SYNTHESIS OF SOME NEW ARYL- AND ARYLOXYALKYL-N-(5-NITRO-2-FURYL)-CARBAMATES AS POTENTIAL ANTIMICROBIAL AGENTS

5-NITROFURAN derivatives are well known for their antibacterial[1] activity. Also many carbamates have been found to possess diverse types of biological activity including antifungal[2] and anthelmentic[3] activities, etc. No biological activity is described for alkyl-N-(5-nitro-2-furyl) carbamates known in literature[4,5]. Furthermore, the presence of aryloxy groups in many antimicrobial agents[6] seems to be their important feature. Fifteen new aryl- and aryloxyalkyl-N-(5-nitro-2-furyl) carbamates (I and II) have been synthesised with a view to evaluate their antifungal and antibacterial activities.

5-Nitro-2-furyl azide was made following the method of Singleton and Edwards[7] by treating an ethereal solution of 5-Nitro-2-furoyl chloride with aqueous sodium azide at 0–5° C when it separated out as an yellow crystalline solid. I.R. (Nujol, cm^{-1}): 2140 s (N=N=N) and 1680 s (C=O). The final carbamates were obtained by condensing various phenols and aryloxyalkanols with 5-nitrofuryl isocyanate obtained *in situ* from above 5-nitrofuroyl azide.

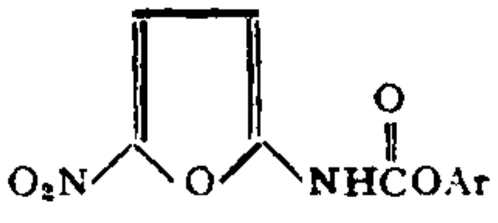
In a typical experiment for the preparation of the aryl carbamates, 5-nitro-2-furoyl azide (0·01 moles) in dry benzene (25 ml) was heated for 4 hours at 75° to liberate 5-nitro-2-furyl isocyanate (small quantity of black powder separated out due to polymerisation). Phenol (0·011 moles) in dry benzene (25 ml) was added to 5-nitro-2-furyl isocyanate, thus obtained, and heating was further continued for 6 hours. Ether (100 ml) was added to the cooled reaction mixture, organic layer washed with 10% hydrochloric acid followed by water and dried (Na_2SO_4). Removal of the organic solvent gave brownish yellow solid which was taken in benzene and chromatographed over silica gel. Elution with benzene afforded phenyl-N-(5-nitro-2-furyl) carbamate as yellow shining needles, which was further purified by recrystallising from benzene-petroleum ether (40–60° C).

The aryloxyalkyl carbamates were prepared by heating the azide and aryloxyalkanols directly without a solvent at 70° till the evolution of nitrogen ceased. The products were worked up as usual.

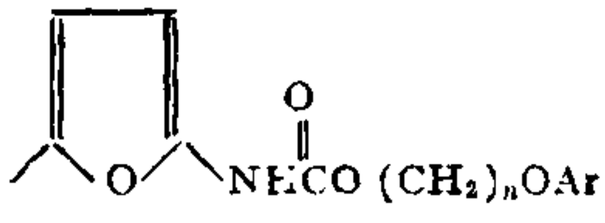
All the carbamates showed characteristic I.R. absorptions (Nujol, cm^{-1}): 3230 m (NH) and 1720 s (ester). Table I gives the details of various compounds prepared together with their melting points, elemental analyses and percentage yields. All compounds were recrystallised from benzene-petroleum ether (40–60°).

All the fifteen carbamates were tested *in vitro* for antifungal activity by agar dilution assay method[8] and for antibacterial activity by serial dilution tube method[9] using various pathogenic test organisms. Some of the compounds were found to possess moderate activity as shown in Table II.

TABLE I



I



II

Compound No.	Structure	*n*	Ar	m.p. °C	Yield %	Molecular formula	% C Found	% C Calcd.	% H Found	% H Calcd.
1	I	..	Phenyl	108–10	50	$C_{11}H_8N_2O_5$	53·38	53·22	3·65	3·22
2	I	..	*p*-Chlorophenyl	176–78	70	$C_{11}H_7ClN_2O_5$	46·65	46·73	2·70	2·47
3	I	..	*p*-Tolyl	121–23	66	$C_{12}H_{10}N_2O_5$	55·44	54·96	4·00	3·81
4	I	..	Thymyl	124–26	50	$C_{15}H_{16}N_2O_5$	59·27	59·21	5·35	5·26
5	I	..	4-Chlorothymyl	138–40	54	$C_{15}H_{15}ClN_2O_5$	53·56	53·19	4·59	4·43
6	I	..	*o*-Allyl-*p*-chlorophenyl	127–29 (d)	75	$C_{14}H_{11}ClN_2C_5$	52·20	52·08	3·32	3·41
7	II	2	Phenyl	104–5	48	$C_{13}H_{12}N_2O_6$	53·90	53·42	4·55	4·11
8	II	2	*p*-Chlorophenyl	126–28	52	$C_{13}H_{11}ClN_2O_6$	48·09	47·77	3·40	3·37
9	II	2	3-Nitrophenyl	162–64 (d)	65	$C_{13}H_{11}N_3O_8$	46·50	46·29	3·54	3·26
10	II	2	Thymyl	98–100	60	$C_{17}H_{20}N_2O_6$	58·43	58·61	5·81	5·74
11	II	2	4-Chlorothymyl	90–92	65	$C_{17}H_{19}ClN_2O_6$	52·89	53·32	4·41	4·96
12	II	4	Phenyl	108–10	62	$C_{15}H_{16}N_2O_6$	56·51	56·26	5·30	5·00
13	II	4	*p*-Chlorophenyl	152–53	46	$C_{15}H_{15}ClN_2O_6$	50·93	50·78	4·54	4·23
14	II	6	*p*-Chlorophenyl	130–32	57	$C_{17}H_{19}ClN_2O_6$	53·36	53·32	4·66	4·96
15	II	6	Thymyl	102–4	75	$C_{21}H_{28}N_2O_6$	62·24	62·37	6·82	6·93

TABLE II

Antifungal and antibacterial activities M. I. C. (μ g/ml)

(*a*)

Compound No.	*Fungi*									
	T.m.	*T.r.*	*M.c.*	*M.g.*	*C.a.*	*C.n.*	*S.s.*	*H.c.*	*A.f.*	*A.t.*
1	..	..	..	100	..	..	100	25	..	..
2	100	..	..	..	..	..	100	100	..	..
3	100	100	..	100	..	..	100	100	..	100
4	50	..	100	100	..	..	100	25	..	..
5	50	50	25	25	..	..	50	25	..	..
6	50	50	50	50	100	100	50	25	..	100

(*b*)

	Bacteria						
	S.a.	*S.f.*	*E.c.*	*K.p.*	*Ps.a.*	*S.t.*	*Ag.t.*
5	50	25	..	50	25	..	50
6	..	..	..	..	100	..	..
11	..	..	..	100	25	..	25
13	..	..	..	..	..	..	50

Fungi: *T.m.* = *Trichophyton mentagrophytes*; *T.r.* = *Trichophyton rubrum*; *M.c.* = *Microsporum canis*; *M.g.* = *Microsporum gypseum*; *C.a.* = *Candida albicans*; *C.n.* = *Cryptococcus neoformans*; *S.s.* = *Sporotrichum schenkii*; *H.c.* = *Histoplasma capsulatum*; *A.f.* = *Aspergillus fumigatus*; *A.t.* = *Alternaria tenuis*.

Bacteria: *S.a.* = *Staphylococcus aureus*; *S.f.* = *Streptococcus faecalis*; *E.c.* = *Escherichia coli*; *K.p.* = *Klebsiella pneumoniae*; *Ps.a.* = *Pseudomonas aeruginosa*; *S.t.* = *Salmonella typhi*; *Ag.t.* = *Agrobacterium tumefaciens*.

.. = *Inactive*

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INFLUENCE OF SOLVENTS ON THE CHELATION IN BENZOIN AND METHYL MANDELATE

INTRAMOLECULAR hydrogen bonding in six membered chelates as formed in salicylaldehyde, methyl salicylate, 2-hydroxy acetophenone and enols of β-diketones has been studied earlier[1]. The intramolecular hydrogen bonding leading to the formation of five membered chelate, however, received little attention.

In this communication, evidence for chelation in benzoin and methyl mandelate is furnished. With a view to studying the influence of solvents on chelation the pmr spectra of these compounds have been recorded on Varian A. 60 D in CS_2, $CDCl_3$, DMSO, DMF, acetone and in the presence of traces of trifluoroacetic acid and methanol using TMS as internal standard at 37° C. The