Asian Journal of Chemistry Vol. 11, No. 1 (1999), 59–64

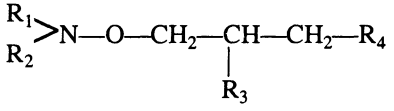
Synthesis of Some Amino-oxy Derivatives of Propane

SONAL RAJORA, DILIP KHATRI and G.L. TALESARA*
Department of Chemistry
University College of Science
Sukhadia University, Udaipur-313 001, India

Some phthalimido-oxy, amino-oxy, biguanidino-oxy and related derivatives of propane have been prepared for the first time using allyl-oxy phthalimide as starting material. This was brominated to give dibromo phthalimido-oxy propane. This on hydrolysis gave dibromo amino-oxy propane. Alternatively this was condensed with N-hydroxy phthalimide to give triphthalimido-oxy propane which on hydrolysis gave triamino-oxy propane. Amino-oxy compounds on condensation with substituted aryl dicyandiamide gave various biguanidino-oxy derivatives.

INTRODUCTION

Many compounds containing —O—N< group, mainly phthalimido-oxy[1], amino-oxy[2] and Biguanidino-oxy[3,4] compounds have shown to possess diverse pharmacological activities[5,6] such as CNS depressant, cardio-vascular agents, antibacterial, antifungal, antimalarial and others.[7,8] It was thought worth while to prepare some compounds having more than one amino-oxy group. This idea prompted us to synthesize some amino-oxy derivatives of propane of the following type:



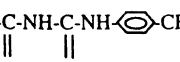
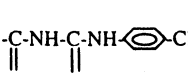
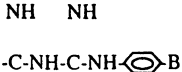
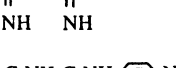
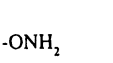
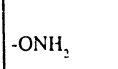
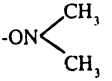
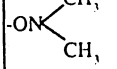
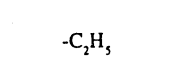
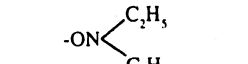
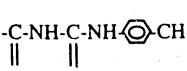
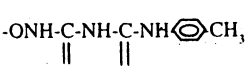
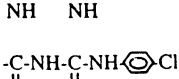
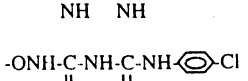
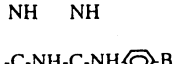
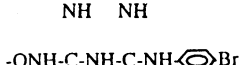
shown in Table-1.

RESULTS AND DISCUSSION

The starting material used was allyl-oxyphthalimide for the synthesis of derivatives of the type Ia–In. Nucleophilic substitution of allylic halide is faster than haloalkanes (confirmed by comparison of rate of reaction with haloalkanes). Substitution of phthalimido-oxy group at allylic carbon was carried out. Stability of these compounds is sufficient towards mild oxidising and reducing agents.

The ethylenic double bond was converted to dibromo derivative by usual addition reaction. Substitution of phthalimido-oxy group took a longer time and

TABLE-1

Comp. No.	R_1	R_2	R_3	R_4
Ia	-H	-H	-Br	-Br
Ib	$-CH_3$	$-CH_3$	-Br	-Br
Ic	$-C_2H_5$	$-C_2H_5$	-Br	-Br
Id	-H		-Br	-Br
Ie	-H		-Br	-Br
If	-H		-Br	-Br
Ig	-H		-Br	-Br
Ih	-H	-H	$-ONH_2$	$-ONH_2$
Ii	$-CH_3$	$-CH_3$		
Ij	$-C_2H_5$	$-C_2H_5$		
Ik	-H			Same as R^3
Il	-H			Same as R^3
Im	-H			Same as R^3
In	-H			Same as R^3

produced tri-phthalimido-oxy derivative (V). Here it may be noted that primary bromine of dibromo compound is replaced with greater ease than secondary; thus the reaction mixture taken out prior to completion is composed of two components: one having bromine on C-2 with incomplete reaction and the other with complete reaction producing triphthalimido-oxy derivative. Formation of monobromo derivative can be explained on the basis of steric hindrance.

Allyl-oxy phthalimide(III) was prepared from N-hydroxy phthalimide(II) and allyl bromide by the modification of the method of Bauer and Suresh.[9] Bromination of this gave 2,3-dibromophthalimido-oxy propane(IV).

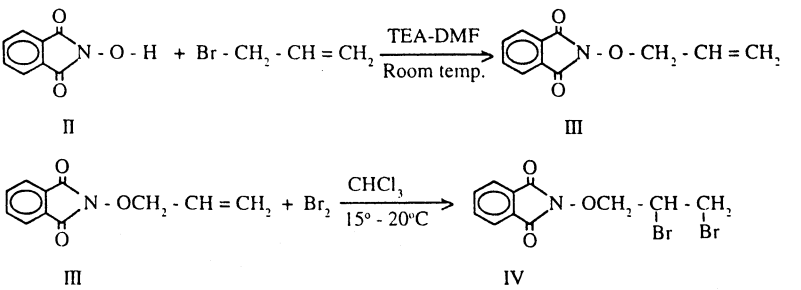
Condensation of IV with II gave tri-phthalimido-oxy propane (V). Both IV and V on hydrolysis with acetic acid and hydrobromic acid gave the corresponding amino-oxy compounds (Ia and Ih).

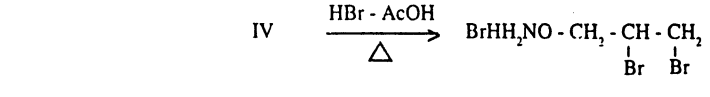
Ia and Ih on condensation with various alkyl halides gave N-substituted amino-oxy compounds. The same on condensation with various aryl dicyandiamides gave the corresponding biguanidino-oxy compounds.

IR spectra

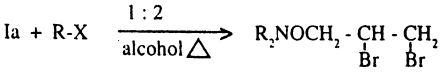
IR spectra of phthalimido-oxy compounds show peak at 1747–1726 cm^{-1} which is due to (C=O) stretching. Peak at 1616–1598 cm^{-1} is asymmetric stretching of (N—O) covalent bond. Out-of-plane bending of aromatic C=C—H appears at 713—700 cm^{-1}. Peak at 1238 cm^{-1} in spectrum of IV is because of CH_2Br group. Peak in the region 1404–1398 cm^{-1} is due to (C—O) stretching. Strong broad absorption between 3024–2997 cm^{-1} in the spectra of amino-oxy compounds is due to asymmetric and symmetric stretching in $\overset{\oplus}{N}H_3$ group. In addition to above, the multiple combination bands of medium intensity occur near 2800 cm^{-1}. Peak at 1242 cm^{-1} in the spectra of Ia is due to CH_2Br group. Peak at 1647–1610 cm^{-1}, 1452–1417 cm^{-1} in the spectra of biguanidino-oxy compounds is due to (C=N) stretching of guanidino-oxy group. (N—O) symmetrical stretching appears at 1388–1253 cm^{-1}. Free secondary (N—H) stretching absorbs at 3440–3411 cm^{-1}. Peak at 1360–1294 cm^{-1} is due to (C—N) stretching of (C—NH—C). Out-of-plane bending of ring C—H appears in the region 817–717 cm^{-1} and in-plane bending absorbs in the region 1087–1003 cm^{-1}.

The Following reaction sequences are used to synthesize the above said compounds:

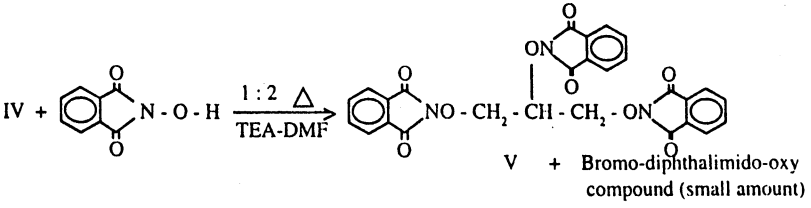




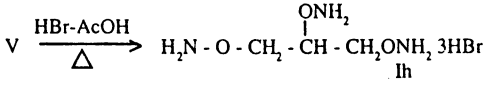
Ia



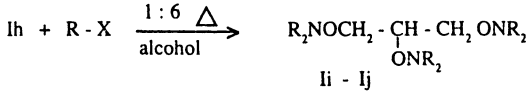
Ib - Ic



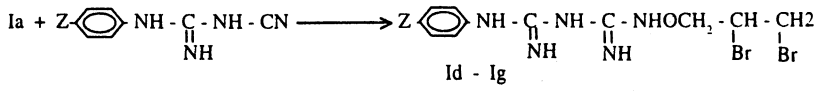
V + Bromo-diphthalimido-oxy compound (small amount)



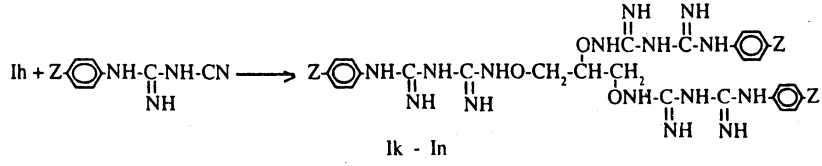
Ih



Ii - Ij



Id - Ig



Ik - In

(Here Z may be $-CH_3$, -Cl, -Br or $-NO_2$)

EXPERIMENTAL

All the melting points are uncorrected; purity of compounds was tested by TLC and other usual methods.

Preparation of allyl-oxy phthalimide

Method of Bauer and Suresh[9] has been used with slight modification. N-hydroxy phthalimide (0.1 mol.) and allyl bromide (0.1 mol.) in DMF 60 mL were stirred for 6 h in presence of triethylamine (0.2 mol). The white solution was filtered and the filtrate added to 500 g crushed ice. White precipitate of allyl-oxyphthalimide (m.p. 48°C) was obtained. It was recrystallised from alcohol. Yield: 75%; m.p. 52°C.

Preparatin of 2,3-dibromo phthalimido-oxy propane

Allyl-oxy phthalimide (0.1 mol) was dissolved in 30 mL chloroform and 10% solution of bromine in chloroform was added dropwise with constant stirring foring 2 h, till the colour of bromine does not disappear. On cooling this at 5°C crystals of 2,3-dibromo phthalimido-oxy propane appeared (m.p. 100°C). Recrystallisation from chloroform raised the m.p. to 102°C. Yield 98%.

Preparation of triphthalimido-oxy propane

2,3-Dibromo phthalimido-oxy propane (0.2 mol) and N-hydroxy phthalimide (0.4 mol) were dissolved in DMF 150 mL and were refluxed with stirring in presence triethylamine (0.4 mol) for 15 h. After cooling, the solution was filtered and the filtrate was added to 1000 g crushed ice. The brown precipitate was filtered and dried (m.p. 182°C). Yield 55%.

Hydrolysis of phthalimido-oxy derivatives

Phthalimido-oxy compounds (0.02 mol.) were boiled in a mixture of 47% HBr (30 mL) and glacial acetic acid (20 mL) for 2 min. On cooling, the phthalic acid obtained was filtered. The filtrate on evaporation *in vacuo* yielded a dirty white solid. This was washed with acetone. Solvent of crystallisation and physical data are presented in Table-2

TABLE-2
PHYSICAL DATA OF AMINO-OXY COMPOUNDS

Comp. No.	Mol. formula	Mol. wt	Solvent cryst.	m.p. °C	Yield %
Ia	$C_3H_8ONBr_3$	314	acetone	245	65
Ih	$C_3H_{14}O_3N_3Br_3$	380	acetone	270	60

Preparation of N-substituted amino-oxy compounds

Amino-oxy compound (0.01 mol) was dissolved in absolute alcohol. Alkyl halide was added to it and it was refluxed on water bath for 5 to 8 h. The mixture was filtered hot, diluted with water and a very dilute solution of base (Na_2CO_3 or $NaHCO_3$) was added dropwise. The precipitate obtained was recrystallised in different solvents. Solvent of crystallisation and physical data of compounds are presented in Table-3.

Preparation of Amino-oxy derivatives of biguanides

Aryl dicyandiamide (0.01 mol.) and amino-oxy compounds (Ia and Ih) were refluxed in absolute alcohol on a water bath for 11 to 22 h. The mixture was filtred hot, diluted with water and a very dilute solution of base (Na_2CO_3 or $NaHCO_3$) was added dropwise. The product formed was recrystallised in different solvents. Solvents of cystallisation and physical data are presented in Table-3.

TABLE-3
PHYSICAL DATA OF SYNTHESIZED COMPOUNDS

Comp. No.	Mol. formula	Mol. wt.	Mol. ratio of reactants	Reflux time (h)	Solvent cryst.	m.p. °C	Yield %
Ib	$C_5H_{11}ONBr_2$	261	1 : 2	6	alcohol	120	65
Ic	$C_7H_{15}ONBr_2$	289	1 : 2	5	alcohol	128	60
Id	$C_{12}H_{17}ON_5Br_2$	407	1 : 1	17	methanol	90	70
Ie	$C_{11}H_{14}ON_5Br_2Cl$	427.5	1 : 1	15	methanol	114	52
If	$C_{11}H_{14}ON_5Br_3$	472	1 : 1	11	ethanol	117	55
Ig	$C_{18}H_{14}O_3N_6Br_2$	438	1 : 1	13	benzene	103	60
Ii	$C_9H_{23}O_3N_3$	221	1 : 6	5	alcohol	205	70
Ij	$C_{15}H_{35}O_3N_3$	305	1 : 6	8	acetone	215	65
Ik	$C_{30}H_{41}O_3N_{15}$	659	1 : 3	14	methanol	190	70
Il	$C_{27}H_{32}O_3N_{15}Cl_3$	720.5	1 : 3	22	methanol	192	75
Im	$C_{27}H_{32}O_3N_{15}Br_3$	854	1 : 3	17	methanol	200	60
In	$C_{27}H_{32}O_9N_{18}$	752	1 : 3	12	methanol	180	55

Percentage compositin has been confirmed by elemental analysis.

ACKNOWLEDGEMENTS

The authors are thankful to the Head, Department of Chemistry, University College of Science, Sukhadia University, Udaipur, for providing necessary departmental facilities and to the Director, CDRI, Lucknow and co-ordinator, Catalysis Division, IIT, Chennai for spectral and elemental analyses.

REFERENCES

1. G.L. Talesara and (Late) K.S. Suresh, *Asian J. Chem.*, **3**, 428 (1991).
2. _____, *Ibid.*, **9**, 635 (1997).
3. Kitagava and Tomiyama, *J. Bio. Chem. Japan.* **11**, 265 (1929).
4. Fuller and King, *J. Chem. Soc.*, 963 (1947).
5. Nyberg and Christensen, *J. Am.. Chem. Soc.*, **78**, 781 (1956).
6. Curd and Rose, *J. Chem. Soc.*, 729 (1946).
7. P. Mamalis, *Xenobiotica*, **4–5**, 569 (1971).
8. D. McHale, J. Green and P. Mamalis, *J. Chem. Soc.*, 225 (1960).
9. L. Bauer and K.S. Suresh, *J. Org. Chem.*, **28**, 1604 (1963).

(*Received*: 22 June 1998; *Accepted*: 21 September 1998) AJC-1568