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Chemical Constituents of *Vallaris solanacea* O. Ktze

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THE latex obtained from *Vallaris solanacea* O. Ktze (Apocyanaceae) is widely used as an anti-inflammatory agent in the treatment of old wounds and sores[1]. Some phytochemical work on this plant is on record[2,3,4]. The present note reports the isolation of some chemical constituents from its leaves.

The powdered airdried leaves of *V. solanacea* were extracted successively with petroleum ether and benzene in a Soxhlet. The petrol extract was chromatographed over Brockmann alumina and the benzene eluates upon concentration and cooling yielded a crystalline sterol m.p. 134-35° ; acetate m.p 126-28° ; benzoate m.p. 141-43°. It was identified as β-sitosterol by direct comparison (m.p., m.m.p. and IR) of the compound and its derivatives with the authentic samples.

The benzene extract on concentration and cooling separated a crystalline mass identified as potassium nitrate. The concentrated mass was chromatographed over Brockmann alumina and the petrol-benzene (10 :2) eluates yielded a triterpene alcohol which crystallised from methanol as needles, m.p. 187-89° ; IR (nujol) broad band between 3300-3400 cm^{-1} (−OH) ; acetate, m.p. 238-39° and benzoate m.p. 229-31°, suggesting its identity with β-amyrin which was further confirmed by direct comparison (m.p., m.m.p., co−TLC and IR) with authentic samples. The chloroform-methanol (1 : 6) eluates furnished a triterpene acid, m.p. 277-79° ; IR(KBr) 3350-3450 cm^{-1} (−OH), 1685 cm^{-1} (C=O) and other peaks at 1380, 1370, 1350, 1305, 1270 and 1247 cm^{-1} characteristic of ursolic acid derivatives[5]. The mass spectrum showed besides molecular ion peak M^+ at m/e 456, prominent fragment ions at m/e 538(5%), 410(8%), 248(100%), 203(53%) and 133(53%) suggesting the compound to be ursolic acid. NMR ($CDCl_3$) exhibited signals for C−12 olifinic proton at δ5.2, polymethylene envelope between δ1.2−2.0 and seven methyl groups as singlets between δ0.66-1.01. The compound formed a methyl ester, m p. 169-70°. Finally, the identity of the compound with ursolic acid was confirmed by direct comparison with an authentic sample.

Acknowledgement

Thanks are due to Dr. A. B. Ray, Dept. of Medicinal Chemistry, Banaras Hindu University for the authentic samples.

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Possible Antibacterial Compounds. Synthesis of Alkyl penta-trans-2, trans-4 dienoic and Alkyl propyl-trans-2-enoic Acid Amides

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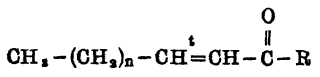
VARIOUS types of acid amide have been shown to be physiological active substances. Conjugated alkyl amides show significant insecticidal activity towards housefly[1]. Many substituted toluamides have been shown to have antibacterial and insect repellant properties[2,3]. In view of this it was thought of interest to synthesise various unsaturated alkyl amides.

The key reaction employed for the synthesis of various alkyl amides was modified Wittig reaction. Aliphatic aldehyde was submitted to modified Wittig reaction with γ-phosphonate of ethyl crotonate or α-phosphonate of ethyl acetate to get the unsaturated esters. It has been shown that Wittig reaction of ylid enjoying resonance stabilization tend to be stereospecific and yield a great preponderance of trans product[4,5]. This has been further proved to be so by spectral data of synthetic products. Various aldehydes such as heptaldehyde, palmatic aldehyde, citronellal and citral were used as starting material for the projected synthesis of various acid amide I to V. Typical procedure for the unsaturated acid amide was as follows.

Heptaldehyde was condensed with γ-phosphonate of ethyl crotonate in the presence of NaH using

tetrahydrofuran as solvent. This resulted in the formation of ethyl trans-2, trans-4 undecadienoate in 65% yield. The conjugated ester so obtained was hydrolysed with alcoholic NaOH to afford the corresponding acid, which was treated with thionyl chloride in benzene. The acid chloride was treated with isobutyl amine or piperidine to get corresponding acid amide in quantitative yield. The various intermediate and final compounds were checked by TLC for their purity. Structure of these compounds were established on the basis of IR and in some cases by NMR data.



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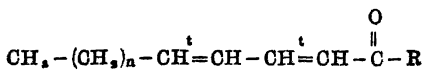

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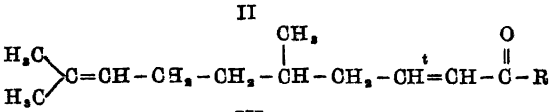

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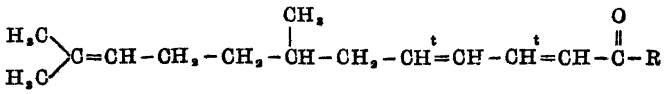

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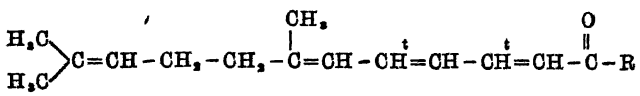

V

These compounds were tested for Juvenils Harmone Activity using last instar nymphs of red cotton bug, *Dysdercus koenigii,* Compared to farnesyl methyl ether all the samples prepared showed low activity.

Typical preparation are described below :

Ethyl trans-2, trans-4-undecadienoate :

A slurry of sodium hydride (4.8 g, 50%) was washed with *n*-hexane and placed in tetrahydrofuran (100 ml) and to this γ-phosphonate of ethyl crotonate (22.4 g) was added dropwise at room temperature (20°) with continuous stirring until the evolution of gas ceased. To the resulting yellow solution was added heptaldehyde (11.4 g) slowly at 10° and the solution further stirred for 2 hr at room temperature and kept overnight. The product was extracted with ether after decomposing with large excess of water and ether extract dried over anhydrous sodium sulphate. Removal of the solvent and distillation under reduced pressure afforded the ester, (12.6 g, 60%). IR : 1715, 1610, 1460, 1300, 1180, 990 cm^{-1}.

Trans-2, trans-4-undecadienoic acid :

The ester (10 g) was hydrolysed with 15% alcoholic sodium hydroxide. The reaction mixture was refluxed for 3 hr, cooled and acidified with hydrochloric acid. The solid acid was filtered and dried. S-benzyl-iso-thiouronium chloride derivative of the acid m.p. 174°. IR: 2810-2550, 1725, *980* (trans-trans-$CH^t=CH-CH^t=CH$ system in conjugation with carbonyl group) cm^{-1}.

N-isobutyl trans-2, trans-4-undecadienoic acid amide :—

The acid (1 g) was taken in dry benzene and thionyl chloride (2 ml) was added at low temperature. The contents were heated to 50° for 30 min. Unreacted thionyl chloride and benzene were removed under reduced pressure and residue furnished the desired acid chloride. The acid chloride was taken in dry benzene, cooled and treated with isobutyl amine (2.2 g). The product was extracted with ether after decomposing with large excess of water. The ether extract washed successively with sodium bicarbonate solution (10%),

TABLE

Compound	Value of n	R	Mol. Formula	BP°C or MP°C	Analysis of Nitrogen Calc(%)	Found(%)
I	5	Isobutyl–NH–	$C_{15}H_{25}NO$	180-85°/8 mm	6.63	6.58
I	5	Piperidine	$C_{14}H_{25}NO$	180-85°/8 mm	6.30	6.21
I	14	Isobutyl–NH–	$C_{22}H_{43}NO$	67° m.p.	4.15	4.00
I	14	Piperidine	$C_{23}H_{43}NO$	72° m.p.	4.01	3.93
II	5	Isobutyl–NH–	$C_{15}H_{27}NO$	150-55°/6 mm	5.90	5.94
II	5	Piperidine	$C_{16}H_{27}NO$	160-70°/8 mm	5.62	5.50
II	14	Isobutyl–NH–	$C_{24}H_{45}NO$	68° m.p.	3.85	3.75
II	14	Piperidine	$C_{25}H_{45}NO$	65-67° m.p.	3.73	3.65
III	—	Isobutyl–NH–	$C_{16}H_{29}NO$	200-10°/15 mm	5.57	5.50
III	—	Piperidine	$C_{17}H_{29}NO$	220-30°/15 mm	5.32	5.21
IV	—	Isobutyl–NH–	$C_{18}H_{31}NO$	220-30°/5 mm	5.05	5.00
IV	—	Piperidine	$C_{19}H_{31}NO$	220-30°/5 mm	4.84	4.70
V	—	Isobutyl–NH–	$C_{19}H_{29}NO$	220-40°/5 mm	5.09	5.01
V	—	Piperidine	$C_{19}H_{29}NO$	220-40°/5 mm	4.88	4.60

hydrochloric acid (10%) and water and dried over anhydrous Na_2SO_4. The solvent was removed and the residue on distillation under reduced pressure afforded the estar. The purity of the product was checked through TLC. IR : 3400 (−NH), 1685 (−$\overset{|}{C}$=O group), 1550 (secondary amine), 980 (trans double bond in conjugation with carbonyl group) cm^{-1}.

Acknowledgement

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Synthesis and Antibacterial Activity of Thiazolyl Guanidines

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A number of biguanides[1] and guanidines have been reported to exhibit antitubercular[2] and antimalarial[3] activities. Bhargava et al[4-7] have shown that benzothiazolyl guanidines are antibacterials, antitubercular and CNS depressants. Besides such compounds are more active against Gram-positive bacteria than Gram-negative ones[8,9].

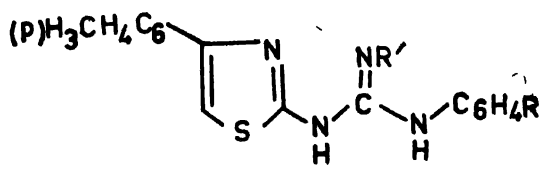
In the present communication, the author has synthesised some new *N*-aryl-*N'*-2-(4-*p*-methylphenyl)-thiazolyl-*N''*-alkyl (or H) guanidines and screened for their antibacterial activities.

Experimental

N-Aryl-N'-2-(4-p-methylphenyl)-thiazolyl thiocarbamides were prepared by the reaction of 2-amino-4-*p*-methylphenyl thiazole and phenyl isothiocyanate or *p*-methoxyphenyl isothiocyanate in dry benzene.

N-Phenyl - N' - 2-(4-p- methylphenyl)- thiazolyl-N''-methyl guanidine (2) :

A mixture of *N*-phenyl-*N'*-2-(4-*p*-methylphenyl)-thiazolyl thiocarbamide (1.6 g), yellow lead oxide (2.5 g) and 33% aqueous methylamine solution (3.0 ml) in 20 ml of ethanol was heated in a steel-autoclave on a water-bath for about three hours with



occasional shaking. The autoclave was opened carefully and the reaction mixture was filtered. The black residue was further extracted with four 10 ml portions of ethanol and filtered hot. The combined filtrate was concentrated and the product was recrystallised from dilute ethanol into yellow coloured crystals.

Similarly, other *N*-phenyl-*N'*-2-(4-*p*-methylphenyl)-thiazolyl-*N''*-alkyl (or H) guanidines were prepared using different alkyl amines or ammonia and are listed in Table 1.

N-p-Methoxyphenyl-N'-2-(4- p- methylphenyl)-thiazolyl-N''-alkyl (or H) guanidines :

These guanidines were prepared as described above using *N*-*p*-methoxyphenyl-*N'*-2-(4-*p*-methylphenyl)-thiazolyl thiocarbamide and different alkyl amines or ammonia and listed in Table 1.

TABLE 1—*N*-ARYL-*N'*-2-(4-*p*-METHYLPHENYL)-THIAZOLYL-*N''*-ALKYL (OR H) GUANIDINES

Sl. No.	Alkyl group R'	Molecular formula	Yield (%)	M.P. (°C)
		R=H		
1.	H	$C_{17}H_{16}N_4S$	64	150
2.	Methyl	$C_{18}H_{18}N_4S$	78	159
3.	Ethyl	$C_{19}H_{20}N_4S$	68	128
4.	*n*-Propyl	$C_{20}H_{22}N_4S$	72	93
5.	*n*-Butyl	$C_{21}H_{24}N_4S$	58	100
6.	*iso*-Butyl	$C_{21}H_{24}N_4S$	85	76
		R=*p*-Methoxy		
7.	H	$C_{18}H_{18}N_4OS$	54	171
8.	Methyl	$C_{19}H_{20}N_4OS$	52	154
9.	Ethyl	$C_{20}H_{22}N_4OS$	73	103
10.	*n*-Propyl	$C_{21}H_{24}N_4OS$	72	105
11.	*iso*-Propyl	$C_{21}H_{24}N_4OS$	68	121
12.	*n*-Butyl	$C_{22}H_{26}N_4OS$	75	100
13.	*iso*-Butyl	$C_{22}H_{26}N_4OS$	81	112

(a) All the melting points are uncorrected.
(b) All the compounds were analysed for C, H, N and S ; the observed values were within a range of ±0.35% of the calculated values.
(c) IR and PMR spectral data were in well agreement with the synthesised compounds.