

Using of 4-(4'-Methylbenzylidene)-1-Hydroxy-2-(N-Phthalimidomethyl)-5-Imidazolone as A Building Block in Synthesis of Some Heterocyclic Compounds

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Summary: 4-(4'-Methylbenzylidene)-1-hydroxy-2-(N-phthalimidomethyl)-5-imidazolone (2) is now newly synthesized. The interactions of 2 with aromatic amines, hydrazines, and aromatic substrates under Friedel-Craft's conditions were studied. Also the phthalyl group used as masking group in the preparation of heterocyclic amines.

Introduction

We report here on the synthesis of 4-(4'-methyl-benzylidene)-1-hydroxy-2-(N-phthalimido-methyl)-5-imidazolone (2) via ring opening of 2-(N-phthalimido-methyl)-4 (4'-methyl-benzylidene)-5(4)-oxazolone [1] (1) with hydroxyl-amine hydrochloride in refluxing pyridine.

The structure of 2 was established from the following assignments : (i) Correct analytical values. (ii) The infrared spectrum [2] of 2 exhibited bands attributable to the carbonyl of imidazolone (1680 cm^{-1}), coupling carbonyl of cyclic imide moiety (1780 and 1730 cm^{-1}), and OH group (basin, centered at 3590 cm^{-1}). (iii) The mass spectrum showed molecular ion $[M^+, m/z\ 361\ (0.28\ \%)]$, (cf. Chart 1).

Interaction of imidazolone derivative 2 with aromatic amines namely, aniline, *p*-toluidine, *p*-anisidine and *p*-aminobenzoic acid in an oil bath at 150°C gave directly the required imidazolones (3_{a-d}).

The structure of the imidazolones 3 was based on: (i) analytical data. (ii). The IR measurements which showed stretching frequencies at 1630 , 1695 , 1780 , 1720 and 3550 cm^{-1} characteristic for -C=N- , -CONAr , and doublet of cyclic imides, and OH for compound 3_d . (iii) The $^1\text{H-NMR}$ spectrum of 3_c in CDCl_3 showed signals at (δ ppm) 1.7 (s, 3H, Ar- CH_3), 2.2 (s, 2H, CH_2), 6.3 (s, 1H, CH), 7.6-8 (m, 13H, ArH). (iv) Compounds 3_{a-d} have been obtained via unambiguous synthesis, by interaction of oxazolone derivative 1 with aniline, *p*-toluidine, *p*-anisidine, and *p*-amino-benzoic acid in boiling acetic

acid, in the presence of fused sodium acetate as catalyst [3].

The phthalyl group has been utilized in variety of cases as masking group in preparation of amines and amino- acids. Thus when compound 2 was allowed to react with excess hydrazine hydrate or phenylhydrazine in refluxing toluene it yielded a mixture of 1,4-phthalazindione (4), and 3-aminomethyl-5-(4'-methylbenzylidene)-1,2-dihydro-1,2,4-triazin-6-one (5) and a mixture of *N*-anilinophthalimide (6) and 1-phenyl-3-aminomethyl-5 (4'-methylbenzylidene)-(1*H*)-1,2,4-triazin-6-one (7) respectively.

The structure of phthalazindione 4 and *N*-anilinophthalimide 6 was established by (i) comparison with authentic samples [4,5], (ii) with the IR spectrum of compound 4 which displayed strong absorption bands at 1760 , and 3320 cm^{-1} attributable to $\nu_{\text{C=O}}$ and ν_{NH} respectively. The IR spectrum of 6 showed ν_{max} of two carbonyl groups at 1790 , 1730 and 3300 cm^{-1} due to mechanical coupling of imides moiety and ν_{NH} .

The following facts supports the structure assigned to the 1,2,4-triazin-6-ones 5 and 7: (i) Their IR spectra exhibit strong absorption bands in the region 1680 - 1690 , attributable to $\nu_{\text{C=O}}$ and 3450 - 3350 cm^{-1} ν_{NH} or ν_{OH} . Such IR data illustrate that compounds 5 and 7 really exists in lactam \rightleftharpoons lactim dynamic equilibrium. (ii) $^1\text{H-NMR}$ of compound 5 showed signals at (δ ppm), 1.8 (s, 3H, Ar- CH_3), 2.1 (s, 2H, CH_2) 6.3 (s, 1H, CH), 7.4 (m, 4H, ArH), 8.1

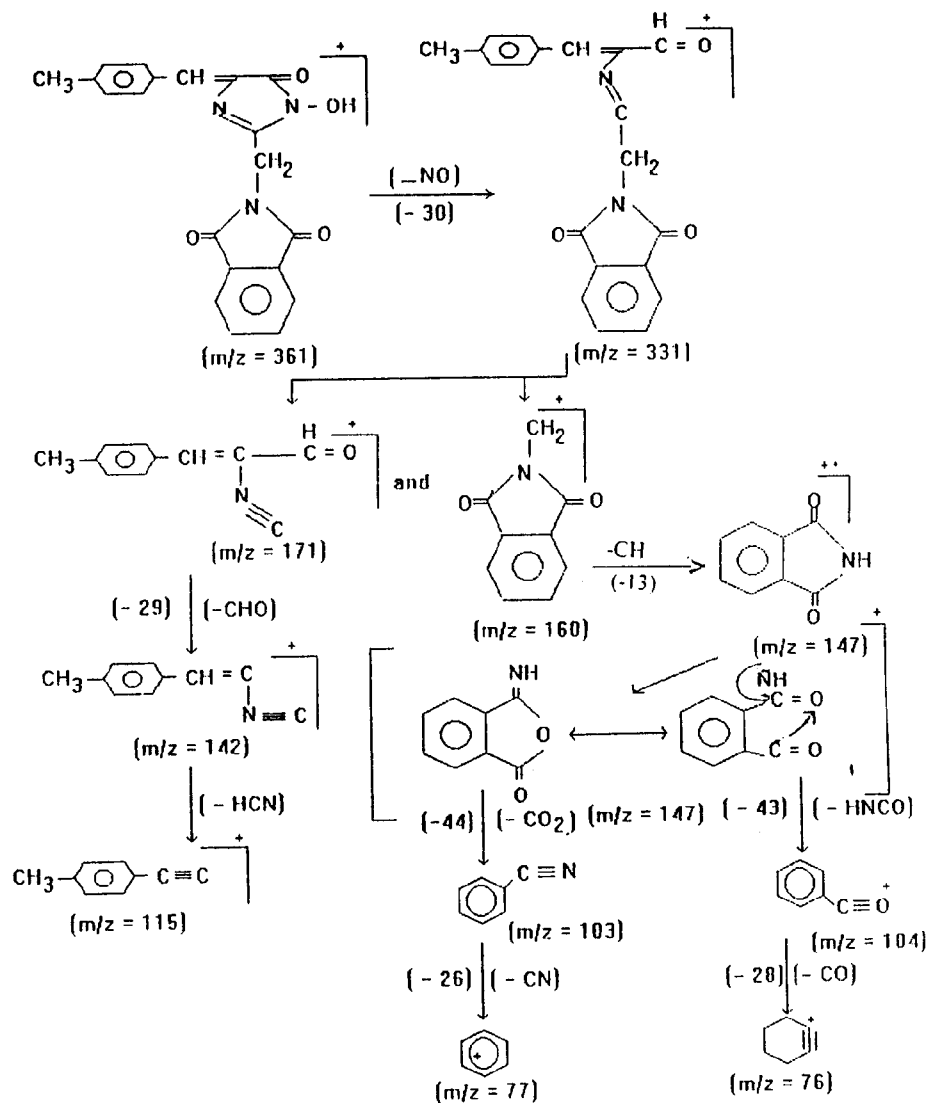


Chart (1)

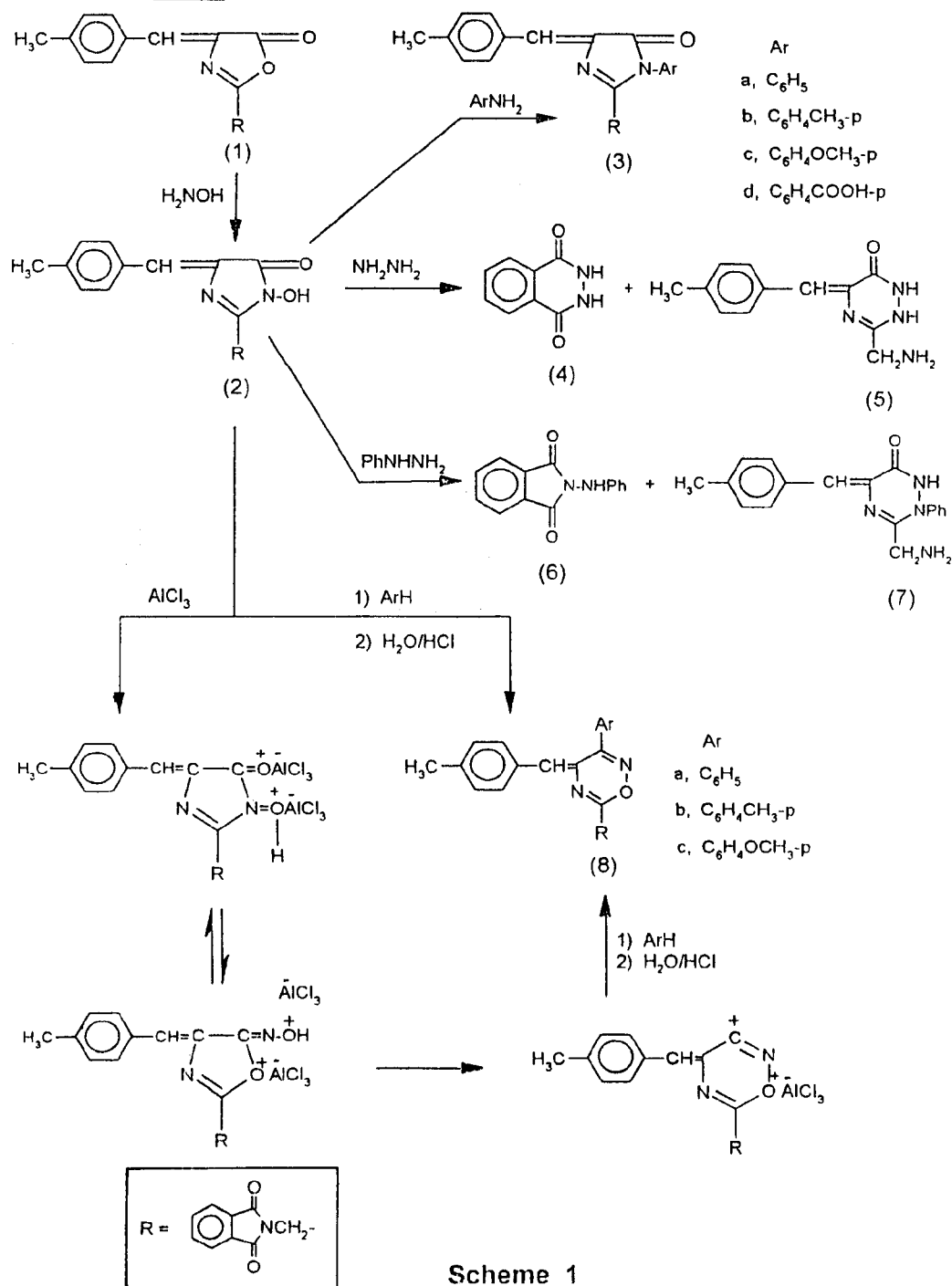
(broad, s, 2H, NH₂), 9.1 (s, 1H, NH) and 9.4 (s, 1H, NH/OH), and compound 7 showed signals at δ 1.6 (s, 3H, ArCH₃), 2.2 (s, 2H, CH₂), 6.1 (s, 1H, CH), 7.2-7.8 (m, 9H, ArH), 8.1 (broad, 2H, NH₂), 8.7 (s, 1H, NH). (iii) Interaction of oxazolone 1 with phenylhydrazine in acetic acid solution and in the presence of sodium acetate gave directly the required 1,2,4-triazine [3] (7). On the other hand, trials for conversion of oxazolone 1 to compound 5 via its interaction with hydrazine hydrate in the

presence of boiling acetic acid and fused sodium acetate were unsuccessful. It seemed that decomposition took place as indicated by rapid evolution of nitrogen (frothing).

El-Hashash *et al.* had reported the hetero-ring opening of the 3,1-benzoxazin-4-one [6], 5(4*H*)-oxazolone [7], and furanone derivatives [8,9] by aromatic hydrocarbons under Friedel-Craft's conditions. Similar work has not been carried out so

far on imidazolone derivative 2. Thus, when imidazolone 2 was submitted to react with aromatic hydrocarbons namely, benzene, toluene, and anisole under Friedel-Craft's conditions afforded 4-(4'-methylbenzylidene)-3-aryl-6-(*N*-phthalimido-methyl)-1,2,5-oxadiazine (8_{a-c}) (cf. Scheme 1).

The structure of compounds 8_{a-c} was confirmed by : (i) The correct elemental analysis, (ii) the IR spectra exhibited strong absorption bands at (1790-1780), (1720-1710), (1630-1620) and (1610-1600) cm⁻¹ attributable to mechanical coupling of ν_{C=O} of cyclic imides, ν_{C-N} and ν_{C-C}



Scheme 1

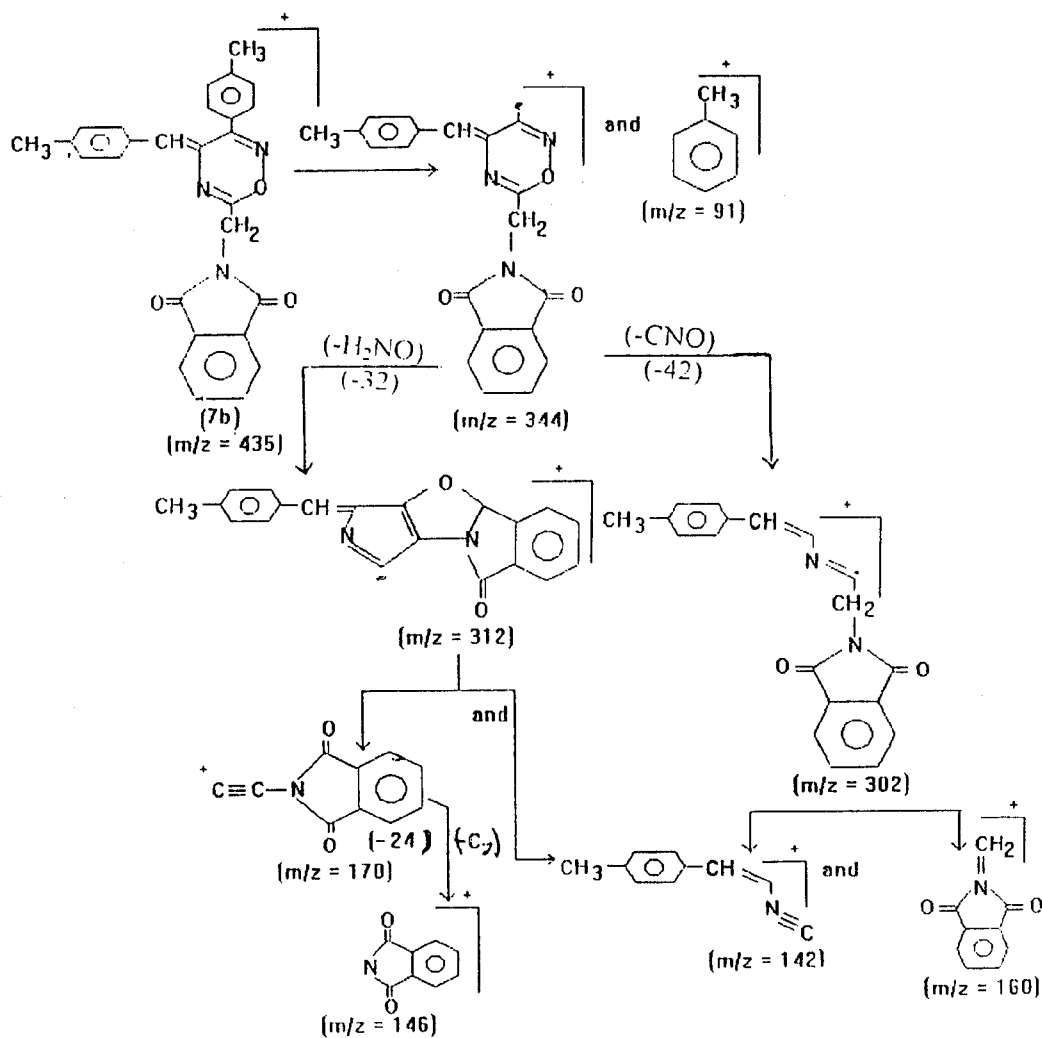


Chart (2)

functions respectively, (iii) 1H -NMR spectrum of **8_a** showed signals at: δ (ppm), 2(s, 3H, ArCH₃), 3.4 (s, 2H, CH₂), 5.5 (s, 1H, CH) and 7.4-7.8 (m, 13H, ArH), (iv) the mass spectrum of **8_b** and **8_c**. (cf. Charts 2 and 3).

Experimental

Melting points are uncorrected. IR spectra were measured on a Unicam SP-1200 infrared spectrophotometer using KBr Wafer technique (National Research Centre, Giza, Egypt.) and 1H -NMR spectra on Joel FX 90 Q MHz spectrometer (National Research Centre, Giza, Egypt) using TMS

as an internal standard in CDCl₃ chemical shifts in δ ppm), and Mass spectra were recorded on HP model : MS 5988 (Cairo University, Cairo.) instrument.

Synthesis of 4-(4'-methylbenzylidene)-1-hydroxy-2-(N-phthalimidomethyl)-5-imidazolone (2).

A mixture of 2-(N-phthalimidomethyl)-4-(4-methyl benzylidene)-5(4)-oxazolone (**1**) (0.01 mole) and hydroxylamine hydrochloride (0.015 mole) in pyridine (30 ml) was refluxed for 2 h. The reaction mixture was poured on ice-cold dilute HCl. The solid that separated out was crystallized from xylene to give **2** (cf. Table 1).

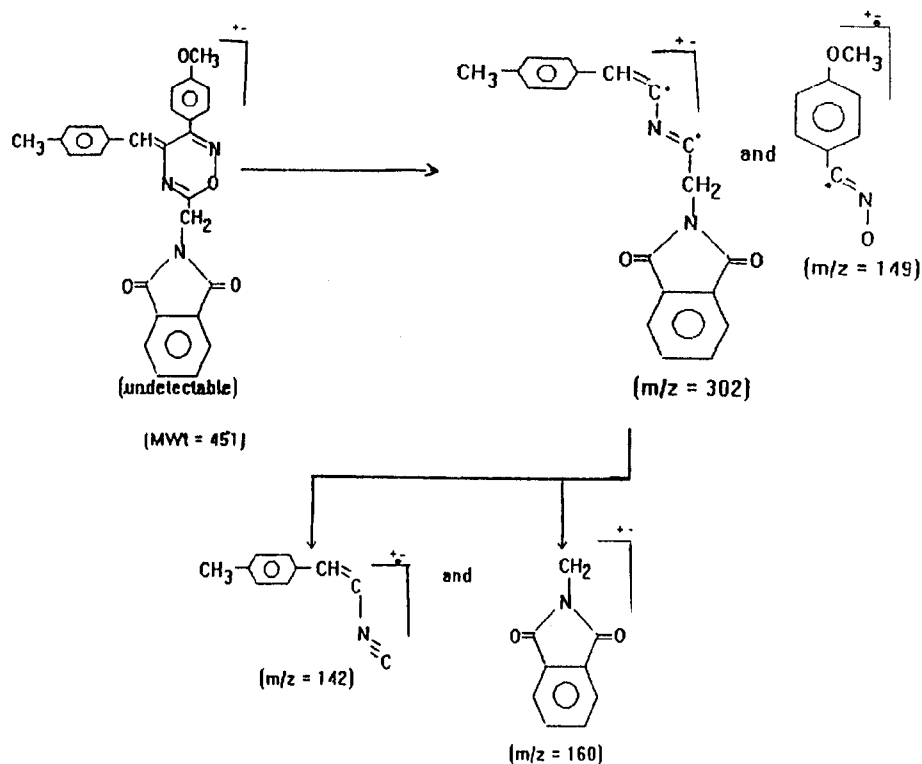


Chart (3)

Table I : Physical and analytical data of compounds (1-7)

Compd. No.	M.p. ^a (Yield)	Ref.	Mol. Formula (M.WL)	Analysis % Found (Calcd.)		
				C	H	N
2	164-166 ^b (80)	-	C ₂₈ H ₁₇ N ₃ O ₄ (361)	66.30 (66.48)	4.10 (4.16)	11.40 (11.63)
3 _a	216-218 ^b (65)	-	C ₂₆ H ₁₇ N ₃ O ₃ (421)	74.20 (74.11)	4.40 (4.51)	9.70 (9.97)
3 _b	133-135 ^c (72)	-	C ₂₇ H ₂₁ N ₃ O ₃ (435)	74.20 (74.48)	4.70 (4.83)	9.40 (9.66)
3 _c	184-186 ^c (63)	-	C ₂₇ H ₂₁ N ₃ O ₄ (451)	71.60 (71.84)	4.60 (4.65)	9.20 (9.31)
3 _d	156-158 ^b (60)	-	C ₂₇ H ₁₉ N ₃ O ₃ (465)	69.40 (69.68)	4.10 (4.09)	9.10 (9.03)
4	300 ^c (42)	3	C ₉ H ₈ N ₂ O ₂ (162)			
5	201-203 ^d (40)	-	C ₁₂ H ₁₄ N ₄ O (230)	62.40 (62.61)	6.10 (6.08)	24.10 (24.35)
6	171-173 ^c (49)	4	C ₁₄ H ₁₆ N ₂ O ₂ (238)			
7	228-230 ^c (35)	-	C ₁₈ H ₁₈ N ₄ O (306)	70.30 (70.59)	5.90 (5.88)	18.10 (18.30)
8 _a	179-181 ^b (62)	-	C ₂₆ H ₁₉ N ₃ O ₃ (421)	74.30 (74.11)	4.40 (4.51)	9.60 (9.97)
8 _b	230-232 ^d (68)	-	C ₂₇ H ₂₁ N ₃ O ₃ (435)	74.30 (74.48)	4.60 (4.83)	9.60 (9.66)
8 _c	118-120 ^b (61)	-	C ₂₇ H ₂₁ N ₃ O ₄ (451)	71.70 (71.84)	4.50 (4.65)	9.20 (9.31)

^a Recrystallized from : (a) xylene, (b) benzene, (c) ethanol, (d) benzene-ethanol.

EIMS for compound 2 : m/z 361 (0.28 %), 331 (0.17 %), 160 (100 %), 171 (1.3 %), 147 (1.11 %), 142 (0.48 %), 115 (8 %), 104 (20 %), 103 (3 %), 77 (13 %) and 67 (16.3 %).

Reaction of the imidazolone 2 with aromatic amines and/or *p*-aminobenzoic acid : Formation of (3_{a-d})

A mixture of 2 (0.01 mole) and aromatic amines namely, aniline, *p*-toluidine, *p*-anisidine, and *p*-aminobenzoic acid (0.01 mole) was heated on oil bath at 150 °C for 1h. The resulting Jelly like mass was crystallized from a suitable solvent to give 3_{a-d} (cf. Table 1).

Independent synthesis of the 4-(4-methylbenzylidene)-1-aryl-2-(*N*-phthalimidomethyl)-5-imidazolone (3_{a-d})

A mixture of oxazolone 1 (0.01 mole) and aromatic amines namely, aniline, *p*-toluidine, *p*-anisidine and *p*-aminobenzoic acid (0.01 mole) and

fused sodium acetate (0.3 g) in acetic acid (50 ml) was heated under reflux for 1h. Dilution with water gave products identified as **3_{a-d}** respectively by m.p. and m.m.p. determination.

Reaction of 2 with hydrazine hydrate : Formation of 1,4-phthalazindione (4) and 3-aminomethyl-5(4'-methyl benzylidene)-1,2-dihydro-1,2,4-triazin-6-one (5).

A mixture of **2** (0.01 mole) and hydrazine hydrate (0.03 mole) in toluene (50 ml) was refluxed for 3 h., then cooled. The solid product was filtered off and crystallized from ethanol to give **4**, the mother liquor was concentrated and crystallized from benzene, ethanol to give **5** (cf. Table 1).

Unsuccessful independent synthesis of the 1,2-dihydro-1,2,4-triazin-6-one (5).

Oxazolone **1** (0.01 mole) and hydrazine hydrate (0.02 mole) in acetic acid (60 ml) and in the presence of fused sodium acetate (0.3 g) were heated under reflux for 1h. much frothing took place. Decomposition of the cold reaction mixture with water gave sticky products from which no crystalline materials were obtained.

Reaction of 2-with phenylhydrazine : Formation of N-anilinophthalimide (6), 1-phenyl-3-aminomethyl-5(4'-methylbenzylidene)-(1H)-1,2,4-triazin-6-one (7)

A solution of **2** (0.01 mole) in toluene (40 ml) was treated with phenylhydrazine (0.03 mole). The reaction mixture was refluxed for 3 h., then cooled. The solid product was filtered off and crystallized from benzene to give **6**. The mother liquor was concentrated and crystallized from ethanol to give **7** (cf. Table 1).

Independent synthesis of (1H)-1,2,4-triazin-6-one (7)

The oxazolone **1** (0.01 mole) and phenylhydrazine (0.02 mole) in acetic acid (60 ml) and in the presence of fused sodium acetate (0.3 g) were heated under reflux for 1h. Dilution with water gave a product identified as **7** by m.p. and mixed m.p. determination.

Reaction of 2 with aromatic hydrocarbons : Formation of 4-(4'-methylbenzylidene)-3-aryl-6-(N-phthalimidomethyl)-1,2,5-oxadiazine (8_{a-c})

To a solution of the imidazolone derivative **2** (0.01 mole) in the aromatic hydrocarbons namely,

benzene, toluene and anisole (50 ml), anhydrous AlCl₃ (0.04 mole) was added portionwise while stirring. The stirring was continued for 6 h., the reaction mixture was then refluxed on a steam-bath for 3 h. and left aside overnight. The reaction mixture was decomposed with iced-dil. HCl and the excess solvent was removed by steam-distillation and the organic materials were extracted with ether. Slow evaporation of ether left a solid which was crystallized from the proper solvent to give compounds (**8_{a-c}**). Their physical data are given in Table 1.

EIMS (rel. abun.) for compound **8_b** : *m/z* 435 (8 %), 344 (0.3 %), 312 (100 %), 302 (7 %), 170 (16 %), 160 (46 %), 146 (37 %), 142 (0.4 %), 115 (3.2 %), 104 (22 %), 103 (12 %), 77 (55 %), 76 (36 %).

EIMS (rel. abun.) for compound **8_c** : *m/z* 302 (2.1 %), 160 (100 %), 149 (24 %), 146 (13 %), 142 (7 %), 140 (8 %), 103 (3.3 %), 77 (18.6 %), 76 (21.2 %).

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