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SYNTHESIS OF PERHYDRO-1,5,2-DIOXAZINES
A NOVEL TYPE OF HETEROCYCLIC COMPOUNDS

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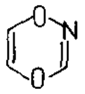
Abstract —— Derivatives of perhydro-1,5,2-dioxazine have been prepared by the reaction of N-substituted 2-hydroxycarbohydroxamic acids with the dimethyl acetals of aromatic aldehydes.

The six-membered ring system of 1,4,2-dioxazine (1) is known since 1967, when McHale [1] synthesized some 5,6-dihydro-3-phenyl-1,4,2-dioxazine-5-ones (2). However, the isomeric heterocyclic system of 1,5,2-dioxazine (3) does not as yet to have been isolated.



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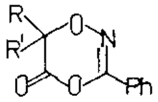
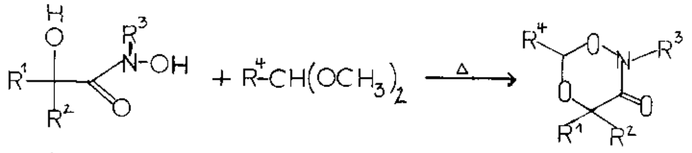


2

3

I now wish to report the synthesis of some derivatives of this novel type of compound by a method [2] used for the cyclisation of unsubstituted hydroxamic acids to 1,4,2-dioxazoles. Thus, treatment of the N-substituted 2-hydroxycarbohydroxamic acids 4a-d with the dimethyl acetals of benzaldehyde or 2-chlorobenzaldehyde in boiling benzene in the presence of p-toluenesulphonic acid gave perhydro-1,5,2-dioxazine-3-ones (5a-d) as crystalline products in yields of 35-60%. Attempts to prepare 5 by refluxing a solution of 4 and benzaldehyde in the presence of p-toluenesulphonic acid under the removal of water were unsuccessfull. The structure of 5 was confirmed by elemental analysis, by ir, by ^{1}H-nmr and by mass spectra. The infrared spectra showed a strong carbonyl band at the expected region [3] (1650 - 1665 cm^{-1}). A one proton signal due to the cyclic acetalic structure was observed at δ = 6,03 - 6,50 . Molecular peaks corresponding to the right molecular weights appeared in the mass spectra.



4a-d

5a-d

5	R^1	R^2	R^3	R^4
a	C_6H_5	C_6H_5	CH_3	C_6H_5
b	C_6H_5	H	CH_3	2-(Cl)C_6H_4
c	C_6H_5	C_6H_5	$CH_2C_6H_5$	C_6H_5
d	C_6H_5	H	$CH_2C_6H_5$	2-(Cl)C_6H_4

Experimental Part

General procedure:

A mixture of 0.01 mole of hydroxamic acid 4 [4], 0.012 mole dimethyl acetal of benzaldehyde or 2-chlorobenzaldehyde and 50 mg p-toluenesulphonic acid in 50 ml anhydrous benzene was refluxed for 4 hours. After removing the solvent the remaining oil was purified on a silica gel column (benzene/dichloromethane 1:1).

2-Methyl-4,4,6-triphenylperhydro-1,5,2-dioxazine-3-one (5a)

Yield 1.2g (35%); mp 99-100°C (cyclohexane), colorless prisms; ir(KBr) 1665 cm^{-1} (C=O); ^{1}H-nmr ($CDCl_3$) δ 3.40 (3H, s, CH_3), 6.17 (1H, s, O-CH-O), 7.27 - 7.77 (15H, m, ArH); MS m/e 345 (M^+), 317 (M^+ - CO), 239 (M^+ - PhCHO).

$C_{22}H_{19}NO_3$ (345.4)	calc.	C 76.50	H 5.54	N 4.06
	found	C 76.44	H 5.67	N 4.23

6-(2-Chlorophenyl)-2-methyl-4-phenylperhydro-1,5,2-dioxazine-3-one (5b)

Yield 1.8g (60%); mp 88°C (cyclohexane), colorless prisms; ir(KBr) 1665 cm^{-1}(C=O) ^{1}H-nmr ($CDCl_3$) δ 3.40 (3H, s, CH_3), 5.63 (1H, s, $\geq$CH), 6.50 (1H, s, O-CH-O), 7.26 - 7.86 (9H, m, ArH); MS m/e 303/305 (M^+), 258 (M^+ - CH_3NO).

$C_{16}H_{14}ClNO_3$ (303.7)	calc.	C 63.28	H 4.65	Cl 11.67	N 4.61
	found	C 63.03	H 4.72	Cl 11.42	N 4.75

2-Benzyl-4,4,6-triphenylperhydro-1,5,2-dioxazine-3-one (5c)

Yield 1.7g (40%); mp 96-97°C (cyclohexane), colorless prisms; ir (KBr) 1650 cm^{-1} (C=O); ^{1}H-nmr ($CDCl_3$)δ 4.96 (2H, q, N-CH_2, J 7 Hz), 6.03 (1H, s, O-CH-O), 7.26 - 7.70 (20H, m, ArH); MS m/e 421 (M^+), 316 (M^+ - PhCHO), 301 (M^+ - $PhCH_2NO$).

$C_{28}H_{23}NO_3$ (421.5) calc. C 79.79 H 5.50 N 3.32
found C 79.94 H 5.48 N 3.32

<u>2-Benzyl-6-(2-chlorophenyl)-4-phenylperhydro-1,5,2-dioxazine-3-one</u> (<u>5d</u>)
Yield 1.4g (37%); mp 121°C (benzene/n-hexane), colorless prisms; ir(KBr) 1665 cm^{-1} (C=O); ^1H-nmr ($CDCl_3$) δ 4.90 (2H, q, N-CH_2, J 7 Hz), 5.70 (1H, s, ⟩CH), 6.40 (1H, s, O-CH-O), 7.26 - 7.87 (14H, m, ArH); MS m/e 379/381 (M^+), 256/260 (M^+ - $PhCH_2NO$).

$C_{22}H_{18}ClNO_3$ (379.9) calc. C 69.56 H 4.78 Cl 9.33 N 3.69
found C 69.72 H 4.82 Cl 9.64 N 3.71

References

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