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Reactions of 3-Isopropenyl- and 3-Acetyltropolone with Quarternary Ammonium Tribromides

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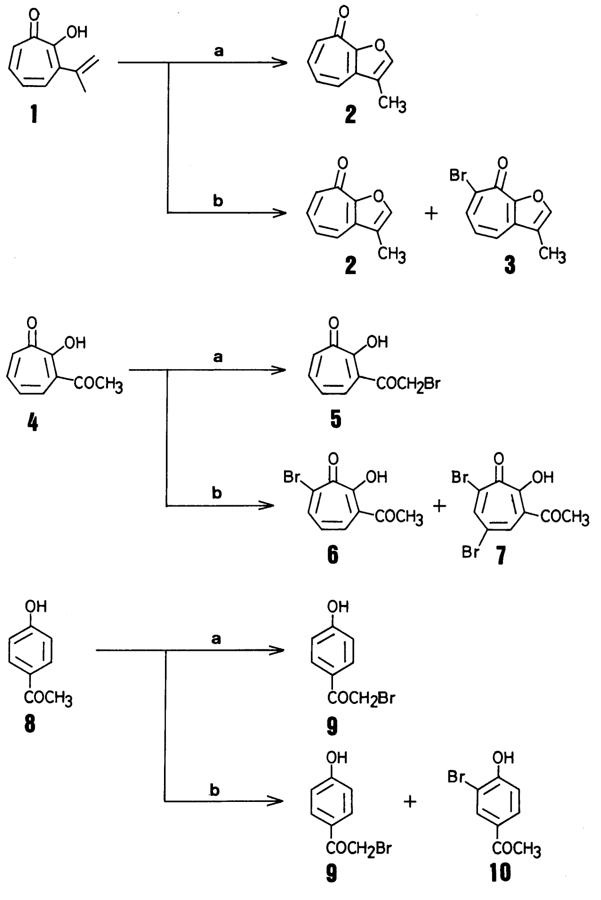
Synopsis. Treatments of 3-isopropenyltropolone with quarternary ammonium tribromides in tetrahydrofuran afforded 3-methyl-8*H*-cyclohepta[*b*]furan-8-one. The reactions in methanol–dichloromethane gave 7-bromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one. Bromination of 3-acetyltropolone with the tribromides in tetrahydrofuran produced 3-(bromoacetyl)tropolone, while the reaction in the methanolic solvent gave 7-bromo- and 5,7-dibromo-substituted 3-acetyltropolones. The brominations of 4′-hydroxyacetophenone were also carried out.

It is well-known that, on bromination with bromine, tropolones generally give substitution products.[1-3] 3-Acetyltropolone was brominated to yield 3-acetyl-5,7-dibromotropolone,[4] while 3-isopropenyltropolone gave 3-methyl-8*H*-cyclohepta[*b*]furan-8-one and its 5,7-dibromo-substituted product.[5]


Scheme 1. a: Quarternary ammonium tribromide/Tetrahydrofuran. b: Quarternary ammonium tribromide/CH$_3$OH–CH$_2$Cl$_2$.

Recently, solid quarternary ammonium tribromides have been used as brominating agents in order to avoid the disadvantage of volatile, toxic, and corrosive properties of liquid bromine.[6,7] In the treatment of 3-acetyltropolone with phenyltrimethylammonium tribromide, an acetyl group was brominated to yield 3-(bromoacetyl)tropolone, which is applicable as a useful synthon for syntheses of tropolones bearing heterocyclic side chain.[8]

The present paper deals with the reactions of 3-isopropenyl- (**1**) and 3-acetyltropolone (**4**) with tetrabutylammonium tribromide (TBABr$_3$), benzyltrimethylammonium tribromide (BTMABr$_3$), and phenyltrimethylammonium tribromide (PTMABr$_3$). We investigated the differences in the reactivity of the reagents and the effects of solvents on the reactions.

Results and Discussion

Previously, it was found that alkenes are treated with BTMABr$_3$ to give dibromo adducts on the carbon–carbon double bond.[9] A solution of 3-isopropenyltropolone (**1**) in an aprotic solvent, tetrahydrofuran, was stirred for 2 h at room temperature in the presence of an equimolar amount of TBABr$_3$. From the reaction mixture, a cyclized product, 3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**2**),[10] was isolated in a 41% yield. The reactions with BTMABr$_3$ and PTMABr$_3$ under the same conditions also gave the compound **2**. These results are summarized in Table 1.

On the other hand, the reactions of **1** with TBABr$_3$, BTMABr$_3$, and PTMABr$_3$ in a protic solvent, methanol–dichloromethane (2:5), yielded the cyclized product **2** and its 7-bromo-substituted product **3** (Table 1). The treatment of the compound **2** with quarternary ammonium tribromide did not give the brominated compound **3**. This means that **1** was initially brominated to produce 7-bromo-3-isopropenyltropolone (not isolated) as an intermediate, which cyclized to the product **3**.

Previously, we reported that bromination of 3-acetyltropolone (**4**) with PTMABr$_3$ in tetrahydrofuran yielded 3-(bromoacetyl)tropolone (**5**).[8] In a similar manner, **4** was treated with an equimolar amount of TBABr$_3$, BTMABr$_3$, and PTMABr$_3$ by stirring for 2 h at room temperature to afford **5** (Table 1). From the reaction with TBABr$_3$, the starting material **4** was also recovered.

The reactions of 3-acetyltropolone (**4**) with quarternary ammonium tribromide in methanol–dichloromethane (2:5) for 1 h gave 3-acetyl-7-bromotropolone (**6**) and 3-acetyl-5,7-dibromotropolone (**7**)[4] as substitution products (Table 1).

In the chemistry of benzenoid compounds, it was

Table 1. Reactions with Quarternary Ammonium Tribromide

Substrate	Reagent	Solvent	Reaction time/h	Product (Yield/%)
1	$\mathrm{TBABr_3}$	THF	2	**2** (41)
1	$\mathrm{BTMABr_3}$	THF	2	**2** (46)
1	$\mathrm{PTMABr_3}$	THF	2	**2** (56)
1	$\mathrm{TBABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	2	**2** (54) **3** (7)
1	$\mathrm{BTMABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	2	**2** (52) **3** (6)
1	$\mathrm{PTMABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	2	**2** (56) **3** (3)
4	$\mathrm{TBABr_3}$	THF	2	**5** (22) **4**[a] (13)
4	$\mathrm{BTMABr_3}$	THF	2	**5** (38)
4	$\mathrm{PTMABr_3}$	THF	2	**5** (46)
4	$\mathrm{TBABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	1	**6** (15) **7** (34)
4	$\mathrm{BTMABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	1	**6** (16) **7** (31)
4	$\mathrm{PTMABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	1	**6** (19) **7** (54)
8	$\mathrm{TBABr_3}$	THF	3	**9** (49) **8**[a] (16)
8	$\mathrm{BTMABr_3}$	THF	2	**9** (51) **8**[a] (27)
8	$\mathrm{PTMABr_3}$	THF	2	**9** (55) **8**[a] (19)
8	$\mathrm{TBABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	0.5	**9** (21) **10** (59)
8	$\mathrm{BTMABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	0.5	**9** (16) **10** (69)
8	$\mathrm{PTMABr_3}$	$\mathrm{CH_3OH\text{-}CH_2Cl_2}$	0.5	**9** (15) **10** (76)

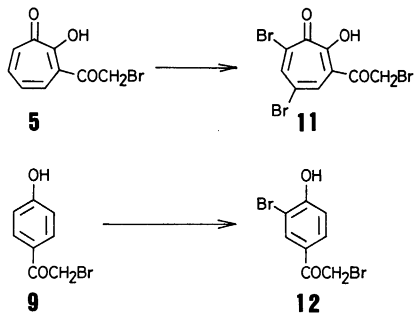
a) Recovered substrate.

reported that the reactions of phenols with $\mathrm{BTMABr_3}$ gave 2,4,6-tribromophenols,[11] while the reactions of acetophenones gave 2-bromoacetophenones by using an equimolar amount of $\mathrm{BTMABr_3}$[12] and 2,2-dibromoacetophenones by using three molar amount of the reagent.[13] However, the bromination reactions of hydroxyacetophenones bearing both the hydroxyl and acetyl group with quarternary ammonium tribromides were not reported. Thus, in comparison with the reactions of 3-acetyltropolone (**4**), the bromination of 4′-hydroxyacetophenone (**8**) with quaternary ammonium tribromides was carried out.

When a solution of **8** in tetrahydrofuran was treated with an equimolar amount of $\mathrm{TBABr_3}$ at room temperature, the color of the reagent disappeared after stirring for 2 h. The reaction mixture was worked up to give 2-bromo-4′-hydroxyacetophenone (**9**) in a 49% yield, besides the unchanged **8**. The reactions with $\mathrm{BTMABr_3}$ and $\mathrm{PTMABr_3}$ also gave **9** and the unchanged **8** (Table 1). On the other hand, in the reactions in methanol–dichloromethane (2:5), the color of the reagents disappeared after stirring for 30 min and then **9** and 3′-bromo-4′-hydroxyacetophenone (**10**) were obtained in 15—21 and 59—76% yields, respectively (Table 1).

The yields of the reactions by using three quarternary ammonium tribromides increased in order of $\mathrm{TBABr_3}<\mathrm{BTMABr_3}<\mathrm{PTMABr_3}$ in both tetrahydrofuran and methanolic solvent. It can be said that four inductively electron-donating alkyl groups of $\mathrm{TBABr_3}$ repressd the bromination reaction, while the electron-attracting phenyl group of $\mathrm{PTMABr_3}$ accelerated the reactions.

We also found a striking difference in the effects of the solvents on the bromination reactions. As shown in Table 1, the bromination of 3-acetyltropolone (**4**) in the aprotic tetrahydrofuran took place at the side-chain acetyl group, while the reaction in the protic methanol–dichloromethane took place at the 5- and 7-positions in the tropolone nucleus. The reactions of 4′-hydroxyacetophenone (**8**) in tetrahydrofuran afforded the 2-brominated product **9**. The reaction in the methanolic solvent gave two types of products **9** and **10**. The latter was preferential to the former. When the compounds **5** and **9** were stirred at room temperature in the methanolic solvent in absence of the brominating agent, they were recovered quantitatively, respectively. On the other hand, the compounds **5** and **9** were treated with an equimolar amount of $\mathrm{PTMABr_3}$ in methanol-dichloromethane to afford 5,7-dibromo-3-(bromoacetyl)tropolone (**11**) and 2,3′-dibromo-4′-hydroxyacetophenone (**12**) in 58 and 85% yields, respectively. In the reaction of 3-isopropenyltropolone (**1**), the 7-brominated product **3** was found in the methanolic solvent, besides the product **2**.



Scheme 2.

Thus, in the methanolic solvent, the brominating agent might react with methanol to produce methyl hypobromite[11,13] which brominates the tropolone and benzene nucleus as a more active brominating species.

Experimental

The melting points were determined with a Yanagimoto MP-

S2 apparatus and are uncorrected. The IR spectra were taken on a JASCO A-102 spectrophotometer. The ^{1}H NMR spectra were recorded with a JEOL JNM-PMX60SI spectrometer. The mass spectra were measured on a JEOL DX3-3HF spectrometer.

Reactions of 3-Isopropenyltropolone (1) with Quarternary Ammonium Tribromide. General Procedure. a) Reactions in Tetrahydrofuran. To a solution of 3-isopropenyltropolone (**1**) (486 mg, 3 mmol) in tetrahydrofuran (10 ml) was added quarternary ammonium tribromide (3 mmol) little by little. After stirring for 2 h at room temperature, the color of the reaction mixture changed gradually from orange to yellow. The mixture was diluted with water (100 ml) and extracted with ether (40 ml×4). The extract was evaporated, chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate–chloroform (1:1), and recrystallized from methanol to give 3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**2**): Mp 95—97 °C (lit,[10] 95—96 °C).

b) Reactions in Methanol–Dichloromethane. A solution of 3-isopropenyltropolone (**1**) (486 mg, 3 mmol) in methanol (20 ml)-dichloromethane (50 ml) was treated with quarternary ammonium tribromie (3 mmol) for 2 h and worked up, as described above. The evaporation residue was chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate–chloroform (1:1). The lower fraction was recrystallized from methanol to give 3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**2**). The upper fraction was recrystallized from methanol to give 7-bromo-3-methyl-8*H*-cyclohepta[*b*]furan-8-one (**3**): Pale yellow needles; mp 118—120 °C; IR (CHCl$_3$) 1597 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ=2.27 (3H, s, CH$_3$), 6.83 (1H, dd, J=9, 9 Hz, H-5), 7.70 (1H, m, H-2), 7.74 (1H,d , J=9 Hz, H-6), 8.23 (1H, d, J=9 Hz, H-4). Found: C, 49.98; H, 2.97%. Calcd for $C_{10}H_7BrO_2$: C, 50.24; H, 2.95%.

Reactions of 3-Acetyltropolone (4) with Quarternary Ammonium Tribromide. General Procedure. a) Reactions in Tetrahydrofuran. A solution of 3-acetyltropolone (**4**) (492 mg, 3 mmol) in tetrahydrofuran (10 ml) was treated with quanternary ammonium tribromide (3 mmol) for 2 h and worked up, as described above. The extract was evaporated and recrystallized from petroleum ether to give 3-(bromoacetyl)tropolone (**5**): Mp 95—97 °C (lit,[8] 97—98 °C).

b) Reactions in Methanol–Dichloromethane. A solution of 3-acetyltropolone (**4**) (492 mg, 3 mmol) in methanol (20 ml)-dichloromethane (50 ml) was treated with quarternary ammonium tribromide (3 mmol) for 1 h and worked up, as described above. The extract was evaporated and chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate. The lower fraction was recrystallized from methanol to give 3-acetyl-7-bromotropolone (**6**): Yellow needles; mp 87—89 °C; IR (CHCl$_3$) 3220 (OH), 1693 (COCH$_3$), 1603 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ=2.76 (3H, s, CH$_3$), 7.03 (1H, dd, J=10, 10 Hz, H-5), 7.50 (1H, d, J=10 Hz, H-6), 8.70 (1H, d, J=10 Hz, H-4); MS m/z (%) 244 [(M+2)$^+$, 45], 242 (M$^+$, 46), 201 [(M+2)$^+$−COCH$_3$, 91], 199 (M$^+$−COCH$_3$, 92), 163 (M$^+$−Br, 100). Found: C, 44.25; H, 2.84%. Calcd for $C_9H_7BrO_3$: C, 44.47; H, 2.90%.

The upper fraction was recrystallized from methanol to give 3-acetyl-5,7-dibromotropolone (**7**): Mp 171—173 °C (lit,[4] 173—174 °C).

Reactions of 4′-Hydroxyacetophenone (8) with Quarternary Ammonium Tribromide. General Procedure. a) Reactions in Tetrahydrofuran. A solution of 4′-hydroxyacetophenone (**8**) (408 mg, 3 mmol) in tetrahydrofuran (10 ml) was treated with quanternary ammonium tribromide (3 mmol) for 3 h (TBABr$_3$) or 2 h (BTMABr$_3$ and PTMABr$_3$) and worked up, as described above. The extract was evaporated, chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate, and recrystallized from benzene to give 2-bromo-4′-hydroxyacetophenone (**9**): Mp 128—130 °C (lit,[14] 130 °C).

b) Reactions in Methanol-Dichloromethane. A solution of 4′-hydroxyacetophenone (**8**) (408 mg, 3 mmol) in methanol (20 ml)-dichloromethane (50 ml) was treated with quarternary ammonium tribromide (3 mmol) for 30 min and worked up, as described above. The extract was evaporated and chromatographed on a Wakogel B-10 plate (30×30 cm) with ethyl acetate. The lower fraction was recrystallized from benzene to give 2-bromo-4′-hydroxyacetophenone (**9**). The upper fraction was recrystallized from petroleum ether to give 3′-bromo-4′-hydroxyacetophenone (**10**): Mp 93—94 °C (lit,[15] 92—95 °C).

Reaction of 3-(Bromoacetyl)tropolone (5) with PTMABr$_3$. A solution of **5** (122 mg, 0.5 mmol) in methanol (3 ml)-dichloromethane (8 ml) was treated with PTMABr$_3$ (188 mg, 0.5 mmol) for 1 h and worked up, as described above. The extract was evaporated and recrystallized from methanol to give 5,7-dibromo-3-(bromoacetyl)tropolone (**11**): Yield 116 mg (58%); yellow crystals; mp 162 °C (decomp); IR (CHCl$_3$) 3200 (OH), 1695 (COCH$_2$), 1600 cm^{-1} (C=O); ^{1}H NMR (CDCl$_3$) δ=4.59 (2H, s, CH$_2$), 8.02 (1H, d, J=2 Hz, H-6), 8.49 (1H, d, J=2 Hz, H-4). Found: C, 26.71; H, 1.50%. Calcd for $C_9H_5Br_3O_3$: C, 26.96; H, 1.26%.

Reaction of 2-Bromo-4′-hydroxyacetophenone (9) with PTMABr$_3$. A solution of **9** (108 mg, 0.5 mmol) in methanol (3 ml)-dichloromethane (8 ml) was treated with PTMABr$_3$ (188 mg, 0.5 mmol) for 30 min and worked up, as described above. The extract was evaporated and recrystallized from benzene to give 2,3′-dibromo-4′-hydroxyacetophenone (**12**): Mp 140—142 °C (lit,[16] 143 °C).

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