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Synthesis of New 5-Substituted Pyrazolinyl Oxazolophenoxazine Derivatives

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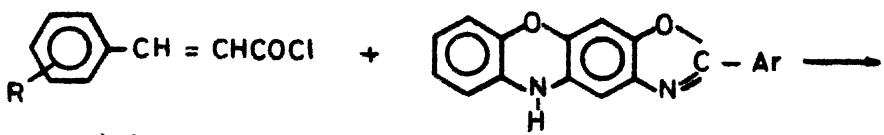
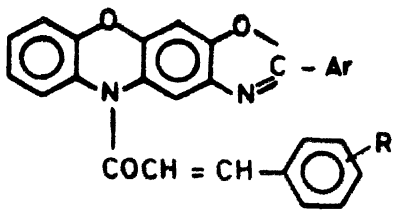
Substituted cinnamoyl chloride (I) reacted with 2-aryl-5H-oxazolo(4,5-*b*) phenoxazines in dioxane in the presence of triethylamine to give 5-substituted benzalacetyl oxazolophenoxazine derivatives (III). (III) reacted easily with hydrazine hydrate, phenyl hydrazine and hydroxylamine giving the corresponding pyrazolines and isozazolines respectively.

IN our previous work[1-4], the synthesis and reaction of oxazolophenoxazine, and some of its derivatives with substituted acid chlorides has been described. In the present work attempts were made to prepare 5-substituted benzalacetyl oxazolophenoxazines to cover other classes of 5-oxazolophenoxazine derivatives. This was conducted by interaction of substituted cinnamonyl chloride[5-8] (I) with oxazolophenoxazines (II) in dioxane using triethylamine as a catalyst given 5- substituted benzalacetyl oxazolophenoxazines (III).

The IR spectra of compounds III showed absorption bands at 1700–1696 cm^{-1} (C = O) and 1808–1606 cm^{-1} (C = C)[9].



(I) (II)

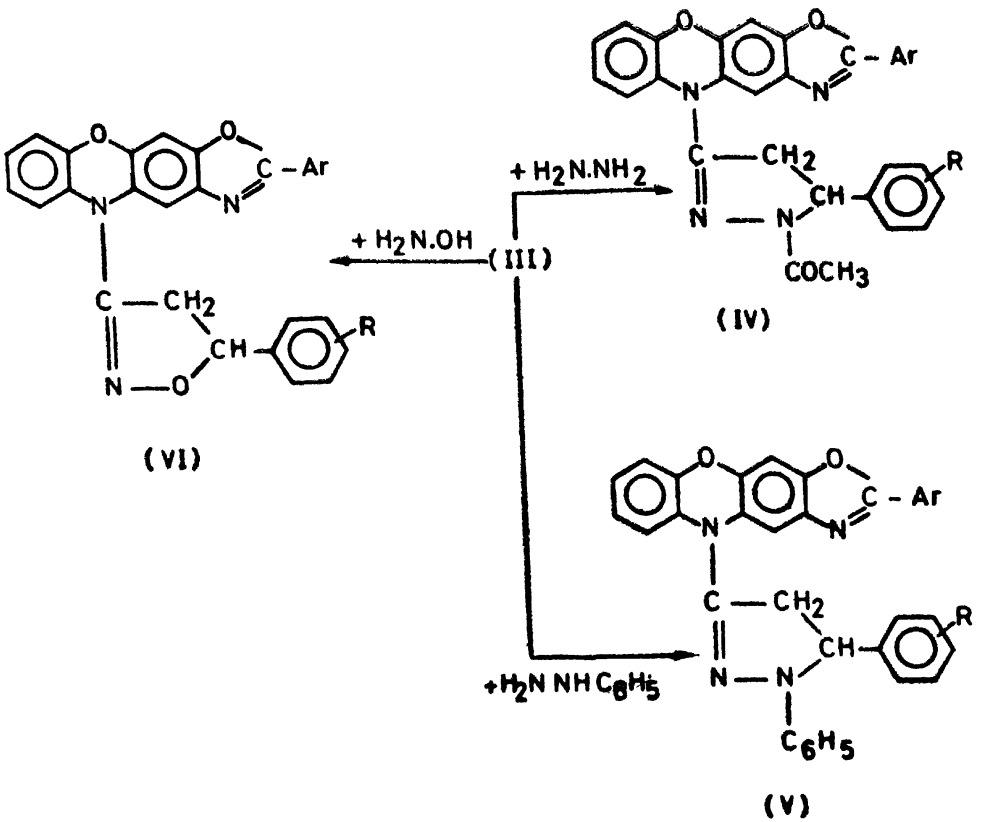


(III)

The additive property of the exo-cyclic C = C in compounds (III) conjugated with the carbonyl group prompted us to investigate their behaviour towards the action of hydrazine hydrate, phenylhydrazine and hydroxylamine hydrochloride. Interaction of (III) with hydrazine under suitable conditions gave a variety of pyrazolines. Hydrazine hydrate itself interacted with (III) in dioxane giving unstable pyrazolines, but when this was treated with glacial acetic acid or when the reaction itself was carried out in presence of glacial acetic acid, the stable N-monoacetyl pyrazolines (IV) were obtained.

The structure of compounds (IV) has been established from their correct analytical data (cf. Table 2) The IR spectra of compounds(IV) showed absorption bands at 1687–1613 cm^{-1} (C = N) and at 1250-1227 cm^{-1} (C–N), and the absence of the –NH stretching frequency. Phenylhydrazine reacted with (III) in presence of a base catalyst. The reaction was carried out in dioxane in presen ceof piperidine giving N-phenyl pyrazolines (V).

The structure of these compounds (V) was established from their correct analytical data (cf. Table



3), and IR spectra showed absorption bands at 1608–1592 cm^{-1} (C = N) and at 1242–1220 cm^{-1} (C–N). Also, compounds (V) proved to be stable on boiling with a mixture of acetic acid and concentrated sulphuric acid at room temperature or on heating above its melting points which are the conditions that bring out the cyclization of phenyl hydrazones to pyrazolines. The prepared pyrazolines gave colour test characteristic for aryl pyrazolines[10,11].

Also when compounds (III) and hydroxylamine hydrochloride in dioxane and in the presence of sodium hydroxide was refluxed, the isoxazoline derivatives (VI) were obtained.

The structure of compounds (VI) has been established from their correct analytical data (cf. Table 4). The IR spectra showed absorption band at 1688–1612 cm^{-1} (C = N).

Experimental

All melting points were uncorrected. The IR absorption spectra were determined in KBr pellets on Unicam SP 200 G infrared spectrophotometer.

Cinnamoyl chloride, and substituted cinnamoyl chloride were prepared by the known methods.

General method for preparation of 4-substituted benzalacetyl oxazolophenoxazine derivatives (III)

Substituted cinnamoyl chloride (1 mol) in dioxane (10 ml) and triethylamine (1 mol) was refluxed with 2-aryl-5*H*-oxazolo(4,5-b) phenoxazine derivatives (1 mol) for 2 hr. The reaction mixture was then allowed to stand at room temperature overnight. The precipitated triethylamine hydrochloride was filtered, the filtrate was evaporated under vacuum and the residue was crystallized from ether and recrystallized from ethyl acetate to give 5-substituted benzalacetyl oxazolophenoxazine derivatives. The results are listed in Table 1.

Preparation of 5-substituted-N-acetyl-pyrazolinyl-oxazolophenoxazines (IV)

To a solution of (III) (0·01 mole) in dioxane (10 ml), few drops of glacial acetic acid, hydrazine hydrate (50%, 4 ml), was added and the mixture was refluxed for 5 hrs. Upon concentration a yellow product separated out which crystallized from alcohol to give N-monoacetyl derivatives. The results are listed in Table 2.

TABLE 1—5-SUBSTITUTED BENZALACETYL OXAZOLOPHENOXAZINE DERIVATIVES (III)

Ar	R	yield %	m.p. °C	Molecular Formula	Found/Calcd. %C	%H	%N
-C_6H_5	H	90	264–5	$C_{28}H_{18}N_2O_3$	78·35 78·14	4·31 4·18	6·69 6·51
-C_6H_4-*p*-OCH_3	H	87	155–6	$C_{29}H_{20}N_2O_4$	75·80 75·65	4·51 4·34	6·27 6·09
-C_6H_4-*o*-OH	H	91	120–2	$C_{28}H_{18}N_2O_4$	75·55 75·33	4·19 4·03	6·35 6·27
-C_6H_4-*o*-Cl	H	85	130–3	$C_{28}H_{17}N_2O_3Cl$	72·69 72·41	3·75 3·66	6·21 6·03
-C_6H_5	-*p*-OCH_3	90	230–1	$C_{29}H_{20}N_2O_4$	75·79 75·64	4·48 4·34	6·18 6·09
-C_6H_4-*p*-OCH_3	-*p*-OCH_3	90	215–7	$C_{30}H_{22}N_2O_5$	73·63 73·47	4·61 4·49	5·83 5·71
-C_6H_5	-*m*-NO_2	87	203–5	$C_{28}H_{17}N_3O_5$	70·89 70·73	3·70 3·58	8·91 8·84
-C_6H_4-*p*-OCH_3	-*m*-NO_2	85	219–21	$C_{29}H_{19}N_3O_6$	69·07 68·91	3·89 3·76	8·50 8·31
-C_6H_5	-*p*-$N(CH_3)_2$	90	285–7	$C_{30}H_{23}N_3O_3$	76·26 76·11	4·93 4·86	8·97 8·88
-C_6H_4-*p*-OCH_3	-*p*-N-$(CH_3)_2$	90	220–3	$C_{31}H_{25}N_3O_4$	74·08 73·95	5·06 4·97	8·50 8·35

TABLE 2—5-SUBSTITUTED--N-ACETYL-PYRAZOLINYL OXAZOLOPHENOXAZINE DERIVATIVES (IV)

Ar	R	yield %	m.p. °C	Molecular Formula	Found/Calcd %C	%H	%N
-C_6H_5	H	70	294–5	$C_{30}H_{22}N_4O_3$	74·21 74·07	4·55 4·33	11·69 11·52
-C_6H_4-*p*-OCH_3	H	72	280–2	$C_{31}H_{24}N_4O_4$	72·21 72·09	4·69 4·65	10·93 10·85
-C_6H_4-*o*-OH	H	75	259–60	$C_{30}H_{22}N_4O_4$	71 89 71·71	4·51 4·38	11·33 11·15
-C_6H_4-*o*-Cl	H	78	277–80	$C_{30}H_{21}N_{11}O_3Cl$	69·38 69·23	4·21 4·04	10·91 10·77
-C_6H_5	-*p*-OCH_3	70	292–5	$C_{31}H_{24}N_4O_4$	72·23 72·09	4·79 4·65	10·98 10·85
-C_6H_4-*p*-OCH_3	-*p*-OCH_3	75	245–7	$C_{32}H_{26}N_4O_5$	70·51 70·33	4·89 4·76	10·47 10·25
-C_6H_5	-*m*-NO_2	76	257–9	$C_{30}H_{21}N_5O_5$	67·92 67·79	4·08 3·95	13·23 13·18
-C_6H_4-*p*-OCH_3	-*m*-NO_2	80	285–7	$C_{31}H_{25}N_5O_6$	66·57 66·31	4·23 4·09	12·61 12·47
-C_6H_5	-*p*-$N(CH_3)_2$	79	248–9	$C_{32}H_{27}N_5O_3$	72·72 72·58	5·23 5·13	13·39 13·13
-C_6H_4-*p*-OCH_3	-*p*-$N(CH_3)_2$	75	279–81	$C_{33}H_{29}N_5O_4$	70·97 70·83	5·38 5·19	12·67 12·52

TABLE 3—5-SUBSTITUTED-N-PHENYL-PYRAZOLINYL OXAZOLOPHENOXAZINE DERIVATIVES (V)

Ar	R	yield %	m.p. °C	Molecular Formula	Found/Calcd. %C	%H	%N
$-C_6H_5$	H	73	280–2	$C_{34}H_{24}N_4O_2$	78·58 78·46	4·73 4·61	10·91 10·77
$-C_6H_4$-*p*-OCH_3	H	70	220–3	$C_{35}H_{26}N_4O_3$	76·50 76·36	4·88 4·72	10·35 10·18
$-C_6H_4$-*o*-OH	H	69	177–80	$C_{34}H_{24}N_4O_3$	76·25 76·12	4·68 4·47	10·58 10·44
$-C_6H_4$-*o*-Cl	H	75	230–3	$C_{34}H_{23}N_4O_2Cl$	73·81 73·64	4·28 4·15	10·17 10·01
$-C_6H_5$	-*p*-OCH_3	72	276–8	$C_{35}H_{26}N_4O_3$	76·54 76·33	4·85 4·72	10·29 10·18
$-C_6H_4$-*p*-OCH_3	-*p*-OCH_3	80	168–70	$C_{36}H_{28}N_4O_4$	74·63 74·48	5·02 4·81	9·73 9·65
$-C_6H_5$	-*m*-HO_2	74	221–23	$C_{34}H_{29}N_5O_4$	72·39 72·20	4·18 4·07	12·55 12·40
$-C_6H_4$-*p*-OCH_3	-*m*-NO_2	78	215–18	$C_{35}H_{26}N_5O_5$	70·73 70·58	4·37 4·20	11·89 11·76
$-C_6H_5$	-*p*-$N(CH_3)_2$	70	209–11	$C_{36}H_{29}N_5O_2$	76·89 76·73	5·33 5·15	12·55 12·45
$-C_6H_4$-*p*-OCH_3	-*p*-$N(CH_3)_2$	79	233–7	$C_{37}H_{31}N_5O_3$	74·98 74·87	5·57 5·22	11·98 11·80

TABLE 4—5-SUBSTITUTED ISOXAZOLINYL OXAZOLOPHENOXINE DERIVATIVES (VI)

Ar	R	yield %	m.p. °C	Molecular Formula	Found/Calcd. %C	%H	%N
$-C_6H_5$	H	70	270–3	$C_{28}H_{19}N_3O_3$	75·68 75·52	4·39 4·27	9·57 9·43
$-C_6H_4$-*p*-OCH_3	H	75	235–7	$C_{29}H_{21}N_3O_4$	73·39 73·26	4·61 4·42	9·03 8·84
$-C_6H_4$-*o*-OH	H	69	158–60	$C_{28}H_{19}N_3O_4$	73·05 72·88	4·33 4·12	9·29 9·11
$-C_6H_4$-*o*-Cl	H	76	205–7	$C_{28}H_{18}N_3O_3Cl$	72·48 72·23	3·91 3·75	8·93 8·76
$-C_6H_5$	-*p*-OCH_3	79	285–7	$C_{29}H_{21}N_3O_4$	73·38 73·26	4·61 4·42	9·05 8·84
$-C_6H_4$-*p*-OCH_3	-*p*-OCH_3	80	215–7	$C_{30}H_{23}N_3O_5$	71·45 71·28	4·66 4·55	8·48 8·31
$-C_6H_5$	-*m*-NO_2	73	217–9	$C_{28}H_{18}N_4O_5$	68·71 68·57	3·88 3·67	11·51 11·43
$-C_6H_4$-*p*-OCH_3	-*m*-NO_2	75	223–5	$C_{29}H_{20}N_4O_6$	67·11 66·92	4·02 3·84	10·91 10·77
$-C_6H_5$	-*p*-$N(CH_3)_2$	76	218–20	$C_{30}H_{24}N_4O_3$	73·95 73·77	5·12 4·91	11·63 11·48
$-C_6H_4$-*p*-OCH_3	-*p*-$N(CH_3)_2$	77	210–12	$C_{31}H_{26}N_4O_4$	72·05 71·81	5·28 5·01	10·92 10·81

Preparation of 5-substituted-N-phenyl pyrazolinyl-oxazolophenoxazines (V)

A solution of (III) (0·005 mole) and phenyl hydrazine (0·007 mole) in dioxane (10 ml), and few drops of piperidine was refluxed for 3 hrs. On concentration and cooling crystalline product separated out. These were filtered and crystallized from ethanol as pale yellow crystals. The results are listed in Table 3.

Preparation of 5-substituted isoxazolinyl-oxazolophenoxazines (VI)

A solution of equimolar quantities of (III) and hydroxylamine hydrochloride in dioxane (10 ml), and few crystals of NaOH was refluxed for 6 hrs. On concentration and cooling the product was crystallized from alcohol. The results are listed in Table 4.

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