J. Chem. Sci., Vol. 118, No. 3, May 2006, pp. 249–256.

Curtius rearrangement reactions of 3-(4-azidocarbonyl) phenylsydnone. Synthesis of 4-(sydnon-3-yl) phenyl carbamates, N-aryl-N′-[4-(sydnon-3-yl)] phenyl ureas and their antimicrobial and insecticidal activities

P R LATTHE[a], P S SHINGE[a,+], BHARATI V BADAMI[a,]*, P B PATIL[b] and S N HOLIHOSUR[b,]*

[a]Department of Chemistry, and [b]Department of Zoology, Karnatak University, Dharwad 580 003
[+]Present address: Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012
e-mail: bbadami@rediffmail.com

MS received 1 September 2005; revised 4 January 2006

Abstract. 3-[4-(Azidocarbonyl)]phenylsydnone (**2**) obtained from 3-(4-hydrazinocarbonyl) phenylsydnone (**1**) on Curtius rearrangement with alcohols, water and amines afforded the corresponding carbamates (**3a**–**h**), 4,4′-(sydnone-3-yl) diphenyl urea (**4**) and 4-(heterocyclyl)phenyl ureas (**5a**–**l**). Compounds (**5a**–**l**) on one-pot ring conversion yielded the 1,3,4-oxadiazolin-2-one derivatives (**6a–l**), which on reaction with N_2H_4 gave the 4-amino-1,2,4-triazolin-3-ones (**7a–l**). All these compounds exhibited moderate antimicrobial activity against the few microbes tested. The carbamates have been found to be more toxic against fourth instar larvae of *Aedes aegypti*, in particular, the *n*-butyl derivative (**3e**).

Keywords. 3-(4-Azidocarbonyl)phenylsydnone; Curtius rearrangement; 4-(sydnon-3-yl)phenyl carbamates; N-aryl-N′-[4-(sydnon-3-yl)] phenyl ureas.

1. Introduction

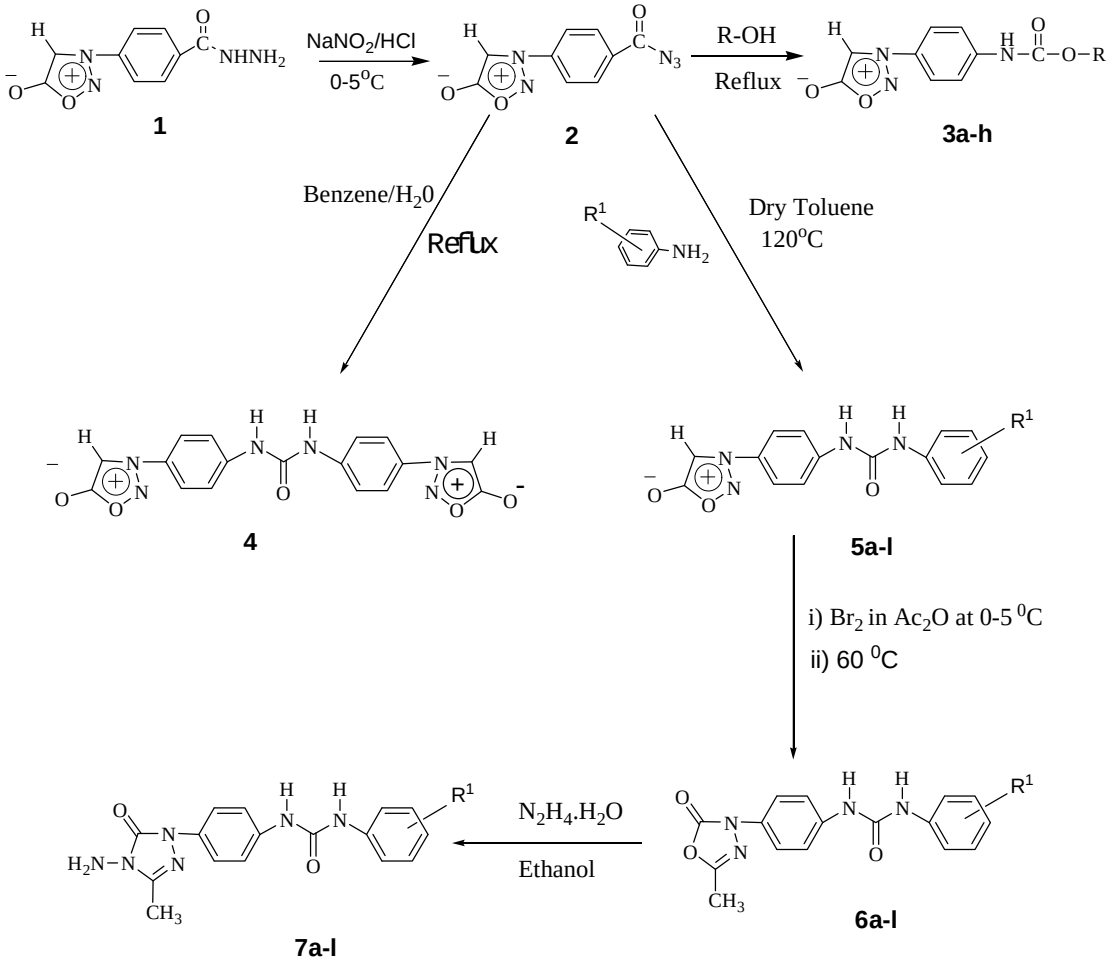
Synthesis and biological properties of sydnone derivatives incorporated with biologically active heterocycles have been reported from this laboratory for the past several years.[1–4] Though many of these compounds showed promising pharmacological properties at the preliminary testing, none of them have exhibited sufficient activity to justify further screening. Hence, much needs to be done in the form of synthesis and screening of many more derivatives, before we can conclude anything definite about structural modifications and pharmacological properties. So, it was thought of interest to synthesise some more sydnone derivatives containing other biologically potent moieties. In view of the diverse and remarkable biological properties of several heterocyclic systems with pendant carbamates[5,6] and diphenylureas[7,9] we thought of coupling these moieties with sydnones.

*For correspondence

2. Results and discussion

In this paper we report the synthesis and biological properties of some carbamates (**3a–h**) and ureas (**4**, **5a–l**, **6a–l** and **7a–l**) incorporated with the sydnone ring, using the well-known Curtius rearrangement.[10] 3-(4-Hydrazinocarbonyl)phenylsydnone (**1**) used as the starting material is converted to the acylazide derivative (**2**), which when subjected to Curtius rearrangement with alcohols, water and aromatic amines, affords the carbamates (**3a–h**), symmetrical urea (**4**) and ureas (**5a–l**) respectively.

3-(4-Hydrazinocarbonyl)phenylsydnone (**1**) on nitrosation with sodium nitrite gives 3-(4-azidocarbonyl) phenylsydnone (**2**) in 75% yield. IR analysis of this compound shows a strong band at 2184 cm^{-1} for the azide group stretching vibration. The ^{1}H-NMR (300 MHz) spectrum shows two doublets at *d* 7·95 (2H, *J* = 8·1 Hz) and *d* 7·83 (2H, *J* = 8·1 Hz) assigned to the aromatic protons and a singlet at *d* 7·69 due to the sydnone CH. This compound is sufficiently pure for further use in rearrangement reactions. Compound (**2**) undergoes Curtius rearrangement



1 **2** **3a-h** **4** **5a-l** **6a-l** **7a-l**

3a	R=Me	**5a, 6a, 7a**	R^1=H	**5i, 6i, 7i**	R^1=3- NO_2
3b	R=Et	**5b, 6b, 7b**	R^1=2-Me	**5j, 6j, 7j**	R^1=4- NO_2
3c	R=Pr	**5c, 6c, 7c**	R^1=4-Me	**5k, 6k, 7k**	R^1=2-OCH_3
3d	R=i-Pr	**5d, 6d, 7d**	R^1=2-Cl	**5l, 6l, 7l**	R^1=4-OCH_3
3e	R=n-Bu	**5e, 6e, 7e**	R^1=4- Cl		
3f	R=t-Bu	**5f, 6f, 7f**	R^1=4- $COCH_3$		
3g	R=2-methoxyethyl	**5g, 6g, 7g**	R^1=4- COOH		
3h	R=2-ethoxyethyl	**5h, 6h, 7h**	R^1=2-NO_2		

Scheme 1.

in boiling ethanol to afford the carbamate (**3b**) in good yield (80%) (scheme 1). The absence of an azide band at 2184 cm^{-1} and the presence of a $n_{N–H}$ band at 3246 cm^{-1} in its IR spectrum is evidence for the rearrangement of azide to carbamate. This is further substantiated by the ^{1}H-NMR (300 MHz) spectrum, which shows signals at *d* 10·15 (*s*, 1H, NH D_2O exchanged), *d* 7·85 (*d*, 2H Ar-H), *d* 7·71 (*d*, 2H Ar-H), *d* 7·61 (*s*, 1H sydnone C–H), *d* 4·28 (*q*, 2H, CH_2) and *d* 1·3 (*t*, 3H CH_3). This is further confirmed by its mass spectrum that shows molecular ion peak *m*/*z* at 249, which agrees with the molecular weight of the compound. A series of carbamates (**3a–h**) were prepared using different alcohols. All these compounds were characterized by their spectral data.

In another reaction, 3-(4-azidocarbonyl)phenylsydnone (**2**) on refluxing with water also underwent Curtius rearrangement to give the symmetrical urea, 4,4′-(sydnone-3-yl) diphenyl urea (**4**) (scheme 1). The IR spectrum of this compound shows broad bands at 3353 cm^{-1} and 3125 cm^{-1} due to $n_{N–H}$ and $n_{C–H}$ of sydnone respectively. The $n_{C=O}$ of sydnone and amide appear as sharp bands at 1759 cm^{-1} and 1705 cm^{-1} respectively. The ^{1}H-NMR spectrum shows signals at *d* 9·51 (*s*, 2H, NH D_2O exchanged), *d* 7·85 (*d*, 4H Ar-H), *d* 7·71 (*d*, 4H Ar-H), *d* 7·61(*s*, 2H sydnone C–H) indicating magnetic equivalency of protons in both halves of the molecule.

Another Curtius rearrangement of 3-(4-azidocarbonyl)phenylsydnone (**2**) in presence of various

aromatic amines gives the corresponding N-aryl-N′-[4-(sydnon-3-yl)phenyl] ureas (**5a–l**) (scheme 1). The IR spectra of all these compounds shows two sharp bands at 3357 cm^{-1} and 3125 cm^{-1} due to n_{N-H} and n_{C-H} of sydnone respectively. The $n_{C=O}$ of sydnone and amide appears as sharp bands at 1739 cm^{-1} and 1701 cm^{-1} respectively. The absence of the azide band at 2184 cm^{-1} also confirms the formation of compounds (**5a–l**). The ^{1}H-NMR spectrum (compound **5l**) shows signals at *d* 9·20 (*s*, 1H, NH D_2O exchanged), *d* 8·72 (*s*, 1H, NH attached to the aryl ring, (D_2O exchanged). The protons of the phenyl ring attached to the sydnone resonate as two doublets at *d* 7·80 (2H, *J* = 8·0 Hz) and *d* 7·70 (2H, *J* = 8·0 Hz), while the protons of methoxy phenyl ring are observed as two doublets at *d* 7·35 (2H, *J* = 7·9 Hz) and *d* 6·91 (2H, *J* = 7·9 Hz). The sydnone C–H and the OCH_3 protons appear as singlets at *d* 7·61 and 3·75 respectively. We have obtained the X-ray crystal[11] structure for one of these compounds, **5f**.

Our recent reports[12,13] on one-pot sydnone ring transformation to 1,3,4-oxadiazolin-2-ones and their subsequent conversion to the 4-amino-1,2,4-triazolin-3-ones prompted us to convert these newly synthesized compounds to the corresponding oxadiazolinone and triazolinones.

Compounds (**5a–l**) on reaction with bromine in acetic anhydride undergo ready one- pot ring conversion to yield N-aryl-N′ [4-(5-methyl-1,3,4-oxadiazolin-2-one-3yl) phenyl]ureas (**6a–l**) (scheme 1). The absence of sydnone C–H band at 3125 cm^{-1} and shift in the carbonyl frequency from 1739 cm^{-1} to 1787 cm^{-1} in the IR spectra clearly indicate ring transformation of sydnone to oxadiazolinones. The amide $n_{C=O}$ appears at 1705 cm^{-1}. The ^{1}H-NMR spectrum (compound **6l**) shows signals at *d* 10·29 (*s*, 1H, NH D_2O exchanged), *d* 10·18 (*s*, 1H, NH attached to the aryl ring, D_2O exchanged). The protons of the phenyl ring attached to the oxadiazolinone resonate as two doublets at *d* 8·00 (2H, *J* = 8·7 Hz) and *d* 7·81 (2H, *J* = 8.7 Hz) while the protons of the methoxy phenyl ring are observed as two doublets at *d* 7·62 (2H, *J* = 8·9 Hz) and *d* 6·92 (2H, *J* = 8·9 Hz). The OCH_3 and CH_3 protons appear as singlets at *d* 3·76 and *d* 2·30 respectively.

In the next part the N-aryl-N′ [4-(5-methyl-1,3,4-oxadiazolin-2-one-3yl) phenyl]ureas (**6a–l**) on reaction with hydrazine hydrate afford the N-aryl-N′ [4-(4-amino-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-one-2yl)] phenyl ureas (**7a–l**) (scheme 1). The IR spectra of compounds (**7a–l**) are characterized by the presence of two new bands at 3325 cm^{-1} and 3214 cm^{-1} for n_{NH_2} and a sharp band at 1713 cm^{-1} for the $n_{C=O}$. This lowering of the carbonyl frequency from 1787 cm^{-1} to 1713 cm^{-1} confirms the ring transformation. The amide $n_{C=O}$ is now observed at 1635 cm^{-1}, perhaps due to intermolecular H-bonding with the amino group. ^{1}H-NMR spectrum (compound **7l**) shows signals at *d* 10·23 (*s*, 1H, NH D_2O exchanged), *d* 10·05 (*s*, 1H, NH attached to the aryl ring, D_2O exchanged). The aromatic protons resonate at *d* 8·05–7·11 (*m*, 8H) while the two singlets at *d* 5·42 and *ä* 2·23 are assigned to the NH_2 and CH_3 of triazolinone. Another singlet at *d* 3·75 is due to the OCH_3 protons. No significant changes are observed in the characteristic spectral data of other derivatives of all these compounds.

3. Biological activity

3.1 *Antimicrobial activity*

Preliminary antimicrobial testing has been carried out by the cup-plate method. The antimicrobial activity was carried out against two pathogenic bacteria, *Escherichia coli* (Gram –ve) and *Micrococcus luteus* (Gram +ve) and two fungal strains, *Asperigillus niger* and *Penicillium notatum.* The reference drugs used were Norfloxacin and Griseofulvin respectively. The activity of the samples and the reference drugs was assayed under identical conditions at 50 *m*g concentration in DMSO as the control. N-aryl-N′-[4-(sydnon-3yl)]phenyl ureas (**5a–l**) with halogen substitution (**5d**, **5e**) on the phenyl ring showed better activity only against the Gram + bacteria while rest of the compounds showed moderate activity against both the bacteria (table 1). However, moderate antifungal activity was observed for all the compounds against both the fungi.

3.2 *Insecticidal activity against aedes aegypti*

Aedes aegypti mosquito is the vector responsible for dangerous diseases like dengue hemorrhagic fever and yellow fever. An attempt has been made to study the newly synthesized carbamate compounds with respect to their insecticidal properties against fourth instar larvae of *Aedes aegypti* under laboratory conditions.

3.2a *Materials and methods:* Eggs of *Aedes aegypti* were obtained from "The Viral Research Insti-

Table 1. Antimicrobial activity (N* = Norfloxacin, G* = Griseofulvin).

	Antibacterial		Antifungal			Antibacterial		Antifungal	
Compd	*E. coli* zone of inhibition (mm)	*M. luteus* zone of inhibition (mm)	*A. niger* zone of inhibition (mm)	*P. notatum* zone of inhibition (mm)	Compd	*E. coli* zone of inhibition (mm)	*M. luteus* zone of inhibition (mm)	*A. niger* zone of inhibition (mm)	*P. notatum* zone of inhibition (mm)
3a	13	12	12	10	**6d**	19	12	15	12
3b	15	10	13	11	**6e**	21	10	15	10
3c	18	11	12	10	**6f**	–	–	10	09
3d	14	10	11	12	**6g**	–	–	08	09
3e	15	09	12	11	**6h**	11	10	–	–
3f	–	–	10	11	**6i**	15	12	12	11
3g	14	14	11	11	**6j**	13	11	13	10
3h	–	–	11	10	**6k**	14	10	09	10
5a	14	10	10	13	**6l**	–	–	13	10
5b	18	11	13	12	**7a**	15	09	–	–
5c	15	10	15	14	**7b**	17	11	09	10
5d	23	12	15	14	**7c**	13	11	14	10
5e	26	13	09	14	**7d**	15	10	13	13
5f	17	10	10	13	**7e**	14	14	14	12
5g	16	09	12	12	**7f**	17	12	11	07
5h	20	11	09	14	**7g**	09	11	09	07
5i	20	10	14	13	**7h**	–	–	–	–
5j	19	12	13	14	**7i**	14	10	13	11
5k	20	10	11	11	**7j**	12	12	12	10
5l	12	09	13	12	**7k**	13	10	–	–
6a	–	–	09	11	**7l**	13	11	10	11
6b	12	10	12	11					
6c	14	11	10	10	**DMSO**	06	06	06	06
N*	31	15	–	–	**G***	–	–	18	15

Table 2. Emergence inhibition (EI) of fourth instar larvae of *Aedes aegypti* exposed to the compounds **3b**, **3c** and **3e** and methoprene.

Compounds	EI_{50} (ppm)*	EI_{90} (ppm)*
3b	15·80	25·86
3c	6·76	9·94
3e	3·17	5·24
Standard (methoprene)	0·05	0·09

*Calculated value of emergence inhibition (EI) of 50 and 90% adults of the larvae exposed at different concentrations.

tute, Pune" and this culture has been maintained under laboratory conditions for about four years. Eggs thus obtained were flooded with water in an enamel tray and the larvae that hatched were transferred to fresh water containers frequently. The larvae were provided with a mixture of finely ground dog biscuits and yeast in 2 : 1 ratio as food in the form of pellets. Pupae formed were separated in plastic cups and were kept in oviposition cages designed for rearing adults. Male adults were provided with 2% honey diluted with distilled water in petridishes with a lining of cotton. Females were provided with rat blood meal. A constant wet surface was provided for egg laying in each petridish with cotton lining it and a cover of blotting paper on to which water was added frequently. The eggs thus collected were used for experiments as and when required.

Stock solutions were prepared by dissolving the compounds (only the straight chain derivatives) in 1 ml of acetone and this was made up to 100 ml with distilled water with a drop of tween 85 as emulsifier. Concentrations of prepared stock solutions of (**3a**), (**3b**), (**3c**), (**3d**), (**3e**), (**3f**), (**3g**) and (**3h**) were 0·5%, 1%, 0·5%, 1%, 1%, 1%, 1% and 1% respectively. A standard solution of Methoprene (Altosid) of 0·01% in absolute alcohol was prepared for comparative analysis. Experiments were carried out according to the WHO method.[14] Further dilutions of the stock solutions were made using tap water to obtain stipu-

Table 3. Physical and analytical data of compounds **3a–h**.

Compd	R	Solvent	Melting point (°C)	Yield (%)	Molecular formula	Elemental analysis – found (calculated) (%)		
						C	H	N
3a	Methyl	Ethanol	107–109	78	$C_{10}H_9N_3O_4$	51·00 (51·06)	3·78 (3·82)	17·85 (17·87)
3b	Ethyl	Ethanol	121–123	80	$C_{11}H_{11}N_3O_4$	52·95 (53·01)	4·89 (4·94)	16·80 (16·86)
3c	Propyl	Ethanol	113–115	69	$C_{12}H_{13}N_3O_4$	54·70 (54·75)	3·96 (4·00)	15·92 (15·96)
3d	Iso-propyl	Ethanol	131–133	73	$C_{12}H_{13}N_3O_4$	54·72 (54·75)	3·94 (4·00)	15·90 (15·96)
3e	*n*-Butyl	Ethanol	147–149	68	$C_{13}H_{15}N_3O_4$	56·25 (56·31)	5·39 (5·41)	15·14 (15·16)
3f	*t*-Butyl	Ethanol + dioxane	181–183	63	$C_{13}H_{15}N_3O_4$	56·27 (56·31)	5·38 (5·41)	15·12 (15·16)
3g	2-Methoxy ethyl	Ethanol	120–122	70	$C_{12}H_{13}N_3O_5$	51·57 (51·61)	4·61 (4·65)	15·01 (15·05)
3h	2-Ethoxy ethyl	Ethanol	153–155	67	$C_{13}H_{15}N_3O_5$	53·21 (53·24)	5·08 (5·11)	14·30 (14·33)

Table 4. Physical and analytical data of compounds **5a–l**.

Compd	R	Solvent	Melting point (°C)	Yield (%)	Molecular formula	Elemental analysis – found (calculated) (%)		
						C	H	N
5a	H	Ethanol	190–192	81	$C_{15}H_{12}N_4O_3$	60·76 (60·81)	4·01 (4·05)	18·88 (18·91)
5b	2-CH_3	Ethanol	189–191	74	$C_{16}H_{14}N_4O_3$	61·90 (61·93)	4·47 (4·51)	18·03 (18·06)
5c	4-CH_3	Ethanol	201–203	78	$C_{16}H_{14}N_4O_4$	61·88 (61·93)	4·49 (4·51)	18·01 (18·06)
5d	2-Cl	Ethanol + dioxane	211–213	68	$C_{15}H_{11}ClN_4O_3$	54·48 (54·54)	3·28 (3·33)	16·94 (16·96)
5e	4-Cl	Ethanol + dioxane	222–224	79	$C_{15}H_{11}ClN_4O_3$	54·50 (54·54)	3·31 (3·33)	16·91 (16·96)
5f	4-$COCH_3$	Ethanol+ DMF	216–217	79	$C_{17}H_{14}N_4O_4$	60·30 (60·35)	4·09 (4·14)	16·50 (16·54)
5g	4-COOH	Ethanol + DMF	242–244	67	$C_{16}H_{12}N_4O_5$	56·43 (56·47)	3·49 (3·52)	16·44 (16·47)
5h	2-NO_2	Ethanol + DMF	281–283	75	$C_{15}H_{11}N_5O_5$	52·74 (52·78)	3·15 (3·22)	20·46 (20·52)
5i	3-NO_2	Ethanol + DMF	267–269	69	$C_{15}H_{11}N_5O_5$	52·72 (52·78)	3·18 (3·22)	20·43 (20·52)
5j	4-NO_2	Ethanol + DMF	241–243	72	$C_{15}H_{11}N_5O_5$	52·75 (52·78)	3·14 (3·22)	20·48 (20·52)
5k	2-OCH_3	Ethanol	189–191	64	$C_{16}H_{14}N_4O_4$	58·84 (58·89)	4·21 (4·29)	17·11 (17·17)
5l	4-OCH_3	Ethanol + dioxane	204–206	76	$C_{16}H_{14}N_4O_4$	58·82 (58·89)	4·25 (4·29)	17·14 (17·17)

lated concentrations for the experiments with volume made up to 100 ml in 250 ml polythene cups with three replicates, in which 25 freshly moulted fourth instar larvae were introduced. Controls with acetone and

tween 85, and others with water alone were maintained. Food was provided *ad libitum*. Biostatistical analysis to calculate emergence inhibition of adults (i.e. EI_{50} and EI_{90}) was done according to Finney.[15]

Compounds **3a**, **3d**, **3f**, **3g**, and **3h** did not show any activity while compounds **3b**, **3c**, and **3e** demonstrated insect growth regulatory activity against fourth instar larvae of *Aedes aegypti*. The EI_{50} and EI_{90} for the ethyl (**3b**), propyl (**3c**) and *n*-butyl (**3e**) derivatives and the standard (Methoprene) were found to be 15·8 and 25·86, 6·76 and 9·94, 3·17 and 5·24 and 0·05 and 0·09 ppm respectively (table 2). From the results it was found that the *n*-butyl derivative (**3e**) was more effective at low concentration compared to the ethyl and the propyl derivatives. The EI_{50} for the *n*-butyl derivative is 5 times more effective compared to the ethyl and twice as compared to the propyl, but is 60 times less effective compared to the standard Methoprene.

Methoprene, an insect growth regulatory compound, has been recommended by WHO for use against mosquito larvae.[16] However, this compound is not in use for vector control in India. The results of the present study showed the delayed efficacy of *n*-butyl derivative (**3e**) against *Aedes aegypti* larvae. The occurrence of delayed mortality indicated the effective developmental inhibition potential of this compound. The other compounds did not show any activity at these test doses.

4. Experimental

IR spectra were recorded on Nicolet-Impact 410 FT-IR spectrophotometer as KBr pellets.^{1}H-NMR spectra were recorded on a Brucker 300 MHz FT-NMR spectrometer in $CDCl_3$/DMSO-d_6 with TMS as internal standard. Purity of compounds was checked by TLC on silica gel plates.

4.1 *3-[4-(Azido carbonyl)] phenylsydnone (2)*

To a stirred solution of 3-(4-hydrazinocarbonyl) phenylsydnone (**1**) (2·21 g, 0·01 m) in 25% HCl, a solution of sodium nitrite (2·85 g, 0·05 m) was added dropwise at 0–5°C. After complete addition

Table 5. Physical and analytical data of compounds **6a–l**.

Compd	R	Solvent	Melting point (°C)	Yield (%)	Molecular formula	Elemental analysis – found (calculated) (%)		
						C	H	N
6a	H	Ethanol	153–155	83	$C_{16}H_{14}N_4O_3$	61·87 (61·93)	4·45 (4·51)	18·00 (18·06)
6b	2-CH_3	Ethanol	171–173	80	$C_{17}H_{16}N_4O_3$	62·93 (62·96)	4·90 (4·93)	17·20 (17·28)
6c	4-CH_3	Ethanol + DMF	194–196	84	$C_{17}H_{16}N_4O_4$	62·90 (62·96)	4·88 (4·93)	17·23 (17·28)
6d	2-Cl	Ethanol + dioxane	291–293	81	$C_{16}H_{13}ClN_4O_3$	55·76 (55·81)	3·71 (3·77)	16·24 (16·27)
6e	4-Cl	Ethanol + dioxane	279–281	85	$C_{16}H_{13}ClN_4O_3$	55·72 (55·81)	3·74 (3·77)	16·22 (16·27)
6f	4-$COCH_3$	Ethanol + DMF	212–214	76	$C_{18}H_{16}N_4O_4$	61·31 (61·36)	4·50 (4·54)	15·85 (15·90)
6g	4-COOH	Ethanol + DMF	280–282	74	$C_{17}H_{14}N_4O_5$	57·57 (57·62)	3·89 (3·95)	15·78 (15·81)
6h	2-NO_2	Ethanol + DMF	245–247	84	$C_{16}H_{13}N_5O_5$	54·00 (54·08)	3·63 (3·66)	19·64 (19·71)
6i	3-NO_2	Ethanol + DMF	283–285	80	$C_{16}H_{13}N_5O_5$	54·05 (54·08)	3·58 (3·66)	19·67 (19·71)
6j	4-NO_2	Ethanol + DMF	261–263	85	$C_{16}H_{13}N_5O_5$	54·02 (54·08)	3·60 (3·66)	19·65 (19·71)
6k	2-OCH_3	Ethanol + DMF	203–205	79	$C_{17}H_{16}N_4O_4$	59·93 (60·00)	4·67 (4·70)	16·43 (16·47)
6l	4-OCH_3	Ethanol + dioxane	241–243	83	$C_{17}H_{16}N_4O_4$	59·96 (60·00)	4·64 (4·70)	16·40 (16·47)

Table 6. Physical and analytical data of compounds **7a–l**.

Compd	R	Solvent	Melting point (°C)	Yield (%)	Molecular formula	Elemental analysis – found (calculated) (%)		
						C	H	N
7a	H	Ethanol + dioxane	181–183	63	$C_{16}H_{16}N_6O_2$	59·20 (59·25)	4·89 (4·93)	25·87 (25·92)
7b	2-CH_3	Ethanol + dioxane	172–174	69	$C_{17}H_{18}N_6O_2$	60·28 (60·35)	5·28 (5·32)	24·76 (24·85)
7c	4-CH_3	Ethanol + dioxane	161–163	61	$C_{17}H_{18}N_6O_2$	60·31 (60·35)	5·26 (5·32)	24·78 (24·85)
7d	2-Cl	Ethanol + dioxane	175–177	60	$C_{16}H_{15}ClN_6O_2$	56·60 (56·63)	4·15 (4·18)	23·42 (23·46)
7e	4-Cl	Ethanol + dioxane	187–189	62	$C_{16}H_{15}ClN_6O_2$	56·58 (56·63)	4·12 (4·18)	23·44 (23·46)
7f	4-$COCH_3$	Ethanol + dioxane	169–171	68	$C_{18}H_{18}N_6O_3$	58·97 (59·01)	4·87 (4·91)	22·92 (22·95)
7g	4-COOH	Ethanol + DMF	191–193	53	$C_{17}H_{16}N_6O_4$	55·38 (55·43)	4·30 (4·34)	22·78 (22·82)
7h	2-NO_2	Ethanol + DMF	231–233	59	$C_{16}H_{15}N_7O_4$	51·98 (52·03)	4·03 (4·06)	26·50 (26·55)
7i	3-NO_2	Ethanol + DMF	248–250	55	$C_{16}H_{15}N_7O_4$	52·00 (52·03)	4·01 (4·06)	26·49 (26·55)
7j	4-NO_2	Ethanol + DMF	237–239	61	$C_{16}H_{15}N_7O_4$	51·95 (52·03)	4·03 (4·06)	26·51 (26·55)
7k	2-OCH_3	Ethanol + DMF	198–200	52	$C_{17}H_{18}N_6O_3$	57·59 (57·62)	5·05 (5·08)	23·69 (23·72)
7l	4-OCH_3	Ethanol + dioxane	184–186	57	$C_{17}H_{18}N_6O_3$	57·57 (57·62)	5·02 (5·08)	23·65 (23·72)

of sodium nitrite solution, the reaction mixture was stirred at room temperature for 1 h. The pale yellow azide that separated was filtered and washed with water.

4.2 *4-(Sydnon-3-yl) phenyl carbamates (**3a–h**)*

A suspension of 3-(4-azido carbonyl) phenylsydnone (**2**) (2·31 g, 0·01 m) in absolute alcohol (15 ml) was refluxed on a steam bath for 3 h. The reaction mixture was concentrated and then diluted with water. The product that separated was collected and recrystallised from ethanol to get brown needles (table 3).

4.3 *4,4¢-(Sydnone-3-yl) diphenyl urea (**4**)*

A solution of 3-(4-azidocarbonyl) phenylsydnone (**2**) (2·31 g, 0·01 m) in benzene (20 ml) was treated with distilled water (2 ml) and the reaction mixture refluxed on a steam-bath for 3 h. The solid product formed was filtered.

4.4 *N-Aryl-N¢-[4-(sydnon-3yl)] phenylureas (**5a–l**)*

3-(4-Azidocarbonyl) phenylsydnone (**2**) (2·31 g, 0·01 m) and aromatic amines (0·01 m) were refluxed in anhydrous toluene (15 ml) for 4 h at 120°C. The crystalline product that separated was collected and washed with petroleum ether (table 4).

4.5 *N-Aryl-N¢ [4-(5-methyl-1,3,4-oxadiazolin-2-one-3yl)] phenyl ureas (**6a–l**)*

To a solution of compounds (**5a–l**) (0·005 M) in acetic anhydride (10 ml) at 0°C was added bromine (0·3 ml) in acetic anhydride (5 ml) with constant stirring. After complete addition of bromine for 30 min, the reaction mixture was then heated at 60°C. The reaction mixture was cooled and poured into ice. The solid that separated was filtered and recrystallised from DMF (table 5).

4.6 *N-Aryl-N¢[4-(4-amino-5-methyl-2,4-dihydro-3H-1,2,4-triazol-3-one-2yl)]phenylureas (**7a–l**)*

To a suspension of compounds (**6a–l**) (0·01 m) in dry alcohol (15 ml) hydrazine hydrate (1·5 ml) was added and the mixture was refluxed on a water-bath for 8 h. The reaction mixture was then diluted with water and the solid obtained after filtration was

crystallized from suitable solvents to obtain light brown crystals (table 6).

Acknowledgments

We thank Dr G S Puranik for encouragement and suggestions. Authors also wish to thank the Sophisticated Instrumentation Facility, Indian Institute of Science, Bangalore, Indian Institute of Chemical Technology, Hyderabad and University Sophisticated Instrumentation Centre of Karnatak University for providing spectral data.

References

1. Upadhya K G, Badami B V and Puranik G S 1980 *Arch. Pharm. (Weinheim)* **313** 684
2. Tikare R K, Upadhya K G Badami B V and Puranik G S 1984 *Indian J. Chem.* **B23** 798
3. Patil B M, Badami B V and Puranik G S 1995 *Indian Drugs* **32** 439
4. Kavali J R and Badami B V 2000 *J. Chem. Res.* 547(*s*), 1137(*M*)
5. Canan Kus and Nurten Altanlar 2003 *Turk. J. Chem.* **27** 35
6. Ramesh D and Sreenivasulu B 2004 *Indian J. Chem.* **43B** 897
7. Xie Jiugao and Li Shuiqing 2002 *Nongyaoxue Xuebao* **4** 62; 2002 *Chem. Abstr*. **139** 209231
8. Dumas, Boyer J, Riedl S, Wilhelm B and Scott *PCT Int. Appl. 68 Chem. Abstr.* **142** 197889
9. Scozzafava A and Supuran C T 1999 *J. Enzyme Inhib.* 1999 **14** 343
10. Smith P A S *Org. React.* 1946 **3** 337
11. Thamotharan S, Parthasarathi V, Satishkumar P, Latthe P R, Badami B V and Ravikumar K 2004 *Acta Crystallogr*. **E60** o1015–o1016
12. Mallur S G and Badami B V 2000 *Il Farmaco* **55** 65
13. Kavali J R, Kotresh O and Badami B V 2003 *J. Chem. Res.* 275(s)
14. World Health Organization, 1981 Instructions for determining the susceptibility or resistance of mosquito larvae to insecticides *WHO/VBC*/**81**, 807, 1981
15. Finney D J 1971 *Probit analysis* 3rd edn (Cambridge: University Press)
16. Chavasse D C and Yap H H 1997 Chemical methods for the control of vector and pests of public health importance. WHO/CTD/WHOPES/97.2, p. 27