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1,2,4-Triazoles from 1,3-Dipolar Cycloaddition Reaction of Nitrilimines with Aliphatic Ketohydrazones Carrying Electron Withdrawing Groups

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Alkanone and cycloalkanone hydrazones (**3**) carrying electron withdrawing groups ($OCOCH_3$, $COCH_3$, COPh) react with C-benzoyl-and C-2-naphthoylnitrilimines to give the cycloaddition triazole products (**6–11**). IR, ^1H NMR, ^{13}C NMR and mass spectral data are consistent with the assigned triazole ring system. Compounds (**8, 9**) having an acetyl group, show signal doubling in their ^{13}C NMR spectra, apparently owing to their presence in two different mesomeric structures.

Key Words: 1,2,4-Triazoles, 1,3-Dipolar cycloaddition, Nitrilimines, Aliphatic ketohydrazones.

INTRODUCTION

1,2,4-Triazoles have been found to have many useful synthetic and analytical applications[1]. They are also widely used as biological reagents as fungicides[2,] insecticides[3,] antimicrobes[4,] herbicides[5] and against animal parasites[1.] Some 1,2,4-triazole derivatives are widely used as dyes, photographic chemicals[6] and in polymer synthesis[7]. 1,2,4-Triazoles can be prepared by various methods[1]. They can be prepared from hydrazine derivatives[1] by the reaction of C═N multiple bonds with nitrilimines[8,9] or *via* ring transformation of other heterocycles[10]. The reactin of nitrilimines with methyl hydrazones of aliphatic ketones is reported to give the cyclocondensation products 1,2,4,5-tetrazine rather then the cycloaddition triazole products at C═N, apparently because of the strong nucleophilicity of the nitrogen carrying the methyl group, where the reaction starts[11].

Simple hydrazones react in a similar manner giving initially the acyclic electrophilic addition products, which cyclize to 1,2,4,5-tetrazines upon heating with charcoal[12]. We understand it may be significant to investigate the reaction of C-benzoyl and C-2-naphthoyl-N-aryl nitrilimines with hydrazones carrying electron withdrawing groups ($OCOCH_3$, $COCH_3$, COPh). It is expected in this case to obtain the cycloaddition products (1,2,4-triazoles) owing to the weak nucleophilicity of the nitrogen atom carrying the electron withdrawing groups.

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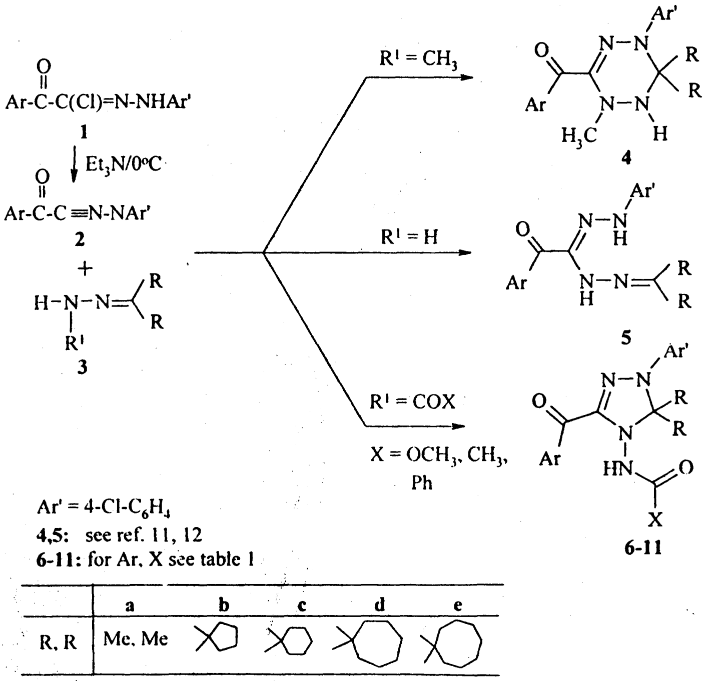

SCHEME-1

EXPERIMENTAL

Melting points were determined on an Electrothermal Mel. Temp. apparatus and are uncorrected. IR spectra were obtained by using Perkin-Elmer 237 infrared spectrometer (KBr discs). ^{1}H and ^{13}C NMR spectra were recorded on a Brucker 300 MHz instrument for solutions in $CDCl_3$ at 21°C, using TMS as an internal reference. Electron impact mass spectra were run on Finnigan Mat 8200 and 8400 spectrometers at 70 eV. C-Benzoyl[13] and C-2-naphthoyl-hydrazonoyl halides[14] (1), hydrazones (3) were prepared by standard procedures[15] which involve heating an alcohol solution of equimolar amounts of the ketone and substituted hydrazine plus a few drops of acetic acid.

Reaction of nitrilimines (2) with hydrazones (3)

Triethylamine (5.0 g, 0.05 mol) in tetrahydrofuran (20 mL) was dropwise added to a stirred solution of the appropriate hydrazonoyl halides (1) (0.01 mol) and hydrazones (0.01 mol) in tetrahydrofuran (100 mL) at −5 to 0°C. The reaction temperature was allowed to rise slowly to room temperature and stirring was continued for 4–6 h. The precipitated triethylammonium salt was filtered off, and the solvent was evaporated under reduced pressure. The residue was washed with water, triturated with ethanol, collected and recrystallized from appropriate solvent.

RESULTS AND DISCUSSION

The reaction of nitrilimines (2) with hydrazones of aliphatic ketones (3) was carried out by applying a two-fold excess of the hydrazones with hydrazonoyl halides (1)—precursors of nitrilimines (2)—in presence of triethylamine in THF at 0°C. The products were separated in moderate yields and recrystallized from ethanol.

Structure assignment of the title compounds was carried out by analytical and spectral data. The compounds show satisfactory elemental analysis and give correct molecular weight in their mass spectra in accordance with the suggested structure (Table-1).

TABLE-1
PHYSICAL DATA AND MOLECULAR ION PEAKS FOR COMPOUNDS **6–11**

Compd.	Ar	X	m.p. (°C)	Yield (%)	m.f.	$M^{+\cdot}$
6a	Ph	OCH_3	174–6	65	$C_{19}H_{19}N_4O_3Cl$	386/388
6b	Ph	OCH_3	160–2	75	$C_{21}H_{21}N_4O_3Cl$	412/414
6c	Ph	OCH_3	190–2	72	$C_{22}H_{23}N_4O_3Cl$	426/428
6d	Ph	OCH_3	144–6	65	$C_{23}H_{25}N_4O_3Cl$	440/442
6e	Ph	OCH_3	150–2	60	$C_{24}H_{27}N_4O_3Cl$	454/456
7a	2-Na	OCH_3	178–9	82	$C_{23}H_{21}N_4O_3Cl$	436/438
7b	2-Na	OCH_3	186–8	80	$C_{25}H_{23}N_4O_3Cl$	462/464
7c	2-Na	OCH_3	174–6	86	$C_{26}H_{25}N_4O_3Cl$	476/478
7d	2-Na	OCH_3	174–5	74	$C_{27}H_{27}N_4O_3Cl$	490/492
7e	2-Na	OCH_3	168–9	72	$C_{28}H_{29}N_4O_3Cl$	504/506
8a	Ph	CH_3	160–2	50	$C_{19}H_{19}N_4O_2Cl$	370/372
8b	Ph	CH_3	189–90	55	$C_{21}H_{21}N_4O_2Cl$	396/398
8c	Ph	CH_3	194–6	65	$C_{22}H_{23}N_4O_2Cl$	410/412
8d	Ph	CH_3	184–6	60	$C_{23}H_{25}N_4O_2Cl$	424/426
8e	Ph	CH_3	172–4	55	$C_{24}H_{27}N_4O_2Cl$	438/440
9a	2-Na	CH_3	183–5	50	$C_{23}H_{21}N_4O_2Cl$	420/422
9b	2-Na	CH_3	173–5	55	$C_{25}H_{23}N_4O_2Cl$	446/448
9c	2-Na	CH_3	186–8	65	$C_{26}H_{25}N_4O_2Cl$	460/462
9d	2-Na	CH_3	190–2	62	$C_{27}H_{27}N_4O_2Cl$	474/476
9e	2-Na	CH_3	180–2	60	$C_{28}H_{29}N_4O_2Cl$	488/490
10a	Ph	Ph	202–4	65	$C_{24}H_{21}N_4O_2Cl$	432/434
10b	Ph	Ph	178–9	75	$C_{26}H_{23}N_4O_2Cl$	458/460
10c	Ph	Ph	196–8	75	$C_{27}H_{25}N_4O_2Cl$	472/474
10d	Ph	Ph	173–5	70	$C_{28}H_{27}N_4O_2Cl$	486/488
10e	Ph	Ph	150–2	65	$C_{29}H_{29}N_4O_2Cl$	500/502
11a	2-Na	Ph	184–6	65	$C_{28}H_{23}N_4O_2Cl$	482/484
11b	2-Na	Ph	186–8	80	$C_{30}H_{25}N_4O_2Cl$	508/510
11c	2-Na	Ph	189–9	85	$C_{31}H_{27}N_4O_2Cl$	522/524
11d	2-Na	Ph	190–2	75	$C_{32}H_{29}N_4O_2Cl$	536/538
11e	2-Na	Ph	168–9	75	$C_{33}H_{31}N_4O_2Cl$	550/552

TABLE-2: CHARACTERISTIC IR, ^{1}H- and ^{13}C-NMR SPECTRAL DATA OF COMPOUNDS **6–11**

Compd.	IR cm^{-1}			^{1}H-NMR	^{13}C-NMR			
	N—H	ArC=O	XC=O	N—H	ArC=O	XC=O	C=N	C6
6a	3252	1638	1734	7.1	184.2	158.0	145.0	88.4
6b	3259	1648	1726	7.1	183.7	158.0	144.2	96.5
6c	3299	1636	1727	7.0	183.5	157.8	145.7	87.4
6d	3319	1624	1736	6.9	183.4	157.8	145.0	92.3
6e	3261	1655	1730	7.0	187.5	158.5	146.0	92.7
				6.7	183.6	157.8	145.2	92.3
7a	3237	1643	1736	6.9	183.2	157.9	145.0	88.27
7b	3198	1636	1720	7.1	183.1	158.1	144.4	96.5
7c	3280	1644	1726	7.1	183.0	157.5	145.9	87.5
7d	3286	1618	1726	7.2	183.5	157.9	145.3	92.3
7e	3286	1618	1726	7.2	183.6	157.9	146.2	89.2
8a	3350	1639	1689	8.2	184.1	177.9	146.2	88.8
					182.5	171.9	145.5	88.7
8b	3257	1641	1678	8.8	183.9	178.3	145.6	97.1
					182.6	171.6	145.5	97.0
8c	3296	1627	1686	8.9	183.9	177.8	147.1	88.2
					183.0	171.6	147.2	88.1
8d	3303	1631	1690	8.9	184.0	178.1	146.6	93.4
					183.2	171.7	145.8	92.7
8e	3304	1635	1684	8.9	184.1	177.9	146.9	93.4
					183.0	171.7	146.8	92.6
9a	3262	1646	1688	8.8	184.0	177.6	146.9	88.9
					183.0	171.5	145.7	88.8
9b	3294	1626	1677	8.8	184.4	177.9	146.0	97.0
					183.6	171.7	145.5	96.9
9c	3286	1638	1685	8.8	184.3	177.6	147.1	88.2
					183.5	171.6	146.3	87.9
9d	3291	1639	1691	8.8	184.4	173.5	146.5	93.4
					183.6	171.9	146.0	92.6
9e	3294	1640	1685	8.8	185.9	177.8	147.1	93.0
					183.7	171.7	146.9	92.5
10a	3272	1639	1667	9.2	184.2	168.8	146.5	89.1
10b	3247	1637	1676	9.4	184.0	168.9	145.7	97.2
10c	3338	1619	1667	9.7	183.8	168.9	146.2	88.3
10d	3319	1620	1681	8.9	183.8	169.1	145.9	92.9
10e	3337	1622	1669	9.2	184.0	169.2	146.9	93.3
11a	3215	1637	1670	9.3	184.0	168.8	146.6	89.0
11b	3244	1641	1681	9.3	183.7	169.0	145.8	97.1
11c	3321	1647	1680	8.9	183.3	169.0	146.2	88.1
11d	3315	1621	1676	9.8	183.7	169.1	146.3	93.0
11e	3327	1611	1671	9.2	183.7	169.2	147.0	93.2

The IR spectra of these compounds rèveal the presence of one N—H and two C=O signals that are attributed to Ar(C=O) and X(C=O) (Table-2).

^{1}H NMR play an important role in structure determination of these compounds. The signal at 7–9 ppm is that of the amine N—H of these compounds. The N—H of the cyclocondensation products **(4)** appears at 4–5 ppm[11], which is not the case here.

^{13}C NMR spectra account for the different carbon atoms of these triazoles. Or special significance is the signal at 80–100 ppm, which is attributed to C5 (quaternary or spiro carbons) of the triazole ring. This is similar to reported values of C5 carbon of triazoles.[9] Signal doubling is observed in ^{13}C NMR spectra of compounds **(6e, 8, 9)**, apparently owing to the presence of two mesomeric structures in solution.

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