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THE BF_3-CATALYZED DECOMPOSITION OF DIAZO CARBONYL COMPOUNDS IN NITRILES. FORMATION OF ENAMIDES

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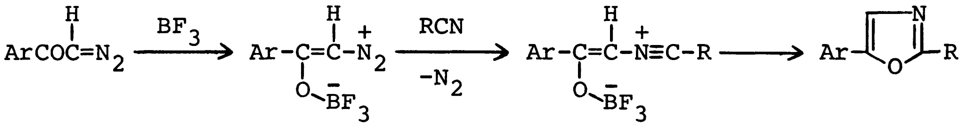
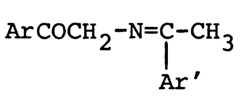
The BF_3-catalyzed decomposition of α-diazoacetopheones in acetonitrile, propionitrile, or methyl thiocyanate in the presence of 1,3,5-trimethoxybenzene produced enamides (7) in good yield.

The chemistry of enamides has recently been the subject of extensive studies from the synthetic standpoint.[1)] We wish to report here a novel formation of enamides, as an extension of the works on the acid-catalyzed decomposition of diazo carbonyl compounds.[2,3)] The intervention of a nitrilium ion type betaine intermediate (3) was postulated in the formation of oxazoles by the BF_3-catalyzed decomposition of diazo carbonyl compounds in nitriles.[2,4)] In a hope to intercept 3, we tried the reaction in the presence of electron-rich benzene, such as 1,3,5-trimethoxybenzene and 1,4-dimethoxybenzene. If 3 reacts in the Friedel-Crafts fassion with 1,3,5-trimethoxybenzene, imine derivatives (5) will be produced.



(1) (2) (3) (4)

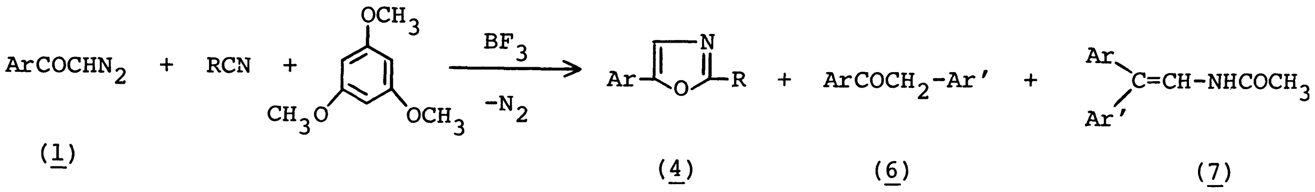


$$ArCOCH_2\text{-}N\text{=}\underset{Ar'}{C}\text{-}CH_3$$

(5)

Into a cold (0-5°C) vigorously stirring mixture of acetonitrile (10 ml), 1,3,5-trimethoxybenzene (2.5 g, 15 mmol), BF_3-etherate (0.6g, 4 mmol), and carbon tetrachloride (20 ml), α-diazoacetophenone (0.44 g, 3 mmol) was added in small portions.

Column chromatography of the product mixture on silica gel gave two enamides in 79% and 7% yields, accompanied by small amounts of phenyl 2,4,6-trimethoxybenzyl ketone (6a),5) [Ar=Ph; yield 5%, mp 90-91°C; ^{1}H-NMR($CDCl_3$) δ 3.70 (s, 6H, OCH_3), 3.77 (s, 3H, OCH_3), 4.21 (s, 2H, CH_2), 6.11 (s, 2H, Ar-H), 7.2-8.1 (m, 5H, Ph); IR(KBr) 1680 cm^{-1} (C=O)] and 2-methyl-5-phenyloxazole (4a: Ar=Ph, R=CH_3, 3% yield).2) The results of combustion analysis of the enamide (7a) agreed with the molecular formula, $C_{19}H_{21}O_4N$, of the expected imine (5a). However, the spectroscopic properties were not in accord with the imine structure (5a) but were compatible with the structure of enamide (7a), N-[2-phenyl-2(2,4,6-trimethoxyphenyl)vinyl]-acetamide. The major product (7a-A; Ar=Ph) shows spectroscopic properties as follows: IR(KBr) 1635 (amide C=O) and 3255 cm^{-1} (NH); ^{1}H-NMR($CDCl_3$) δ 1.92 (s,3H, $COCH_3$), 3.63 (s, 6H, OCH_3), 3.83 (s, 3H, OCH_3), 6.23 (s, 2H,Ar'-H), 7.17 (s, 5H, Ph), 7.55 (d, 1H, =CH), and 6.9 (broad d, 1H, NH); MS m/e 327 (M^+). Minor product (7a-B; Ar=Ph) has following spectral properties:



Ar'=2,4,6-trimethoxyphenyl

Table 1 The Results of the Reactions of α-Diazoacetophenones with Nitriles and 1,3,5-Trimethoxybenzene

run	Ar	R	Enamide (7-A) yield (%)	Enamide (7-A) mp (°C)	Enamide (7-B) yield (%)	Enamide (7-B) mp (°C)	Oxazole (4) yield (%)	Ketone (6) yield (%)
a	C_6H_5	CH_3	79	180-181	7	216-217	-	5
b	p-$CH_3C_6H_4$	CH_3	74	183-184	6	193-195	5	4
c	p-$CH_3OC_6H_4$	CH_3	53	195-196	8	194-195	30	2
d	p-ClC_6H_4	CH_3	54	206-208	8	202-203	6	4
e	p-BrC_6H_4	CH_3	69	202-203	9	177-179	-	2
f	C_6H_5	C_2H_5	63	145-146	35	215-216	-	-
g	p-$CH_3OC_6H_4$	CH_3S	71	174-176	-	-	3	7

IR(KBr) 1630 (amide C=O) and 3265 cm^{-1} (NH); ^1H-NMR($CDCl_3$) δ 1.95 (s, 3H, $COCH_3$), 3.62 (s, 6H, OCH_3), 3.80 (s, 3H, OCH_3), 6.10 (s, 2H, Ar'-H), 7.27 (s, 5H, Ph), 6.90 (d, 1H, =CH), and 7.5 (broad d, 1H, NH); MS m/e 327 (M^+). Each enamide has a doublet signal of vinyl proton and a broad doublet signal of amide proton in addition to the signals of acetyl, phenyl and tri-metnoxyphenyl groups. The markedly large coupling constants, $J_{H-C-N-H}$ (=11.0 and 12.0 Hz), may be explained by the enriched anti arrangement of vinyl and amide protons caused by the sterically restricted rotation about the C_α-N bond.

Similarity of the IR and NMR spectra of the two enamides suggests that these are geometrical isomers. The most significant differences in the NMR spectra of the enamides are the signals of vinyl and amide protons which couple each other. The vinyl proton of the major product (7a-A) shows its doublet signal at about 0.6 ppm down field from that of the minor product (7a-B). This may be attributable to the deshielding effect of the methoxy groups at the ortho positions.[6)] Therefore, the major enamide

Table 2 Analitical and NMR Data of Enamides

Enamide	Observed			Calculated			Molecular Formula	=CH	NH[a)]	J_{CH-NH}
	C	H	N	C	H	N				
7a-A	69.47	6.53	4.30	69.70	6.47	4.28	$C_{19}H_{21}O_4N$	7.55(d)	6.9	11.0
7a-B	69.77	6.47	4.07					6.90(d)	7.5	12.0
7b-A	70.55	6.78	4.13	70.36	6.79	4.10	$C_{20}H_{23}O_4N$	7.60(d)	6.8	11.0
7b-B	70.60	6.68	4.05					6.39(d)	7.1	11.5
7c-A	66.97	6.52	3.73	67.21	6.49	3.92	$C_{20}H_{23}O_5N$	7.48(d)	6.8	11.0
7c-B	67.17	6.58	3.74					6.77(d)	7.2	11.5
7d-A	63.10	5.58	3.74	63.07	5.57	3.87	$C_{19}H_{20}O_4NCl$	7.57(d)	6.9	11.0
7d-B	63.25	5.68	3.65					6.87(d)	7.3	11.5
7e-A	56.26	4.98	3.08	56.17	4.96	3.45	$C_{19}H_{20}O_4NBr$	7.53(d)	6.9	11.0
7e-B	56.52	4.95	3.56					6.88(d)	7.3	11.5
7f-A	70.24	6.85	4.22	70.36	6.79	4.10	$C_{20}H_{23}O_4N$	7.63(d)	6.9	11.5
7f-B	70.12	6.80	4.12					6.97(d)	7.4	11.5
7g-A	61.60	5.91	3.58	61.69	5.95	3.60	$C_{20}H_{23}O_5NS$	6.82(d)	7.3	11.0

a) Broad doublet signals were obtained.

was tentatively assigned to E-isomer, and the minor enamide to the Z-isomer. The enamide structure (7a) was supported by the fact that acid (3M HCl) hydrolysis of 7a-A gave phenyl-2,4,6-trimethoxyphenylacetaldehyde: [mp 85.0-85.5°C; IR(KBr) 1720 cm^{-1} (C=O); NMR($CDCl_3$) 3.72 (s, 6H, OCH_3), 3.77 (s, 3H, OCH_3), 5.03 (s, 1H, CH), 6.12 (s, 2H, Ar'-H_2), 7.22 (s, 5H, Ph), and 9.83 (s, 1H, CHO); Anal. Obsd, C 71.36, H 6.40%. Calcd. for $C_{17}H_{18}O_4$, C 71.31, H 6.34%]. Other substituted α-diazoacetophenones also gave corresponding enamides in addition to small amount of oxazoles (4) and ketones (6) (Table 1, run a-e).

This reaction was also found to be applicable to other nitriles such as propionitrile and methyl thiocyanate (Table 1, run f and g). However, when 1,4-dimethoxybenzene was used in place of 1,3,5-trimethoxybenzene, no enamide was obtained at all but corresponding oxazole was obtained in almost quantitative yield. This suggests that 1,4-dimethoxybenzene is not reactive enough to trap the nitrilium type intermediate (3). The treatment of trimethoxybenzene with the reaction mixture, obtained by the BF_3-catalyzed decomposition of α-diazoacetophenone in an acetonitrile, gave 2-methyl-5-phenyloxazole in high yield without formation of corresponding enamides (7a). This control experiment indicates that oxazole is not the precursor of the enamide formation. The mechanistic study of this reaction is now in progress.

References

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