i,l]	$C_{20}H_{16}N_4O_3$				3390 1700	7-8.2 (m, 15H), 9.5 (broad, 1H, NH)
z	A,B	91,85	178 [k]	$C_{19}H_{16}N_4O$	72.13 (72.01)	5.10 (5.14)	17.71 (17.77)	3390 1700	7-8.1 (m, 13H), 8.7 (d, 2H, pyridyl), 9.65 (s, 1H, NH)
aa	A,B	70,85	180 dec [d]	$C_{18}H_{14}N_4O_4$	61.71 (61.71)	4.03 (4.00)	15.99 (16.08)	3330 1690	7-8 (m, 13H), 9.5 (s, 1H, NH)
ab	B	91	230 [m]	$C_{19}H_{16}N_4O_5$	60.00 (59.92)	4.24 (4.33)	14.73 (14.85)	3400 1700	3.75 (s, 3H), 7-8 (m, 12H), 9.5 (s, 1H, NH)
ac	B	76	195 [e]	$C_{18}H_{13}BrN_4O_4$	50.37 (50.57)	3.05 (2.99)	13.05 (13.14)	3320 1680	7.1-7.9 (m, 12H), 9.6 (s, 1H, NH)
ad	B	97	201 [e]	$C_{18}H_{13}ClN_4O_4$	56.19 (56.12)	3.41 (3.42)	14.56 (14.65)	3370 1700	7-8 (m, 12H), 9.6 (s, 1H, NH)
ae	B	75	230 [e:g]	$C_{18}H_{13}N_5O_6$	54.68 (54.60)	3.31 (3.36)	17.72 (17.69)	3380 1710	6.6-8.4 (m, 12H), 10.1 (broad, 1H, NH)
af	A,B	60,94	222 [e]	$C_{18}H_{14}N_4O_3S$	59.00 (58.85)	3.85 (3.78)	15.29 (15.36)	3320 1670	6.9-7.85 (m, 11H), 8.1 (broad, 2H), 9.45 (broad, 1H, NH)

Table IV continued

2 [18]	Method	Yield %	Mp °C	Formula	Analyses Calcd. (Found) C	H	N	IR, ν cm^{-1} N-H C=O	^{1}H NMR [a] δ ppm
ag	B	88	174 [e]	$C_{19}H_{16}N_4O_4S$	57.56 (57.45)	4.07 (4.20)	14.13 (14.02)	3320 1680	3.8 (s, 3H), 7-7.8 (m, 10H), 8.1 (d, 2H), 9.3 (s, 1H, NH)
ah	B	87	211 [e]	$C_{18}H_{13}BrN_4O_3S$	48.55 (48.64)	2.94 (3.01)	12.58 (12.69)	3320 1680	7.2-7.8 (m, 10H), 8.1 (d, 2H), 9.6 (broad, 1H, NH)
ai	B	85	220 [e]	$C_{18}H_{13}ClN_4O_3S$	53.93 (53.73)	3.27 (3.33)	13.98 (13.88)	3320 1670	7.1-7.8 (m, 10H), 8.1 (d, 2H),9.6 (broad, 1H, NH)

[a] All compounds were measured in DMSO-d_6 except **2a** (in deuterioacetone:deuteriobenzene), **2b** (in deuterioacetone) and **2e,t** (in deuteriobenzene:-DMSO-d_6). [b] Cyclohexane. [c] Lit [16] mp 173°. [d] 1-Butanol. [e] *n*-Butyl acetate. [f] 1-Propanol. [g] Dimethylformamide. [h] Xylene. [i] Benzene. [j] Methanol. [k] Ethanol. [l] Lit [19] mp 198-200°. [m] Ethylene glycol.

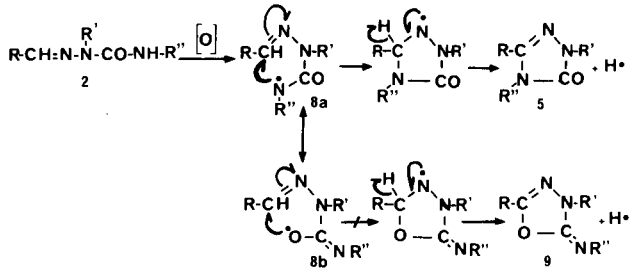
oxidation is carried out at room temperature or at 80-90°. In most cases, the reaction occurs within 30 minutes.

A number of novel triazolones **5** has been synthesized by this method and are listed in Tables III and V with their corresponding reaction mixture.

Scheme IV shows the radical processes that we suggest for the above transformation.

The action of the oxidant proceeds by the loss of an hydrogen radical from **2**, providing thus a radical **8** which canonical forms **8a** and **8b** correspond to the tautomeric forms of the starting compound. The cyclization of such a radical theoretically should give a mixture of triazolone **5**

SCHEME IV



and 2-imino-1,3,4-oxadiazoline **9** (**9** has been synthesized through another path by Huisgen *et al.*, wherein R = R'

Table V

Compounds **5**

5 [18]	Reaction time [a] (minutes)	Yield % [b]	Mp °C	Formula	Analyses Calcd. (Found) C	H	N	IR, ν cm^{-1} C=O	^{1}H NMR [c] δ ppm
e	60 (A)	34 (H)	113 [d]	$C_{20}H_{21}N_3O$	75.21 (75.28)	6.63 (6.57)	13.16 (13.20)	1710	1.2-2.2 (m, 10H), 3.8 (broad, 1H, cyclohexyl), 7.2-8.3 (m, 10H)
f	180 (A)	85 (H)	100 [e]	$C_{21}H_{17}N_3O$	77.04 (77.17)	5.23 (5.32)	12.84 (12.94)	1710	4.7 (s, 2H, CH_2), 7.2-8.3 (m, 15H)
g	10 (B)	95 (C)	221 [f,g]	$C_{20}H_{15}N_3O$				1700	7.3-8.1 (m)
h	20 (B)	81 (D)	176 [h]	$C_{21}H_{17}N_3O_2$	73.45 (73.33)	4.99 (5.06)	12.24 (12.21)	1720	3.6 (s, 3H), 7.2-7.8 (m, 12H), 8.1 (d, 2H)
i	10 (B)	72 (D)	190 [h]	$C_{21}H_{17}N_3O_2$	73.45 (73.29)	4.99 (5.04)	12.24 (12.17)	1700	3.5 (s, 3H), 6.6-7.6 (m, 12H), 8.3 (d, 2H)
j	15 (B)	93 (E)	232 [e,i]	$C_{21}H_{17}N_3O_2$				1710 [i]	[22]
k	300 (A)	40 (C)	194 [j]	$C_{23}H_{19}N_3O_3$	71.67 (71.70)	4.97 (4.92)	10.90 (10.97)	1710	1.45 (t, 3H), 4.5 (q, 2H), 7.3-8.3 (m, 14H)
l	75 (A)	50 (C)	220 [e]	$C_{20}H_{14}BrN_3O$	61.24 (61.39)	3.60(3.64)	10.71 (10.75)	1710	7.2-7.8 (m, 12H), 8.15 (d, 2H)
m	30 (A)	95 (C)	206 [j,k]	$C_{20}H_{14}ClN_3O$				1710 [k]	7-7.5 (m, 12H), 8.45 (d, 2H)
p	15 (B)	78 (C)	158 [f]	$C_{21}H_{17}N_3O$	77.04 (77.17)	5.23 (5.28)	12.84 (12.94)	1690	5 (s, 2H), 6.8-7.8 (m, 15H)
q	20 (B)	63 (C)	155 [f]	$C_{21}H_{17}N_3O$	77.04 (77.04)	5.23 (5.18)	12.84 (12.78)	1710	2.25 (s, 3H), 7.2-7.75 (m, 12H), 8.1 (d, 2H)
r	15 (A)	40 (I)	206 [e]	$C_{21}H_{16}BrN_3O$	62.08 (62.03)	3.97 (4.02)	10.34 (10.27)	1720	2.3 (s, 3H), 7-7.7 (m, 11H), 8.1 (d, 2H)
s	30 (B)	59 (I)	190 [h]	$C_{21}H_{16}ClN_3O$	69.71 (69.70)	4.46 (4.46)	11.61 (11.70)	1710	2.3 (s, 3H), 7-7.7 (m, 11H), 8.1 (d, 2H)
t	20 (B)	85 (C)	174 [f]	$C_{21}H_{17}N_3O_2$	73.45 (73.46)	4.99 (4.94)	12.24 (12.08)	1700	3.8 (s, 3H), 6.9-7.7 (m, 12H), 8.1 (d, 2H)

Table V continued

5 [18]	Reaction time [a] (minutes)	Yield % [b]	Mp °C	Formula	C	H	N	IR, ν cm^{-1} C=O	Analyses Calcd. (Found ^{1}H NMR [c] δ ppm
u	15 (B)	90 (C)	188 [e]	$C_{20}H_{14}ClN_3O$	69.07 (68.89)	4.06 (4.12)	12.08 (12.14)	1710	6.8-7.5 (m, 12H), 8.55 (d, 2H)
v	10 (A)	30 (H)	202 [h:l]	$C_{20}H_{13}BrClN_3O$	56.29 (56.41)	3.07 (2.96)	9.85 (9.74)	1710	7.4-8.3 (m)
x	15 (B)	67 (C)	140-142 [f]	$C_{21}H_{16}N_4O_3$	67.73 (67.67)	4.33 (4.39)	15.05 (15.11)	1700	5.15 (s, 2H), 7.3-7.7 (m, 12H), 8.25 (d, 2H)
y	20 (B)	67 (H)	193 [f:m,n]	$C_{20}H_{14}N_4O_3$				1720	7.3-8.4 (m)
z	20 (B)	83 (C)	187 [f]	$C_{19}H_{14}N_4O$	72.60 (72.45)	4.949(4.53)	17.82 (17.80)	1720	7.3-7.8 (m, 10H), 8.15 (d, 2H), 8.75 (d, 2H, pyridyl)
aa	15 (B)	96 (G)	243 [h]	$C_{18}H_{12}N_4O_4$	62.07 (62.10)	3.47 (3.44)	16.09 (16.06)	1710	6.3 (d, 1H), 7.3-7.7 (m, 9H), 8.1 (d, 2H)
ab	15 (B)	55 (F)	210 [o]	$C_{19}H_{14}N_4O_5$	60.32 (60.17)	3.73 (3.80)	14.81 (14.93)	1720	3.9 (s, 3H), 6.35 (d, 1H), 7.2-8.2 (m, 10H)
ac	30 (A)	40 (H)	217 [e]	$C_{18}H_{11}BrN_4O_4$	50.60 (50.55)	2.60 (2.62)	13.11 (13.16)	1710	[22]
ad	45 (A)	25 (I)	198 [e]	$C_{18}H_{11}ClN_4O_4$	56.48 (56.27)	2.90 (2.95)	14.64 (14.73)	1720	6.5 (d, 1H), 7.2-7.7 (m, 8H), 8 (d, 2H)
ae	480 (B)	20 (K)	185 [l:o]	$C_{18}H_{11}N_5O_6$	54.97 (54.77)	2.82 (2.89)	17.81 (17.90)	1740	6.8 (d, 1H), 7.3-8.2 (m, 8H), 8.5 (d, 2H)
af	60 (B)	97 (H)	222 [h:j]	$C_{18}H_{12}N_4O_3S$	59.33 (59.45)	3.32 (3.35)	15.38 (15.39)	1720	6.9 (d, 1H), 7.3-7.8 (m, 9H), 8.1 (d, 2H)
ag	60 (A)	20 (I)	206 [l]	$C_{19}H_{14}N_4O_4S$	57.86 (57.72)	3.58 (3.64)	14.21 (14.08)	1720	3.9 (s, 3H), 6.9 (d, 1H), 7.2-7.7 (m, 8H), 8 (d, 2H)
ah	90 (A)	60 (J)	165 [h]	$C_{18}H_{11}BrN_4O_3S$	48.77 (48.97)	2.50 (2.54)	12.64 (12.70)	1720	6.9 (d, 1H), 7.3-8.2 (m, 10H)
ai	240 (B)	52 (L)	180 [j]	$C_{18}H_{11}ClN_4O_3S$	54.21 (54.18)	2.78 (2.79)	14.05 (14.17)	1720	6.9 (d, 1H), 7.3-8.2 (m, 10H)

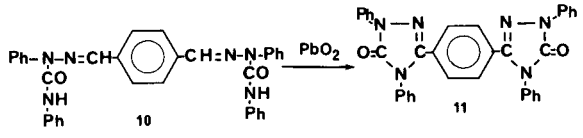
[a] Temperature: A, 25°; B, 80-90°. [b] Reaction mixture: C, acetic acid; D, acetic acid:dichloromethane (1:1); E, acetic acid:dichloromethane (1:2); F, acetic acid:dimethylformamide (2:1); G, acetic acid:dimethylformamide (1:1), H, formic acid:dichloromethane (1:1); I, formic acid:dichloromethane (1:2); J, formic acid:dichloromethane (1:3); K, formic acid:dichloromethane:dimethylformamide (2:1:1); L, formic acid:dichloromethane:dimethylformamide (2:1:2). [c] All compounds were measured in DMSO-d_6 except **5e** (in deuterioacetone:DMSO-d_6), **5l** (in deuteriobenzene:DMSO-d_6), **5m,u** (in deuterioacetone:deuteriobenzene), **5p** (in deuteriobenzene) and **5aa** (in deuteriochloroform). [d] Methanol. [e] Purified by column chromatography (see Experimental). [f] Ethanol. [g] Lit [20] mp 221.5-222°. [h] 1-Butanol. [i] Lit [21] mp 229-232°; ir 1705 cm^{-1} (C=O). [j] *n*-Butyl acetate. [k] Lit [21] mp 204-207°; ir 1715 cm^{-1} (C=O). [l] 3-Methyl-1-butanol. [m] Benzene. [n] Lit [20] mp 193-194°. [o] Ethylene glycol.

= R'' = C_6H_5 [10]). Practically, triazolones **5** are the sole products. This may be ascribed to the preponderance of **8a** over **8b**, owing to a greater resonance energy between the radical center and the aromatic ring R'' in **8a** than in **8b**.

Actually, we noticed that when R'' bears electron-withdrawing groups, the yields are somewhat lower and in some cases, no reaction occurs. Apparently, it is due to a more difficult generation of **8**. When R'' is an alkyl group (with the exception of cyclohexyl) only tar products are formed.

Finally, a double oxidation has been achieved by converting terephthaldehyde bis(2,4-diphenylsemicarbazone) **10** into 1,4-bis(2,4-dihydro-2,5-diphenyl-1,2,4-triazol-3-one-5-yl)benzene (**11**) (Scheme V). This very fluorescent compound is insoluble in organic solvents but slightly soluble in refluxing dimethylformamide.

SCHEME V



Assignment for the structures of the new compounds was provided by ir and ^{1}H-nmr spectra. The ir values correspond to those reported in the literature.

EXPERIMENTAL

Melting points were taken with a Buchi oil heated apparatus and are uncorrected. The ir spectra were recorded on a Perkin Elmer 337 spectrophotometer as potassium bromide disks. The ^{1}H-nmr spectra were obtained on a Varian T-60 spectrometer and are reported as δ values (ppm) relative to tetramethylsilane as an internal standard.

Semicarbazones **2**. Method A.

To a stirred solution of 20 mmoles of **6** in 50 ml of dry benzene, were added 40 ml of arylisocyanate. The mixture was refluxed for 12 hours. After removal of the benzene, the residue **2** was recrystallized from appropriate solvent.

Method B.

To a stirred solution of 10 mmoles of **7** in 15 ml of ethanol at 0°, were added 20 mmoles of primary amine at once. After a few minutes, semicarbazones **2** were isolated by filtration or removal of the ethanol and recrystallized from appropriate solvent.

2-(*N,N*-Disubstitutedamino)-1,3,4-oxadiazoles **3**.

To a solution of 2 mmoles of **1** in 10 ml of formic acid, was added 0.48 g (2 mmoles) of lead dioxide. The mixture was stirred at room temperature for 20 minutes, filtered and extracted with a mixture of dichloro-

methane:water (1:1). The organic layer was dried over anhydrous sodium sulfate and dichloromethane was removed. The residue **3** was recrystallized from appropriate solvent.

2-(*N,N*-Dimethylamino)-5-(4-nitrophenyl)-1,3,4-oxadiazole (**3e**).

This compound had ir: 1630 cm^{-1} (C=N); nmr: δ 3.1 (s, 6H), 7.9-8.5 (m, 4H).

Anal. Calcd. for $C_{10}H_{10}N_4O_3$: C, 51.28; H, 4.30; N, 23.92. Found: C, 51.34; H, 4.32; N, 24.01.

Triazolones **5e, 5f, 5r, 5s, 5v** and **5ac-ai**.

To a stirred appropriate reaction mixture (Table V) containing 1 mmole of **2**, was added 0.72 g (3 mmoles) of lead dioxide at once. Complete oxidation was obtained for some cases by addition of a new excess of lead dioxide, chiefly for **2ae**. Then the solution was filtered, washed with water and dried over anhydrous sodium sulfate. After removal of the dichloromethane, the compounds **5** were recrystallized from adequate solvent except for **5f, 5r, 5ac** and **5ad**. These compounds were purified by column chromatography on silica gel 60 0.05-0.2 mm (Machery-Nagel) using dichloromethane:petroleum ether 40-60 (1:1) as the eluent. For compound **5ai**, a total removal of the solvent was done and the product was recrystallized.

Triazolones **5g-m, 5p, 5q, 5t, 5u** and **5x-ab**.

To a solution of 1 mmole of **2** in acetic acid or a mixture of acetic acid with dichloromethane or dimethylformamide (Table V), was added 0.36 g (1.5 mmole) of lead dioxide at once. In the absence of dichloromethane, the reaction mixture after filtration was poured onto ice-water; in its presence, this solvent was first removed. The products precipitated and were recrystallized from adequate solvent except for **5j, 5l** and **5u** which were chromatographed as above but with ethyl acetate as the eluent for **5j**.

2-Chloroformylhydrazones **7**.

To a solution of 0.2 mole of **6** in 700 ml of dry benzene at 0°, was added 180 ml of a 10% solution of phosgene in dry toluene. Then 20 g of dry pyridine in 200 ml of dry benzene were added at 0° dropwise under vigorous stirring except for **7f**. The completion of the reaction was achieved by refluxing the reaction mixture for 90 minutes. The pyridinium salt was removed by filtration under reduced pressure and the filtrate was evaporated *in vacuo*. A solid was obtained for compounds **7a, 7d** and **7e** which was recrystallized from appropriate solvent. Compounds **7d** and **7e** are relatively stable and therefore their ir and ^{1}H-nmr spectra could be done. Compound **7b** was obtained as an oil which recrystallizes in anhydrous ethyl ether but undergoes rapid decomposition. Compound **7f** was obtained as a salt which was difficult to purify. For better yield in synthesis of **2** (method B) all those compounds **7** must be used within 2 days.

5-Nitro-2-furaldehyde 2-Chloroformyl-2-phenylhydrazone (**7d**).

This compound had ir: 1720 cm^{-1} (C=O); nmr (DMSO-d_6): δ 6.9-8 (m).

Anal. Calcd. for $C_{12}H_8ClN_3O_4$: C, 49.08; H, 2.75; N, 14.31. Found: C, 49.12; H, 2.77; N, 14.36.

5-Nitro-2-thiophenaldehyde 2-Chloroformyl-2-phenylhydrazone (**7e**).

This compound had ir: 1720 cm^{-1} (C=O); nmr (DMSO-d_6): δ 7.1-8.1 (m).

Anal. Calcd. for $C_{12}H_8ClN_3O_3S$: C, 46.53; H, 2.60; N, 13.57. Found: C, 46.68; H, 2.62; N, 13.56.

Terephthaldehyde bis(2,4-Diphenylsemicarbazone) (**10**).

To a stirred solution of 3.14 g (10 mmoles) of terephthaldehyde diphenylhydrazone in 50 ml of dry xylene, was added 4.76 g (40 mmoles) of phenylisocyanate. The mixture was refluxed for 12 hours. After cooling, it was filtered and the residue was recrystallized from xylene giving 3.87 g (70%), mp 288° (Maquenne apparatus); ir: 3350 cm^{-1} (N-H), 1680 cm^{-1} (C=O); nmr [22]; ms: M^+, 555 (M = 552.6).

Anal. Calcd. for $C_{34}H_{28}N_6O_2$: C, 73.89; H, 5.11; N, 15.21. Found: C, 73.75; H, 5.14; N, 15.24.

1,4-bis(2,4-Dihydro-2,5-diphenyl-1,2,4-triazol-3-one-5-yl)benzene (**11**).

To a stirred solution of 0.49 g (0.9 mmole) of **10** in 15 ml of a mixture of acetic acid:dichloromethane (1:1), was added 0.5 g (21 mmoles) of lead dioxide. The mixture was heated at 80-90° for 20 minutes and then filtered. The solvent was evaporated *in vacuo* and gave 0.31 g (63%) of **11** which was recrystallized from dimethylformamide in which it was slightly soluble, mp 284° (Maquenne apparatus); ir: 1720 cm^{-1} (C=O); nmr [22]; ms: M^+, 548 (M = 548.6).

Anal. Calcd. for $C_{34}H_{24}N_6O_2$: C, 74.44; H, 4.41; N, 15.32. Found: C, 74.40; H, 4.43; N, 15.36.

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[17] Compounds **7** react very slowly with ethanol at 0°.

[18] Compounds **2aa-ai** and **5aa-ai** have been synthesized with the view to test them as antibacterian agents.

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[22] This compound is insoluble in the usual deuterio solvents.