REACTION OF o-AMINOTHIOPHENOL WITH α-ACETYLENIC KETONES

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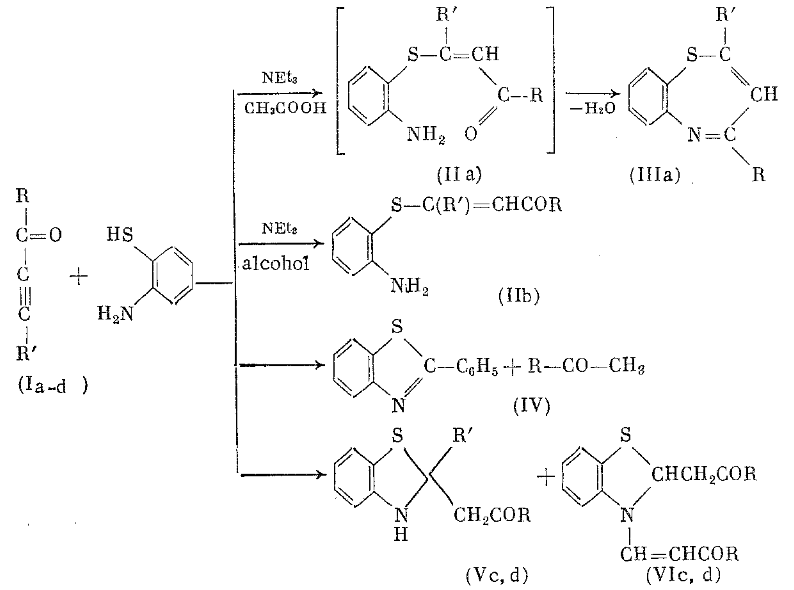
The reaction of o-aminothiophenol (o-ATP) with unsaturated carbonyl compounds is known to take place simultaneously at the $C=O$ and $C=C$ groups, resulting in the formation of seven-membered rings [1-3]. Substituted acetylenic acids also afford seven-membered rings on reaction with o-ATP [4], but with acetylenedicarboxylic acid benzo-1,4-thiazin-2-one is formed [4]. Reaction of 1-phenyl-2-benzoylacetylene (Ia) with o-ATP in methanol in the absence of a catalyst gives 1-benzoyl-2-phenyl-2-(2'-aminophenylthio)ethylene and 2,4-diphenyl-1,5-benzothiazepin (IIIa) [5].

This communication describes the reaction of o-ATP with the terminal α-acetylenic ketones (Ic) and (Id), and with those possessing a substituent at the triple bond (Ia) and (Ib).



R = R' = Ph (a); R = α-C_4H_3S, R' = Ph (b); R = Ph, R' = H (c); R = α-C_4H_3S, R' = H (d)

Reaction of (Ia) with o-ATP in an inert atmosphere (nitrogen) in methanol at 20°C in the presence of triethylamine in glacial acetic acid affords 2,4-diphenyl-6,7-benzo-1-thia-5-azacyclohepta-2,4,6-triene (2,4-diphenyl-1,5-benzothiazepin) (IIIa) in 28% yield. The reaction evidently proceeds via an intermediate ketovinyl sulfide (IIa), followed by cyclization and elimination of a molecule of water. When this reaction is carried out without the addition of AcOH, the yield of (IIIa) is 16%. In the absence of triethylamine, reaction of o-ATP hydrochloride with (Ia) affords, instead of the expected (IIIa), low yields (12%) of a single product, 2-phenyl-4,5-benzothiazole (IV).

The reaction of o-ATP with 1-phenyl-2-thenoylacetylene (Ib) proceeds differently. In methanol solution, in the presence of triethylamine and glacial AcOH, considerable resinification of the reaction mixture occurred, and it was not possible to isolate any reaction products. When the reaction was carried out in the absence of AcOH, the main reaction product, obtained in 61% yield, was 1-thenoyl-2-phenyl-2-(2'-aminophenylthio)ethylene (IIb). The structures of (IIIa) and (IIb) were confirmed by their IR and PMR spectra (see Table 1). The mass

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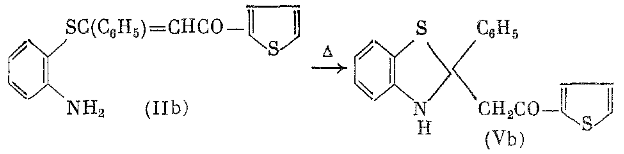
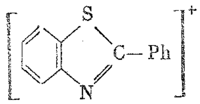
TABLE 1

Compound	Yield, %	Mp, °C (alcohol)	Molecular formula	$\frac{\text{Found}}{\text{Calculated}}$, % C	H	N	S	IR spectrum, ν, cm^{-1}	PMR spectrum, δ, ppm, J, Hz
(IIIa)	28,0	108–110	$C_{21}H_{15}NS$	$\frac{80,47}{80,50}$	$\frac{4,96}{4,81}$	$\frac{4,53}{4,47}$	$\frac{10,17}{10,20}$	690 (CS), 1560 (C=C), 1600 (C=N)	6,77 s (CH=), 7,3–7,6 m (C_6H_5)
(IIb)	61,2	139–141	$C_{19}H_{15}NOS_2$	$\frac{67,70}{67,65}$	$\frac{4,46}{4,45}$	$\frac{4,22}{4,15}$	$\frac{18,79}{18,99}$	710 (CS), 1565 (C=C), 630 (C=O), 3365, 3460 (NH_2)	6,16 s (CH=), 4,35 s (NH_2), 7,2–7,5 m (C_6H_5)
(Vc)	22,7	238–240	$C_{15}H_{13}NOS$	$\frac{70,37}{70,60}$	$\frac{4,86}{5,01}$	$\frac{5,36}{5,49}$	$\frac{12,34}{12,50}$	710 (CS), 1558 (C=C), 1632 (C=O), 3310 (NH)	5,42 t (CH), 3,41 q 3,17 q (CH_2CO), $J_{CHCH_2}=6,0$ 10,07 s (NM), 7,1–7,5 m (C_6H_5)
(Vd)	4,6	219–221	$C_{13}H_{11}NOS_2$	$\frac{60,14}{60,00}$	$\frac{3,94}{4,21}$	$\frac{5,26}{5,36}$	$\frac{24,58}{24,52}$	708 (C–S), 1562 (C=C), 1634 (C=O), 3250 (NH)	5,52 t (CH), 3,48 q 3,22 q (CH_2CO), $J_{CHCH_2}=6,2$ 10,51 s (NH), 6,9–7,7 m (C_6H_4, C_4H_3S)
(VIc)	38,5	179–181	$C_{24}H_{19}NO_2S$	$\frac{75.06}{74,80}$	$\frac{4,82}{4,94}$	$\frac{3,78}{3,64}$	$\frac{8,20}{8,31}$	708 (C–S), 1635, 1685 (C=O), 1560 (C=C)	6,26 d (COCH=), 8,25 d (NCH=), $^3J_{HH}=12,7$ (trans isomer), 6,1 m (CH), 3,8 m (CH_2), 7,0–8,1 m (C_6H_4, C_6H_5)
(VId)	32,3	163–165	$C_{20}H_{15}NO_2S_3$	$\frac{60.44}{60,45}$	$\frac{3,91}{3,78}$	$\frac{3,43}{3,53}$	$\frac{24,05}{24,18}$	710 (C–S), 1555 (C=C), 1640, 1670 (C=O)	6,21 d (COCH=), 8,15 d (NCH=), $^3J_{HH}=13,0$ (trans isomer), 6,1 m (CH), 3,7 m (CH_2), 6,9–8,0 (C_6H_4, C_4H_3S)

spectrum of (IIb) showed peaks for fragments corresponding to 2-thenoylmethyl-2-phenyl-4,5-benzothiazoline (Vb). It appears that, on heating in vacuo (IIb) undergoes intramolecular cyclization to form (Vb)

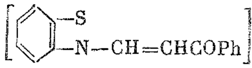
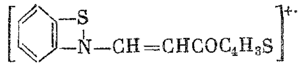


(IIb) (Vb)

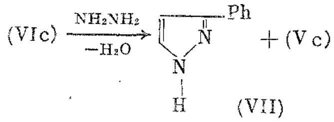
The mass spectrum of (Vb) contains a large peak for the molecular ion with m/z 337 (8%). The peak of highest intensity in the spectrum corresponds to the fragment $[C_4H_3SCO]^+$, with m/z 111 (100%). The spectrum also shows strong peaks for the ions $[M-(C_4H_3SCO)]^+$ with m/z 226 (62%),  with m/z 211 (58%), $[C_4H_3SCOCH_2]^+$ with m/z 125 (35%),  with m/z 108 (51%), $[C_4H_3S]^+$ with m/z 83 (60%), and $[Ph]^+$ with m/z 77 (45%).

Reaction of o-ATP hydrochloride with the ketone (Ib) in the absence of triethylamine afforded 14% of 2-phenyl-4,5-benzothiazole (IV).

Reaction of the terminal α-acetylenic ketones (Ic) and (Id) with o-ATP in alcohol at 60°C under nitrogen in the presence of NEt_3 gave the corresponding 2-acylmethyl-4,5-benzothiazolines (Vc) and (Vd) in 22.7 and 4.6% yields, and the 3-acylvinyl-2-acylmethyl-4,5-benzothiazolines (VIc) and (VId) in 38.5 and 32.3% yields. When the reaction was carried out in the absence of NEt_3 and with a molar ratio of ketone : o-ATP of 2 : 1, only the compounds (VIc) and (VId) were obtained, in yields of 82.3 and 85.4% respectively. The latter are apparently formed as a result of the vinylation of the NH group in the 2-acylmethyl-4,5-benzothiazolines (VIc) and (VId) by a further molecule of the ketone (Ic) or (Id). In the case of the substituted α-acetylenic ketone (Ib), vinylation of the NH group was not observed, possibly due to steric hindrance by the phenyl substituent.

The structures of (Vc), (Vd), (VIc), and (VId) were confirmed by their IR, PMR, and mass spectra. The mass spectrum of (VIc) contained a peak for the molecular ion with m/z 385 (6%), and the ion fragments $[M-(PhCO)]^+$ with m/z 280 (58%), $[M-(PhCOCH_2)]^+$ with m/z 266 (74%),  with m/z 253 (62%), $[PhCO]^+$ with m/z 105 (100%), and $[Ph]^+$ with m/z 77 (45%). The mass spectrum of (VId) contained a substantial peak for the molecular ion with m/z 397 (8%), and for the ion fragments $[M-(C_4H_3SCO)]^+$ with m/z 286 (65%), $[M-(C_4H_3SCOCH_2)]^+$ with m/z 272 (78%),  with m/z 259 (66%), $[C_4H_3SCO]^+$ with m/z 111 (100%), and $[C_4H_3S]^+$ with m/z 83 (50%).

Reaction of 3-benzoylvinyl-2-benzoylmethylbenzo-4,5-thiazoline (VIc) with hydrazine hydrate in ethanol at 78°C resulted in cleavage of the benzoylvinyl fragment with the formation of 3-phenylpyrazole (VII) in 56% yield



(VII)

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument in KBr disks, and PMR spectra were measured on a Tesla 480-B instrument in $CDCl_3$ relative to TMS. Mass spectra were obtained on an MX-1303 mass spectrometer with an ionizing voltage of 30 and 70 eV, ionization chamber temperature 100-150°C.

2,4-Diphenyl-6,7-benzo-1-thia-5-azacyclohepta-2,4,6-triene (IIIa). The ketone (Ia) (1.03 g; 5 mmole) and 0.6 g (5 mmole) of o-ATP were dissolved with stirring and heating in 10 ml of MeOH. The solution was cooled to 20°C, purified nitrogen passed through, 0.7 ml of NEt_3 added, and the mixture was stirred for 4 h. Glacial acetic acid (2 ml) was added, and the mixture stirred at 20°C for a further 2 h. After cooling to 0°C, the bright yellow solid was filtered off and washed on the filter with cold MeOH to give 0.46 g (28%) of (IIIa) (cf. Table 1).

Reaction of o-ATP with 1-Phenyl-2-thenoylacetylene (Ib). To a solution of 0.62 g (5 mmole) of o-ATP in 10 ml of MeOH was added 0.7 ml of NEt_3. A stream of purified nitrogen was passed in, the mixture heated to boiling, and a solution of 1.06 g (5 mmole) of the ketone (Ib) in 10 ml of MeOH added slowly with stirring. The mixture was cooled to 20°C, stirred for 1.5 h, cooled to 0°C, and the solid which separated was filtered off, washed thoroughly on the filter with cold MeOH, and dried in vacuo. The yield of 1-thenoyl-2-phenyl-2-(2'-aminophenylthio)ethylene (IIb) was 61% (see Table 1). When 0.64 g of (IIb) was recrystallized from MeOH or EtOH (heated to 60°C followed by cooling to 0°C), there was obtained 0.34 g (53%) of 2-phenyl-4,5-benzothiazole (IV), mp 110-112°C, cf. [6]. Found: C 74.06; H 4.42; N 6.65; S 14.93%. $C_{13}H_8NS$. Calculated: C 73.93; H 4.26; N 6.63; S 15.16%. IR spectrum (with KBr, ν, cm^{-1}): 1490 (C = N), 708 (C–S).

Reaction of o-ATP with Benzoylacetylene (Ic). A mixture of 0.65 g (5 mmole) of the ketone (Ic) and 0.62 g (5 mmole) of o-ATP in 15 ml of MeOH was heated to boiling under nitrogen, 0.7 ml of NEt_3 added, and the mixture stirred for 0.5 h. The mixture was then cooled to 20°C, stirred for a further 6 h, cooled to 0°C, and the solid which separated was filtered off and dissolved in benzene with heating. The solution was cooled to 0°C, and the bright red crystalline solid filtered off to give 0.29 g of 2-benzoylmethyl-4,5-benzothiazoline (Vc). The benzene solution after removal of (Vc) was evaporated, cooled to 0°C, and kept for 2 days. The resulting solid was filtered off and recrystallized from ethanol to give 0.37 g of 3-benzoylvinyl-2-benzoylmethyl-4,5-benzothiazoline (VIc) as golden needles (cf. Table 1).

3-[(2-Thenoyl)vinyl]-2-[(2-thenoyl)methyl]-4,5-benzothiazoline (VId). Similarly, 0.68 g (5 mmole) of thenoylacetylene (Id) and 0.62 g (5 mmole) of o-ATP in 15 ml of MeOH afforded 0.32 g (32.3%) of (VId) and 0.06 g (4.6%) of 2-(2-thenoyl)methyl-4,5-benzothiazoline (Vd).

Reaction of (VIc) with Hydrazine Hydrate. A mixture of 0.36 g (0.94 mmole) of (VIc), 3 ml of hydrazine hydrate, and 30 ml of ethanol was heated to the boil, and stirred for 3 h. Half of the solvent was removed, the mixture poured into cold water, and kept at 5°C for 1 day. The resulting solid was filtered off and recrystallized from water to give 0.15 g (56%) of 3-phenylpyrazole (VII), mp 77-78°C (cf. [7]). Found: C 75.03; H 5.66; N 19.30%. $C_9H_8N_2$. Calculated: C 75.00; H 5.55; N 19.44%. IR spectrum (with KBr, ν, cm^{-1}): 1580 (C = N), 3490 (NH).

CONCLUSIONS

1. Reaction of 1-phenyl-2-benzoylacetylene and 1-phenyl-2-thenoylacetylene with o-aminothiophenol in alcohol at 20°C in the presence of triethylamine in glacial acetic acid affords 2,4-diphenyl-6,7-benzo-1-thia-5-azacyclohepta-2,4,6-triene and 1-thenoyl-2-phenyl-2-(2'-aminophenylthio)ethylene respectively.

2. The reaction of terminal α-acetylenic ketones with o-aminothiophenol results in the formation of 3-acylvinyl-2-acylmethylbenzothiazolines.

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