Some Reactions of N-(3,4-Dimethylbenzoylacryloyl)-Anthranilic Acid and Its Derivatives

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Summary: N-(3,4-Dimethylbenzoylacryloyl)-anthranilic acid (I) was easily cyclized to the corresponding benzoxazone (IV) by the effect of Ac_2O. Condensation of (IV) with hydrazine hydrate gave rise to the aminoquinazolinones (XIII). Some reactions of the above product have been investigated.

In continuation of our recent study [1-5] on α, β-unsaturated keto-acid derivatives, we report here the influence of introducing electron-repelling substituents in the aroyl group in N-(3,4-dimethylbenzoylacryloyl)-anthranilic acid (I) on the polarization of the ketonic carbonyl group, and to synthesize a number of new-2-substituted 4H-3, 1-benzoxazin-4-ones and their corresponding 4-quinazolones for pharmacological evaluation [6,7].

Thus, condensation of N-[3-3',4'-dimethylbenzoylacryloyl)]-anthranilic acid (I) with urea, thiourea or benzylthiourea in boiling ethanol in the presence of few drops of glacial acetic acid gave the corresponding oxo- and thioxopyrimidine anthranilic acid derivatives (IIa-c) respectively.

The mass spectrum of (IIb) shows a peak at m/e 370 corresponding to the molecular ion. It further supported the structure of (IIb).

Reaction of (I) with hydroxylamine hydrochloride in boiling ethanol in the presence of sodium acetate led to the formation of N-3-(3,4-dimethylphenyl-2-benzisoxazole)-anthranilic acid (III).

Heating a solution of (I) in acetic anhydride affected dehydration and formation of th corresponding 2-[2-(3,4'-dimethylbenzoylvinyl)]-4H-3, 1-benzoxazin-4-one (IV).

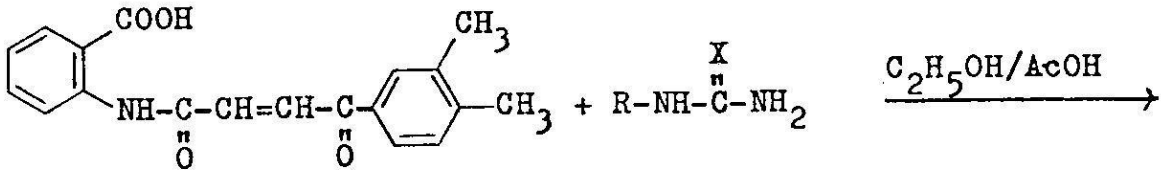
The structure of (IV) was established by alternate synthesis via shaking a pyridine solution of anthranilic acid (1 mole) with β-3,4-dimethylbenzoylacryloyl chloride (2 mole) followed by reflux for 30 minutes.

The reaction of (IV) with methylamine, ethylamine, n-butylamine, benzylamine or dimethylamine in boiling ethanol led to opening of the benzoxazone ring with formation of the corresponding 2'[alkyl-or arylcarbamoyl-β - (3',4'-dimethylphenylacryl)]-anilides (va-e) respectively.

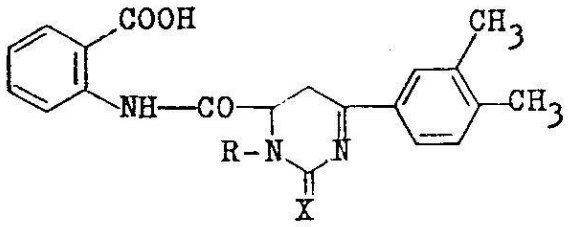
The mass spectrum of (Va) shows a peak at m/e 336 corresponding to the molecular ion. It further supported the structure of (Va).

The mass spectrum of (Vd) shows a peak at m/z 412 corresponding to the molecular ion. It further supported the structure of (Vd).

On the other hand, fusion of (I) with ethylamine or benzylamine in the presence of anhydrous $ZnCl_2$ at 160-170°C for 6 hours led to the formation of the corresponding quinazolinone derivative (VIa and b) respectively.

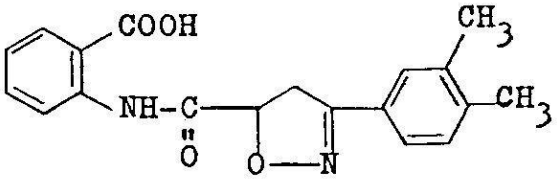


(I)

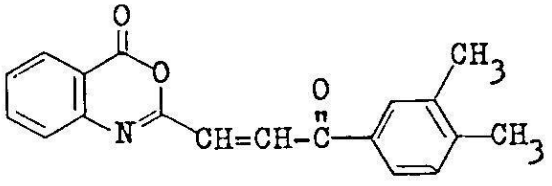


(II)

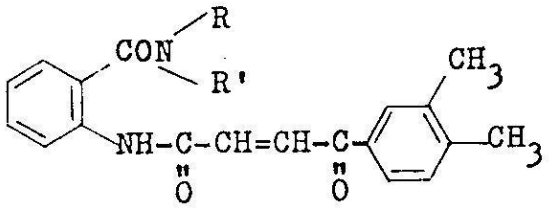
	R	X
a,	H	O
b,	H	S
c,	$CH_2C_6H_5$	S



(III)



(IV)



(V)

	R	R'
a,	H	CH_3
b,	H	C_2H_5
c,	H	$n\text{-}C_4H_9$
d,	H	$CH_2\text{-}C_6H_5$
e,	CH_3	CH_3

The quinazolinone derivatives (VIa) and (VIb) were also synthesized by refluxing (Vb) and (Vd) with acetic anhydride. The identity of these with previous obtained compounds were proved by m.p. and mixed m.p. determinations.

Fusion of (VI) with diethylmalonate in the presence of soidum methoxide under Michael conditions led to opening of the benzoxazone ring with formation of the corresponding ethylbenzamidobenzoylacetate derivative (VII) [8].

Reaction of (VII) with benzylamine (molar ratio 1:1) in boiling ethanol in presence of few drops of piperidine gave rise to the corresponding N-benzylbenzamidobenzoyl acetamide derivative (VIII).

On the other hand reaction of (IV) with diethylamalonate in boiling pyridine under Michael conditions led to opening of the benzoxazone ring and addition on α,β-unsaturated ketonic group to give (IX) [4,5].

Reaction of (IV) with KCN in methanol/water mixture gave rise to the formation of (X) as a result of addition of HCN to the active $>CH=CH<$ followed by hydrolysis of cyano group to carboxyl group with opening of the benzoxazone ring [8].

As expected (X) shows M^+ at m/e 369 in its mass spectrum.

Condensation of (IV) with urea in boiling ethanol and few drops of glacial acetic acid gave the corresponding oxo-pyrimidine derivative (XI).

Alkaline hydrolysis of (XI) gave (IIa) identified by melting point and mixed melting point determinations, without opening of oxo-pyrimidine ring containing less reactive carbonyl group.

Similarly, condensation of (IV) with hydroxylamine hydrochloride in boiling ethanol in the presence of sodium acetate gave rise to the corresponding isoxazoline derivative (XII).

Condensation of (IV) with hydrazine hydrate (molar ratio 1:2) in boiling ethanol, formic, acetic, propionic or n-butyric acid led to the formation of the corresponding pyrazolinylamino and acylamino-quinazolinone derivative (XIIIa-e) respectively.

Compounds (XIIIb and d) can be obtained alternatively via boiling (XIIIa) with formic acid or propionic acid respectively.

The mass spectrum of (XIIIa) shows a peak at m/e 333 corresponding to the molecular ion. It further supported the structure of (XIIIa).

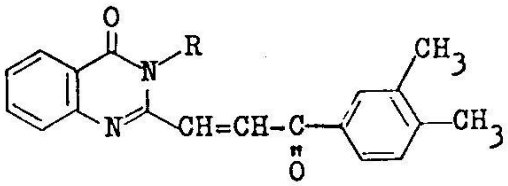
Boiling an ethanolic solution of (XIIIa) with aromatic aldehydes namely benzaldehyde, p-chlorobenzaldehyde, anisaldehyde and piperonal and with acetone led to the formation of the corresponding pyrazolinyl arylidine aminoquinazolinone derivatives (XIVa-e) respectively.

The mass spectra shows a peak at m/e 421 and m/e 451 corresponding to the molecular ions. It further supported the structure of (XIVa) and (XIVc) respectively.

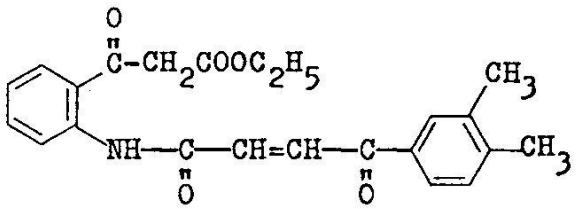
Benzoylation of (XIIIa) using benzoyl chloride in pyridine led to the formation of the corresponding dibenzoyl derivatives (XVa) [10].

The mass spectrum of (XVa) shows a peak at m/e 541 corresponding to molecular ion (XVa). It further supported the structure of (XVa).

Bromination of (XIIIa) using a solution of bromine in chloroform gave rise to formation of 4-bromoderivative (XVb).

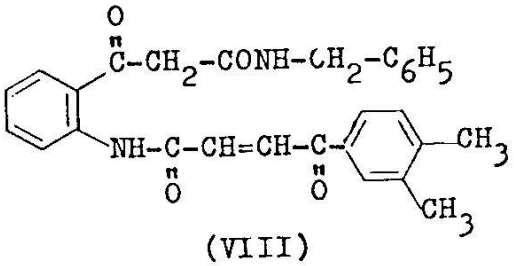


(VI)

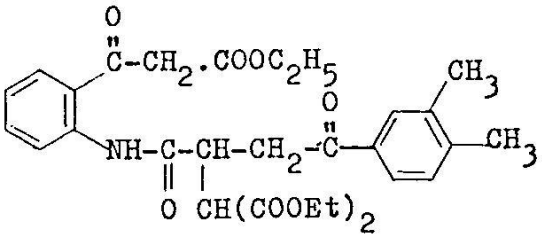


(VII)

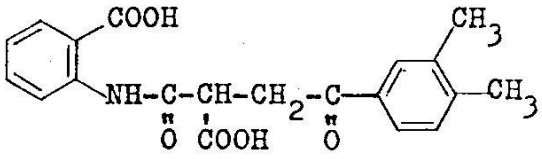
a, R = CH_2CH_3 b, R = $CH_2C_6H_5$



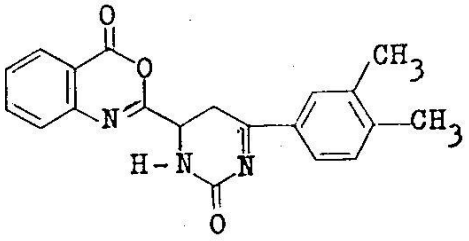
(VIII)



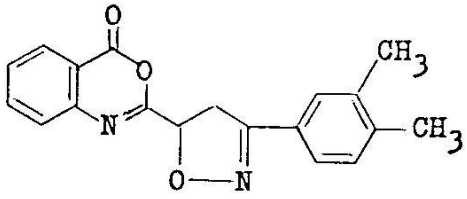
(IX)



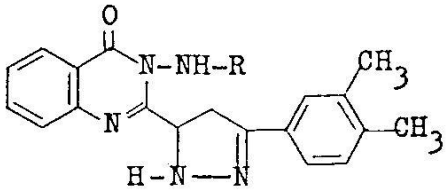
(X)



(XI)



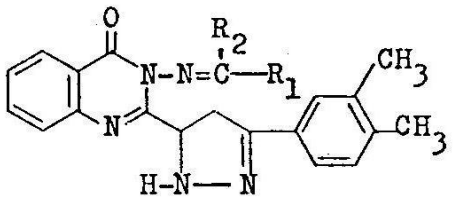
(XII)



(XIII)

a, R = H b, R = CHO c, R = $COCH_3$ d, R = $COCH_2CH_3$

e, R = $COCH_2CH_2CH_3$(n-)



(XIV)

	R_1	R_2
a,	H	C_6H_5
b,	H	$C_6H_4Cl(p)$
c,	H	$C_6H_4OCH_3(p)$
d,	H	piperonyl
e,	CH_3	CH_3

On the other hand, when bromination takes place in glacial acetic acid, the corresponding triacetyl derivative (XVc) obtained without bromination.

The mass spectrum of (XVc) shows a peak at m/e 454 corresponding to the molecular ion. It further supported the structure of (XVc).

As a point of interest, this work investigates also the reaction of (XIIIa) with secondary amines under Mannich conditions [9]. Thus, treatment of ethanolic solution of (XIIIa) with secondary amines namely morpholine, piperidine and dimethylamine in the presence of formaldehyde/ concentrated hydrochloric acid led to the formation of N-Mannich bases (XVd-f) respectively.

Nitrosation of (XIIIa) using sodium nitrite and concentrated hydrochloric acid led to the formation of 3-hydroxy -4-quinazolin-4-one (XVI) which can be obtained alternatively via condensation of (XVII) with hydroxylamine hydrochloride in boiling ethanol and presence of sodium acetate.

Experimental

The infrared spectra were taken on a Perkin-Elmer infrared spectrometer, Model 621. The N.M.R. spectra were determined with a Varian Model 390 spectrometer. The mass spectra were taken on Hitachi Rmv 9 E spectrophotometer.

All melting points were uncorrected.

The physical, I.R. and N.M.R. data were listed in Table 1-3.

Reaction of β-(3,4-dimethylbenzoyl)-acryloyl chloride with anthranilic acid: Formation of (I)

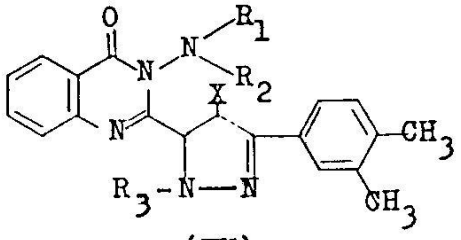
An ether solution of (0.02 mole) of anthranilic acid, was added dropwise to an ether solution of (0.01 mole) of -(3,4-dimethylbenzoyl)-acryloyl chloride. The solid product formed was washed with hot water to get rid of any anthranilic acid hydrochloride, then dried and crystallized from ethanol to give pale brown crystals of (I). (cf. Tables 1-3).

Reaction of (I) and (IV) with urea and thioureas. Formation of (IIa-c) and (XI)

A mixture of (I) or (IV) (0.01 mole), urea, thiourea or benzylthiourea (0.02 mole) and ethanol (15 ml) was treated with few drops of glacial acetic acid and refluxed for 8 hours. The solid product formed after evaporation of most of the solvent and cooling was crystallized from proper solvent to give the corresponding pyrimidone and pyrimidine thione derivatives (IIac) and (XI) respectively. (cf. Tables 1-3).

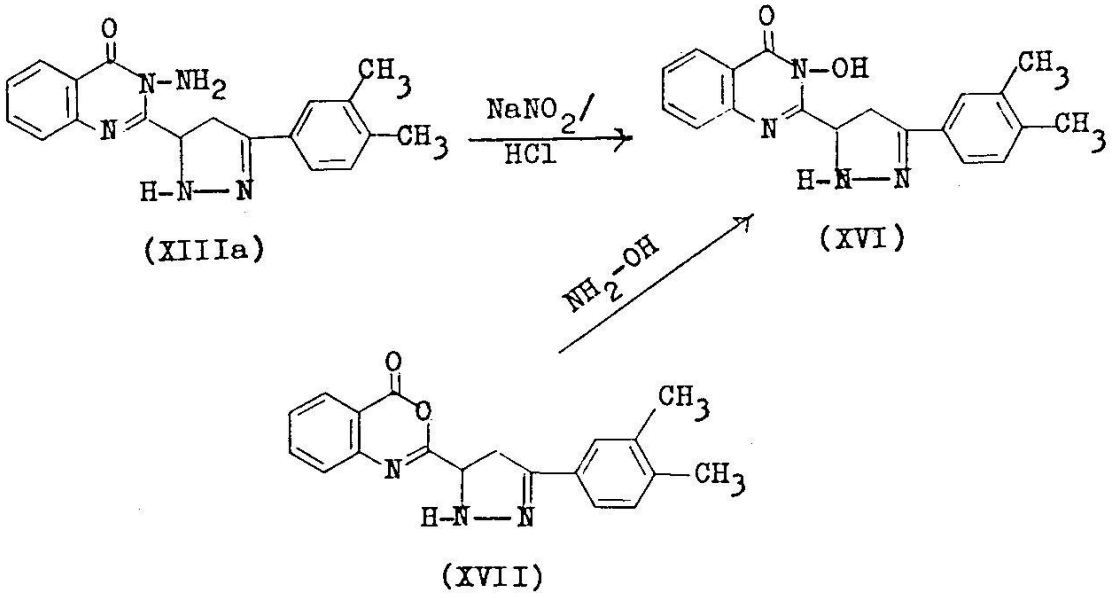
Reaction of (I) and (IV) with hydroxylamine hydrochloride: Formation of (III) and (XII).

A mixture of (I) or (IV) (0.01 mole), hydroxylamine hydrochloride (0.01 mole), sodium acetate (2g),



(XV)

	R_1	R_2	R_3	X
a,	H	COC_6H_5	COC_6H_5	H
b,	H	H	H	Br
c,	$COCH_3$	$COCH_3$	$COCH_3$	H
d,	H	H	$CH_2NC_4H_8O$	H
e,	H	H	$CH_2NC_5H_{10}$	H
f,	H	H	$CH_2N(CH_3)_2$	H



(XIIIa) (XVI)

(XVII)

Table-1: Physical data of new compounds

Comp.d	M.p. °C	Solvent yield (%)	Formula	Found			Required		
				C	H	N	C	H	N
(I)	210	50 (E)	$C_{19}H_{17}O_4N$	70.56	5.11	4.36	70.51	5.29	4.33
(IIa)	198	60(E)	$C_{20}H_{19}O_4N_3$	67.38	5.43	11.27	67.60	5.53	11.83
(IIb)	240	50(E)	$C_{20}H_{19}O_3N_3S$	64.28	5.11	10.83	64.69	5.12	11.32
(IIc)	178	60(E)	$C_{27}H_{25}O_3N_3S$	69.90	4.88	8.37	68.78	5.30	8.91
(III)	198	40(B)	$C_{19}H_{18}O_4N_2$	66.78	5.33	7.90	67.45	5.32	8.28
(IV)	190	60(Bu)	$C_{19}H_{15}O_3N$	74.36	4.42	4.38	74.75	4.91	4.59
(Va)	248	60(Bu)	$C_{20}H_{20}O_3N_2$	71.07	5.56	7.87	71.42	5.95	8.33
(Vb)	230	75(E)	$C_{21}H_{22}O_3N_2$	71.42	6.11	7.71	72.00	6.28	8.00
(Vc)	120	55(E)	$C_{23}N_{26}O_3N_2$	72.81	6.51	6.92	73.01	6.87	7.40
(Vd)	150	60(Bu)	$C_{26}H_{24}O_3N_2$	72.23	5.38	6.66	75.72	5.82	6.79
(Ve)	238	60(B)	$C_{21}H_{22}O_3N_2$	72.50	5.81	8.15	72.00	6.28	8.00
(VIa)	260	50(B)	$C_{21}H_{20}O_2N_2$	75.33	5.80	8.06	75.90	6.02	8.43
(VIb)	210	55(B)	$C_{26}H_{22}O_2N_2$	73.90	5.30	6.81	73.93	5.21	6.63
(VII)	100	55(P)	$C_{23}H_{23}O_5N$	69.88	5.43	3.41	70.22	5.85	3.56
(VIII)	140	60(P/B)	$C_{28}H_{26}O_4N_2$	73.48	5.13	6.12	74.00	5.72	6.16
(IX)	185	75(B)	$C_{30}H_{35}O_9N$	64.68	6.12	2.24	65.09	6.32	2.53
(X)	100	50(P/B)	$C_{20}H_{19}O_6N$	64.87	5.12	3.28	65.04	5.14	3.79
(XI)	165	65(A)	$C_{20}H_{17}O_3N_3$	69.52	4.49	12.29	69.16	4.89	12.10
(XII)	195	40(Bu)	$C_{19}H_{16}O_3N_2$	70.98	5.46	8.20	71.25	5.00	8.75
(XIIIa)	250	80(E)	$C_{19}H_{19}ON_5$	68.12	5.46	20.80	68.46	5.70	21.02
(XIIIb)	235	60(E)	$C_{20}H_{19}O_2N_5$	65.96	4.88	19.11	66.48	5.26	19.39
(XIIIc)	300	50(A)	$C_{21}H_{21}O_2N_5$	66.94	5.32	7.16	67.20	5.60	7.46
(XIIId)	209	70(Bu)	$C_{22}H_{23}O_2N_5$	67.39	5.56	17.76	67.86	5.91	17.99

Table-1: Cont.

Comp.d	M.p. °C	Solvent yield (%)	Formula	Found			Required		
				C	H	N	C	H	N
(XIIIe)	290	70(Bu)	$C_{23}H_{25}O_2N_5$	68.60	6.10	17.68	68.47	6.20	17.36
(XIVa)	200	55(E)	$C_{26}H_{23}ON_5$	73.86	5.41	16.36	74.10	5.46	16.62
(XIVb)	250	70(Bu)	$C_{26}H_{22}ON_5Cl$	64.20	4.83	15.57	68.49	4.82	15.36
(XIVc)	190	60(Bu)	$C_{27}H_{25}O_2N_5$	67.05	5.43	18.51	67.20	5.60	18.66
(XIVd)	204	50(E)	$C_{27}H_{23}O_3N_5$	69.57	4.76	15.00	69.66	4.98	15.04
(XIVe)	210	50(E)	$C_{22}H_{23}ON_5$	70.66	6.07	18.57	70.77	6.16	18.78
(XVa)	224	80(B/E)	$C_{33}H_{27}O_3N_5$	73.02	4.94	12.53	73.19	4.99	12.93
(XVb)	300	40(Bu)	$C_{19}H_{18}ON_5Br$	54.94	4.66	16.48	55.33	4.36	16.99
(XVc)	230	65(A)	$C_{25}H_{25}O_4N_5$	64.77	5.13	15.23	65.35	5.44	15.25
(XVd)	204	50(P/B)	$C_{24}H_{28}O_2N_6$	66.48	6.36	19.43	66.65	6.52	19.43
(XVe)	220	40(P/B)	$C_{25}H_{30}ON_6$	69.18	7.17	19.71	69.74	7.02	19.52
(XVf)	148	45(E)	$C_{22}H_{26}ON_6$	67.38	6.34	21.21	67.66	6.71	21.52
(XVI)	268	50(E)	$C_{19}H_{18}O_2N_4$	68.13	4.99	16.29	68.26	5.38	16.76
(XVII)	189	75(E)	$C_{19}H_{17}O_2N_3$	71.16	5.28	12.86	71.47	5.32	13.16

A = Acetic acid B = Benzene Bu = Butanol
E = Ethanol P = Pet.ether (b.p. 80-100°C)

ethanol (20 ml) and few drops of water was refluxed for 8 hours. The solid product formed after concentration and cooling was crystallized from proper solvent to give the corresponding isoxazole derivatives (III) and (XII) as brown crystals (cf. Tables 1-3).

Ring closure of (I): Formation of (IV)

5 g of (I), was treated with 20 ml of acetic anhydride and then the mixture was refluxed for 6 hrs. The solid crystalline product formed after evaporation of most of acetic anhydride was crystallized from n-butyl alcohol to give yellow crystals of (IV) (cf. Tables 1-3).

Reaction of (IV) and (VII) with amines: Formation of (Va-e) and (VIII)

A mixture of (IV) or (VII) (0.01 mole), methylamine, ethylamine, n-butylamine, benzylamine, p-toluidine or dimethylamine (0.01 mole) and ethanol(20 ml) was refluxed for 4 hours. The solid product obtained after evaporation of most of ethanol and cooling were crystallized from

Table-2: Infrared spectra of new compounds

Compound	Group frequencies (KBr, cm^{-1})
(I)	ν C=O(1710, 1690), νOH or NH (3115, 3150), ν C=C (1610)
(IIa)	νC=O(1690), C=N(1640), νCH_2(2890), ν OH or NH (3320)
(IIb)	νC=O (1670), ν C=N(1650), ν C=S (1235), ν CH(2975), νOH or NH(3260)
(IIc)	ν C=O(1680), ν C=N(1650), ν C=S(1305), ν CH_2(2890), ν OH or NH (3430)
(III)	ν C=O (1710) acid, ν C=O(1685), ν C=N (2870), ν CH_2(3460), ν OH or NH (3460)
(IV)	ν C=O (1690), ν C=N (1680), ν C=C (1600)
Va	ν C=O (1770) anilide, ν C=O (1690) aroyl, ν NH (3200)
Vc	ν C=O(1770) anilide, ν C=O (1660) aroyl, ν NH (3300)
Vd	νC=O (1735) anilide, νC=O (1660) aroyl, ν NH(3350)
Ve	νC=O (1750) anilide, ν C=O (1670) aroyl
(VIa)	νC=O(1770), ν C=O (1720), ν C=N(1660)
(VIb)	νC=O (1790), ν C=O (1700), ν C=N (1640)
(IX)	νC=O (1740, 1720, 1695, 1680), ν CH_2 (2960, 2880), ν NH(3460)
(X)	νC=O (1700), 1685, 1670), ν NH(3280, 3030)
(XI)	νC=O(1770), ν C=O or C=N (1600), ν CH_2(2950), ν NH (3420)
(XIIIa)	ν C=O or C=N (1660), νNH(3190, 3230), ν CH_2(2920, 2955)
(XIIIb-e)	C=O(1705, 1670), ν C=N (1630), νCH_2 (2930), ν OH(3370)
(XIVa)	C=O (1680), ν C=N (1640), νCH_2(2920), ν NH(3270)
(XIVb)	ν C=O (1680), νC=N (1620), ν CH_2 (2925), νNH(3235)
(XIVc)	νC=O (1680), ν C=N (1630), νCH_2 (2945), ν NH(3285)
(XIVd)	ν C=O (1730, 1705), ν C=N (1660), νCH_2 (2940), ν NH (3240)
(XIVe)	ν C=O (1660), νC=N (1640), ν CH_2 (2990, 2945), ν NH (3220)

Table-2: Cont...

Compound	Group frequencies (KBr cm^{-1}
XVa	νC=O (1700), νC=N (1650), ν CH_2 (2920), νNH (3030)
XVb	νC=O (1700), νC=N (1665), ν NH (3240), νC=C (1595)
XVc	νC=O (1740), νC=N (1645, 1625), ν CH_2 (2920), νC=C (1590)
XVf	νC=O or νC=N (1690), ν CH_2(2970, 2920), ν NH(3340)
(XVI)	νC=O or C=N (1690), νCH_2 (2920), νOH or NH (3110, 3150)
(XVI)	νC=O or C=N (1620), νCH_2 (2940), νOH or NH (3200).

proper solvent to give the corresponding amine adduct (Va-e) and (VIII) respectively. (cf. Tables 1-3).

Fusion of (IV) with ethylamine and benzylamine: Formation of (VIa)

A mixture of (0.01 mole) of (IV), ethylamine or benzylamine (0.01 mole) and anhydrous zinc chloride (2 g) was fused in an oil bath for 6 hrs. at 160-170°C. The solid product obtained after washing with hot water was crystallized from benzene to give the corresponding quinazolinone derivatives (VIa and b) respectively (cf. Tables 1-3).

Alternative preparation of (VIa and b)

A solution of(Vb and d)(0.01 mole) in (15 ml) of acetic anhydride was refluxed for 4 hours and left to stand at room temperature for 24 hours. The crystalline solid product obtained after filtration and crystallization proved to be (VIa and b) by melting point and mixed melting points determinations.

Fusion of (IV) with diethylmalonate: Formation of (VII)

A mixture of (IV) (0.01 mole), diethylmalonate (0.01 mole) and sodium methoxide (0.02 mole) was fused in an oil bath at 160-170°C for 6 hours. The solid product obtained was crystallized from petroleum ether (b.p. 60-80°C) to give the corresponding Michael adduct (VII) as colourelss crystals. (cf. Tables 1-3).

Reaction of (IV) with diethylmalonate: Formation of (IX)

A mixture of (0.01 mole) of (IV), diethylmalonate (0.01 mole) and pyridine (20 ml) was refluxed for 6 hours. The solid product obtained was crystallized from benzene to give the corresponding Michael adduct (IX) as colourless crystals. (cf. Tables 1-3).

Reactions of (IV) with KCN: Formation of (X)

A mixture of (IV) (0.01 mole), (1.5 g) of KCN, (5 ml) of water and (15

Table-3: The NMR spectra of some new compounds

Compound	Solvent	δ-Values	J-Values(HZ)	Group
(IIa)	$CDCl_3$	6.92-7.25(m)		7H aromatic protons
		6.30(two d)	$J=7.5_{AX}$	1H-CH-CH-N
			$J=7.5_{BX}$	(Part of ABX system) [11]
		2.80(s)		6H two CH_3 group
		2.30(m)	$J_{AB}=21$	2H cyclic $-CH_2-$
				(Part of ABX system)
(III)	$CDCl_3$	8.25 (s)		1H - NH-CO-
		6.60-7.50(m)		7H aromatic protons
		6.05(d),6.20(d)	$J_{AX}=6.60$	1H - CH_2-CH-O-
			$J_{BX}=6.6$	(Part of ABX system)
		3.10 (m)	$J_{AB}=19.7$	2H cyclic $-CH_2-$
				(part of ABX system)
(IV)	$CDCl_3$	6.85-7.45(m)		7H aromatic protons
		6.30(d), 6.55(d)	10.3(cis)	2H - CO-CH=CH-CO-
(Va)	$CDCl_3$	8.40(s)		1H Ar-NH-CO-
		6.80-7.35(m)		7H aromatic protons
		6.60(d),6.40(d)	10.5(cis)	2H -CO-CH=CH-Ar
		4.75(m)		1H -CONH-CH_3
		3.15(s)		1H NH-CH_3
		2.35(s)		6H two CH_3 groups
(Vd)	$CDCl_3$	8.45(s)		1H -CO-NH-Ar
		7.50(d), 7.40(d)	10.5 (cis)	2H -CO-CH-CH-CO-
		6.80-7.35 (m)		12H aromatic protons
		4.45(s)		1H $-NH-CH_2-C_6H_5$
		3.75(s)		2H-CH_2-C_6H_5
		2.20(s)		6H two CH_3 groups.
(VI)	$CDCl_3$	7.05(d),7.55(d)	10.2 (cis)	2H -CH=CH-CO-
		6.85-6.60(m)		7H aromatic protons
		2.85 (q)		2H $-CH_2-CH_3$
		2.55 (t)		3H - CH_2 $-CH_3$
		2.05 (s), 2.35 (s)		6H two CH_3 groups
(VII)	$CDCl_3$	8.45 (s)		1H -NH-CO-
		7.80(d), 7.70(d)	10.5 (cis)	2H-CO-CH=CH-CO-

Table-3: Cont.

Com-pound	Solvent	δ -Values	J-Values(Hz)	Group
		6.90-7.60(m)		7H aromatic protons
		4.20 (s)		2H -CO-$\underline{CH}_2$-COOET
		3.70(q)		2H -$\underline{CH}_2$-$\underline{CH}_3$
		3.45(t)		3H - CH_2 -$\underline{CH}_3$
		2.15(s)		6H two $\underline{CH}_3$ groups
(VIII)	DMSO	8.15(s)		1H Ar-$\underline{NH}$-CO-
		7.05(d),6.95(d)	10.5 (cis)	2H -CO-$\underline{CH}$=$\underline{CH}$-CO-
		6.20-6.80(m)		2H - CO-$\underline{CH}$=$\underline{CH}$-CO-
				12H aromatic protons
		5.55(s)		1H -CO-$\underline{NH}$-CH_2
		3.65 (s)		2H -CO-$\underline{CH}_2$-CO-
		3.40 (s)		2H -NH-$\underline{CH}_2$-C_6H_5
		2.75(s)		6H two $\underline{CH}_3$ groups
(IX)	$CDCl_3$	8.20(s)		1H - $\underline{NH}$-CO
		7.80(d), 7.70(d)	AX=6.3	1H-NH-CO-$\underline{CH}$-CH_2
			BX-6.3	(Part of ABX system)
		6.15-7.50(m)		7H aromatic protons
		3.85 (m)	AB=19	2H CO-CH-$\underline{CH}_2$-CO
				(part of ABX system)
		3.50(s)		2H - CO-$\underline{CH}_2$-COOEt
		3.20,3.05(t)		6H three -$\underline{CH}_2$-$\underline{CH}_3$
		2.90(q), 2.60 (q)		9H three -CH_2-$\underline{CH}_3$
		2.25 (s)		6H two $\underline{CH}_3$ groups
(X)	$CDCl_3$	8.68-8.70 (s)		1H -CO-$\underline{NH}$-
		7.90 (two d)	AX=6	1H -CO-$\underline{CH}$-COOH
			BX=6	(Part of ABX system)
		6.97-7.60 (m)		7H aromatic protons
		3.30 (m)	AB=19	2H -CH-$\underline{CH}_2$-CO-
				(Part of ABX system)
		2.20 (s)		6H two $\underline{CH}_3$ groups)
(XI)	$CDCl_3$	8.70 (s)		1H -$\underline{NH}$-
		7.10-8.10(m)		7H aromatic protons
		6.80(two d)	AX=7.2	1H -NH-$\underline{CH}$-CH_e
			BX=7.2	(Part of ABX system)

Table-3: Cont.

Compound	Solvent	δ -Values	J-Values(Hz)	Group
		4.20-4.30 (m)	AB=21	2H-CH-$\underline{CH}_2$-
				(Part of ABX system)
		2.30 (s)		6H two $\underline{CH}_3$ groups
(XII)	$CDCl_3$	6.90-7.35 (m)		7H aromatic protons
		6.20 (two d)	AX=6.5	1H -$\underline{CH}$-CH_2-
			BX=6.5	(Part of ABX system)
		3.25 (m)	AB=19.5	2H -CH-$\underline{CH}_2$-C=
				(Part of ABX system)
		2.30 (s)		6H two $\underline{CH}_3$ group
(XIIIa)	DMSO	7.90, 8.05 (s)		1H - CH-$\underline{NH}$-N=
		6.95-7.68 (m)		7H aromatic protons
		6.65 (two d)	AX=12	-NH-$\underline{CH}$-CH_2
			BX=11	(Part of ABX system)
		5.88 (s)		2H N-$\underline{NH}_2$
		3.30, 3.65 (m)	AB=18	2H $\underline{CH}_2$-C=
				(Part of ABX system)
		2.20(s)		6H two $\underline{CH}_3$ groups
(XIIIb)	$CDCl_3$	9.50 (s)		1H - NH-$\underline{CH}$O
		8.30(s), 8.65(s)		2H two -$\underline{NH}$-
		7.35-7.70 (m		7H aromatic protons
		7.05 (m)	AX=11	1H -$\underline{CH}$-CH_2
			BX=11	(Part of ABX system)
		2.35		8H two $\underline{CH}_3$ and -$\underline{CH}_2$-
(XIIIc)	DMSO	8.15(s), 8.25 (s)		2H two -$\underline{NH}$-
		7.10-7.82(m)		7H aromatic protons
		6.85 (two d)	AX=12	1H -$\underline{CH}$-CH_2
			BX=12	(Part of ABX system)
		3.25 (m)	AB=18.3	2H -CH-$\underline{CH}_2$
				(Part of ABX system)
		2.50 (s)		3H -COC$\underline{H}_3$
		2.30 (s)		6H two $\underline{CH}_3$ group
(XIVa)	$CDCl_3$	8.15 (s)		1H -$\underline{NH}$
		7.20-7.75 (m)		12H aromatic protons
		6.50 (s)		1H N-N=$\underline{CH}$-C_6H_4
		5.50 (two d)	AX=12	1H -$\underline{CH}$-CH_2 of pyrazoline
			BX=12	(Part of ABX system)
		3.70 (m)	AB=18.1	2H -CH-$\underline{CH}_2$ of pyrazoline

Table-3: Cont.

Compound	Solvent	δ -Values	J-Values(Hz)	Group
				(Part of ABX system)
		2.25 (s)		6H two CH_3 groups
(XIVb)	$CDCl_3$	8.15(s)		1H - NH-
		6.90-7.60 (m)		11H aromatic protons
		6.60 (s)		1H -N=CH-C_6H_4Cl
		4.45 (two d)	AX=10.8	1H - CH-CH_2-pyrazoline
			BX=10.8	(Part of ABX system
		3.05(m)		2H -CH-CH_2
				(Part of ABX system)
		2.25 (s)		6H two CH_3 groups
(XIVc)	$CDCl_3$	8.05 (s)		1H - NH-
		7.05-7.55 (m)		7H aromatic protons
		5.95 (two d)	AX=11.2	1H -CH-CH_2-pyrazoline
			BX=11.2	(Part of ABX system)
		2.20 (m)	AB=18.1	2H -CH-CH_2-
				(Part of ABX system)
		1.75 (s)		12H three CH_3 groups)
(XVa)	$CDCl_3$	7.80,7.10-7.45 (m)		17H aromatic protons
		5.95 (two d)	AX=12	1H -CH-CH_2-
			BX=12	(Part of ABX system)
		3.50 (m)	AB=18	2H -CH_2-CH
				(Part of ABX system)
		2.15(s)		6H two CH_3 groups
(XVb)	DMSO	8.10(s)		1H -NH-
		7.45-7.80 (m)		7H aromatic protons
		7.25 (d), 7.15 (d)	6.6	2H two -CH-in pyrazoline
		5.50 (s)		2H -NH_2
		2.50 (s)		6H two CH_3 groups
(XVf)	DMSO	6.80-7.80 (m)		7H aromatic protons
		7.35 (two d)	AX=12	1H -CH-CH_2- of pyrazoline
			BX=12	(Part of ABX system
		5.80(s)		2H -NH_2
		3.45 (m)	AB=18.2	2H - CH-CH_2 of pyrazoline
				(Part of ABX system)
		3.30 (s)		2H -CH_2-

Table-3: Cont.

Compound	Solvent	δ -Values	J-Values(Hz)	Group
		2.50(s), 2.25 (s)		12H four CH_3 groups
		2.20(s), 2.10 (s)		
(XVI)	$CDCl_3$	8.20(s)		1H -NH-
		6.90-7.65(m)		7H aromatic protons
		6.60(d), 6.40 (d)	AX=12	1H -CH-CH_2 of pyrazoline
			BX=12	(Part of ABX system)
		3.65 (m)	AB=18.2	2H -CH-CH_2 of pyrazoline
				(Part of ABX system)
		2.45 (s)		6H two CH_3 groups.
(XVII)	$CDCl_3$	8.05(s)		1H -NH-
		7.10-7.85 (m)		7H aromatic protons
		6.80 (d), 6.65 (d)	AX=11.6	1H -CH-CH_2 or pyrazoline
			BX=11.6	(Part of ABX system)
		3.25 (m)	Ab=18.4	2H - CH-CH_2 of pyrazoline
				(Part of ABX system)
		2.25 (s)		6H two CH_3 groups

ml) of methanol was stirred for 6 hours and leave to stand at room temperature for 48 hours. The solid product obtained was washed three times with water, dried, then crystallized from a mixture of petroleum ether (80-100°) and benzene to give the corresponding addition product (X) as colourless crystals (cf. Tables 1-3).

Condensation of (IV) with hydrazine hydrate: Formation of (XIIIa-e)

A mixture of (IV) (0.01 mole), hydrazine hydrate (0.02 mole) and ethanol or formic, acetic, propionic, n-butyric acid (15 ml) was refluxed for 6 hours. The solid product obtained after evaporation of most of ethanol and cooling were crystallized from ethanol to give the corresponding pyrazolinyl aminoquinazolinone derivative (XIII) as colourless crystals. (cf.

Condensation of (XIIIa) with aldehydes and ketones: Formation of (XIVa-e)

A mixture of (XIIIa) (0.01 mole), aromatic aldehdyes (namely benzaldehyde, p-chlorobenzaldehyde, anisaldehyde or piperonal) or acetone (0.01 mole) in ethanol (20 ml) was refluxed for 4 hrs. The solid product separated after evaporation of most of the solvent and cooling was crystallized from proper solvent to give the condensation adducts (XIVa-e) respectively. (cf. Tables 1-3).

Benzylation of (XIIIa): Formation of (XVa).

A mixture of (XIIIa) (0.01 mole) (20 ml) of benzoyl chloride and (20 ml) of pyridine was refluxed for 4 hours then poured into 200 ml of

The solid product obtained was washed several times with boling water, then dried and crystallized from a mixture of benzene and ethanol to give the corresponding dibenzoyl derivative (XVa) as brown crystals (cf. Tables 1-3).

Bromination of (XIIIa). Formation of (XVb and c)

A mixture of (XIIIa) (0.01 mole) in chloroform or glacial acetic acid (20 ml) was treated with a solution of bromine in chloroform or glacial acetic acid. The solid product obtained after complete addition of bromine and evaporation of most of the solvent was crystallized from proper solvent to give 4-bromoderivative (XVb) or the triacetyl derivative (XVc) respectively. (cf. Tables 1-3).

Mannich reaction with (XIIIa): Formation of (XVd-f)

A mixture of (XIIIa) (0.01 mole), formaldehyde (0.02 mole) and morpholine, piperidine or dimethylamine (0.01 mole) in 20% hydrochloric acid was dissolved in 30 ml ethanol. The reaction mixture was heated under reflux for 8 hours and left to stand overnight, the soltuion was diluted with water, then dilute NaOH was added till the solution become alkaline. It was then extract with ether.

The solution was then acidified with acetic acid, diluted with water and the precipitated solid was filtered off, dried and crystalline from proper solvent to give the corresponding Mannich bases (XVd-f) as yellow crystals (cf. Table 1-3).

Nitrosation of (XIIIa). Formation of (XVI)

A solution of (XIIIa) (0.01 mole) in conc. hydrochloric acid (10 ml) was treated with a solution of sodium nitreaction mixture was heated on a water bath for one hour the solution was then poured into ice and the solid separated was crystallized from ethanol to give a colourless crystals of (XVI). (cf. Tables 1-3).

Preparation of (XVII)

A mixture of (IV) (0.01 mole), hydrazine hydrate (0.01 mole) and ethanol (20 ml), was refluxed for 3 hrs. The solid product obtained after evaporation of most of solvent was crystallized from ethanol to give (XVII). (cf. Tables 1-3).

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