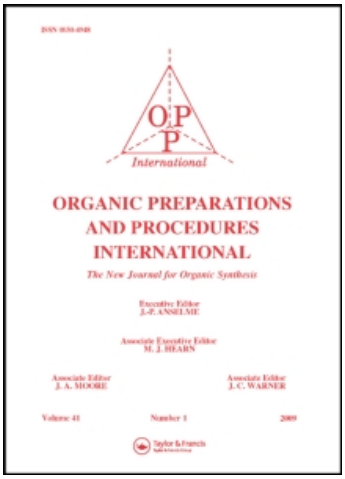

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REDUCTION OF 1,3-AZOLE AND 1,3-BENZAZOLE CARBINOLS WITH SODIUM BOROHYDRIDE-TRIFLUOROACETIC ACID

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REDUCTION OF 1,3-AZOLE AND 1,3-BENZAZOLE CARBINOLS WITH SODIUM BOROHYDRIDE-TRIFLUOROACETIC ACID

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In 1991 we reported that a variety of α-hetero benzyl alcohols and bis-heterocyclic carbinols are readily reduced with sodium borohydride-trifluoroacetic acid (TFA) to the corresponding diarylmethanes.[1] These studies revealed the following reaction parameters: furan, thiophene, benzthiophene, and benzofuran rings are all compatible with the reaction conditions, with the lowest reduction yields

being realized for furan-based substrates. Pyrrole containing compounds afford complex product mixtures, presumably a result of extensive acid catalyzed oligomerization/polymerization of the highly electron-rich heterocycle. Additionally, α-hetero benzyl alcohols, in which the heterocycle is a 1,3-azole or 1,3-benzazole system (1-methylimidazole, benzothiazole, 1-methylbenzimidazole, oxazole) were found to be inert, leading to starting material recovery. The resistance to reduction of the latter systems is likely due to the fact that in an acidic medium the major species in the reaction will be one in which the azole nitrogen is protonated. Since the postulated mechanism for sodium borohydride-TFA reduction of arylcarbinols involves formation of the benzylic carbocation,[2] a high energy dicationic intermediate or a low-probability mono-cationic species (one in which the azole nitrogen is not protonated) would be required for this transformation to be successful. Apparently the resonance stabilization of the carbocation provided by the two aromatic rings (1,3-azole/benzazole and phenyl) is inadequate to compensate for the instability of the requisite dication, and all reduction attempts of these compounds failed. Since the reduction of aromatic carbinols by this methodology utilizes excess TFA, reduction protocols that favor an intermediate containing an azole nitrogen that is not protonated as the major equilibrium species were deemed unfeasible. Therefore, if reductions of azole-based aromatic carbinols were to be realized, the resistance to formation of the dicationic species would need to be overcome. It was anticipated that if enough resonance stabilization of the carbocation could be imparted through the introduction of electron-rich aromatic systems and/or a third aromatic system, to generate a tribenzylic carbocation, formation of the requisite dicationic species might be possible. Successful reduction of 1,3-azole or 1,3-benzazole substituted di- or triaryl carbinols would be an important extension of the borohydride-TFA methodology since heteroaryl-

methanes are of interest to the food and beverage industry due to their presence as natural components in items such as licorice[3] and coffee.[4] Furthermore, most previously published methods for the reduction of heterocyclic alcohols have not included 1,3-azole or 1,3-benzazole substituted carbinols as starting materials; as a result, few of the corresponding methanes are known. We now report that certain 1,3-azole and 1,3-benzazole substituted carbinols can be reduced with sodium borohydride-TFA to afford the corresponding 1,3-azole or 1,3-benzazole substituted methanes in moderate to good yield. The results of these studies are summarized in the Table.

As can be seen in the Table, in addition to the 1,3-azole or 1,3-benzazole heterocycle, two aromatic systems are required to provide enough resonance stabilization of the benzylic carbocation to allow its formation and subsequent hydride reduction. This additional resonance stabilization can be the result of two phenyl rings, two π-excessive heterocyclic rings, or one phenyl ring and one π-excessive heterocyclic ring. However, when only a single π-excessive heterocyclic system is present to contribute resonance stabilization, the reduction fails. The single triarylcarbinol containing two 1,3-azole/benzazole heterocycles and a π-excessive heterocycle that was studied was also inert to the reduction conditions.

TABLE. Reduction of 1,3-Azole and 1,3-Benzazole Alcohols

Substrate	Yield (%)[a]
Het = 2-Thiazolyl; R^1, R^2 = Ph	73
Het = 2-Benzothiazolyl; R^1, R^2 = Ph	58[5]
Het = 2-Benzoxazolyl; R^1, R^2 = Ph	55
Het = 2-(1-Methylimidazolyl); R^1 = Phenyl; R^2 = 2-Thienyl	73
Het = 2-Benzothiazolyl; R^1 = 2-Benzo[b]furyl; R^2 = Phenyl	53
Het = 2-Benzothiazolyl; R^1, R^2 = 2-Thienyl	46
Het = 2-Benzothiazolyl; R^1 = 2-Benzo[b]thienyl; R^2 = 2-Thienyl	39
Het = 2-(1-Methylimidazolyl); R^1 = 2-Thienyl; R^2 = H	0[b]
Het = 2-(1-Methylimidazolyl); R^1 = 2-Furyl; R^2 = H	0[b]
Het = 2-Benzothiazolyl; R^1 = 2-Thiazolyl; R^2 = 2-Thienyl	0[b]

a) Isolated yields after flash chromatography. b) Recovered starting material.

In summary, sodium borohydride-TFA reduction of alcohols has now been extended to systems containing 1,3-azole or 1,3-benzazole heterocyclic substituents provided that two additional aromatic systems (phenyl and/or π-excessive heteroaryl) are present for sufficient resonance stabilization, thus providing a convenient, general route to the corresponding triarylmethanes.

EXPERIMENTAL SECTION

All reactions were performed in oven-dried glassware (120°), and all lithiation reactions were performed under nitrogen. Alkyllithium reagents were purchased from Aldrich and standardized with 2,5-dimethoxybenzyl alcohol.[6] Tetrahydrofuran was distilled from sodium/benzophenone. Thin layer chromatography was performed on precoated (0.25 mm) silica gel 60 F_{254} plastic sheets and were visualized with 254 nm ultraviolet light. Melting points were determined in open capillary tubes with a Mel-Temp Laboratory Devices apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlabs, Norcross GA. Proton and carbon NMR spectra were recorded on a Bruker ACE300 FT-NMR spectrometer; IR spectra were recorded on a Perkin Elmer 1600 FT-IR spectrometer.

Preparation of α-(2-Thiazolyl)diphenylmethanol.- To a magnetically stirred solution of thiazole (1.23 g, 14.5 mmol) in dry THF (10 mL) at -78° under nitrogen was added over 3 min *via* syringe *n*-butyllithium (2.33 M, 6.20 mL, 14.5 mmol). The resulting milky-yellow mixture was stirred at -78° for 30 min and then a solution of benzophenone (2.58 g, 14.2 mmol) in dry THF (10 mL) was added quickly *via* syringe. The resulting mixture was allowed to warm to 25° and stirred at 25° for 5 hrs. The mixture was poured into saturated brine (50 mL) and the resulting aqueous solution was extracted with ether (3 x 50 mL). The combined extracts were dried with sodium sulfate, filtered, and concentrated *in vacuo* to afford a yellow solid. Flash chromatography (9:1 hexanes/ether) gave α-(2-thiazolyl)diphenylmethanol as a white solid (2.30 g, 59%): mp. 111-113°, lit.[7] mp. 114-115°; ^{1}H NMR ($CDCl_3$): δ 7.75 (d, 1H), 7.39-7.27 (m, 11H), 4.48 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 177.3, 145.3, 142.6, 128.1, 127.9, 127.4, 120.0, 80.6; IR (halocarbon oil): 3168 cm^{-1}.

α-(2-Benzothiazolyl)diphenylmethanol was analogously prepared from benzothiazole and benzophenone (64%): mp. 143-144°, lit.[8] mp. 149.5-150°; ^{1}H NMR ($CDCl_3$): δ 7.98 (d, 1H), 7.81 (d, 1H), 7.48-7.43 (m, 5H), 7.38-7.31 (m, 7H), 4.56 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 177.8, 152.8, 144.8, 136.0, 128.2, 128.1, 127.6, 126.1, 125.2, 123.4, 121.6, 81.1; IR (halocarbon oil): 3331 cm^{-1}.

α-(2-Benzoxazolyl)diphenylmethanol was analogously prepared from benzoxazole and benzophenone (60%): mp. 158-160°; ^{1}H NMR ($CDCl_3$): δ 7.58-7.55 (m, 1H), 7.48-7.43 (m, 5H), 7.35-7.28 (m, 8H), 5.01 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 168.5, 151.3, 143.0, 140.1, 128.19, 128.18, 127.4, 125.3, 124.6, 120.3, 111.0, 78.6; IR (halocarbon oil): 3320 cm^{-1}.

Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.72; H, 5.02; N, 4.65. Found: C, 79.66; H, 5.01; N, 4.71

α-(2-(1-Methylimidazolyl))-α-(2-thienyl)benzyl Alcohol was analogously prepared from phenyllithium and 2-(1-methylimidazolyl) 2-thienyl ketone[9] (73%): mp. 156-158°; ^{1}H NMR ($CDCl_3$): δ 7.33 (br s, 6H), 6.97 (d, 1H), 6.93 (dd, 1H), 6.84 (br s, 1H), 6.76 (d, 1H), 3.28 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 149.9, 149.3, 143.6, 128.2, 128.1, 126.9, 126.8, 126.4, 126.3, 126.1, 123.4, 76.2, 34.7; IR (halocarbon oil): 3024 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}N_2OS$: C, 66.64; H, 5.22; N, 10.36; S, 11.86
Found: C, 66.63; H, 5.24; N, 10.31; S, 11.77

α-(2-Benzothiazolyl)-α-(2-benzo[b]furyl)benzyl Alcohol was analogously prepared from benzo[b]furan and 2-benzoylbenzothiazole[10] (72%): mp. 123-125°; ^{1}H NMR ($CDCl_3$): δ 8.02 (d, 1H),

7.82 (d, 1H), 7.64-7.61 (m, 2H), 7.49 (t, 1H), 7.42 (t, 1H), 7.37-7.33 (m, 5H), 7.27-7.16 (m, 3H), 6.71 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 174.5, 157.6, 155.2, 152.4, 141.5, 135.8, 128.5, 128.3, 127.6, 126.7, 126.1, 125.3, 124.7, 123.4, 122.9, 121.6, 121.4, 111.4, 106.6, 77.5; IR (halocarbon oil): 3225 cm^{-1}.

Anal. Calcd for $C_{22}H_{15}NO_2S$: C, 73.93; H, 4.23; N, 3.92; S, 8.97
Found: C, 74.01; H, 4.26; N, 3.89; S, 8.91

2-Benzothiazolyl-*bis*-2-thienylmethanol was analogously prepared from thiophene and 2-benzothiazolyl 2-thienyl ketone (47%): mp. 91-93°; ^{1}H NMR ($CDCl_3$): δ 8.01 (d, 1H), 7.82 (d, 1H), 7.47 (td, 1H), 7.37 (br t, 1H), 7.31 (dd, 2H), 7.08 (d, 2H), 6.96 (dd, 2H), 5.19 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 176.0, 152.3, 148.7, 136.0, 126.8, 126.6, 126.5, 126.3, 125.5, 123.5, 121.7, 76.9; IR (halocarbon oil): 3225 cm^{-1}.

Anal. Calcd for $C_{16}H_{11}NOS_3$: C, 58.33; H, 3.36; N, 4.25; S, 29.20
Found: C, 58.15; H, 3.35; N, 4.25; S, 29.12

2-Benzo[b]thienyl-2-benzothiazolyl-2-thienylmethanol was analogously prepared from benzo[b]thiophene and 2-benzothiazolyl 2-thienyl ketone (78%): mp. 76-78°; ^{1}H NMR ($CDCl_3$): δ 8.05 (d, 1H), 7.85 (d, 1H), 7.80-7.77 (m, 1H), 7.71-7.68 (m, 1H), 7.49 (td, 1H), 7.42 (d, 1H), 7.38-7.30 (m, 4H), 7.16 (dd, 1H), 7.00 (dd, 1H), 5.22 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 175.5, 152.4, 149.2, 148.0, 140.2, 139.0, 135.9, 127.0, 126.7, 126.6, 126.3, 125.6, 124.7, 124.3, 124.1, 123.5, 123.4, 122.3, 121.7, 77.3; IR (halocarbon oil): 3272 cm^{-1}.

Anal. Calcd for $C_{20}H_{13}NOS_3$: C, 63.30; H, 3.45; N, 3.69; S, 25.34
Found: C, 63.21; H, 3.42; N, 3.61; S, 25.25

2-(1-Methylimidazolyl)-2-thienylmethanol was analogously prepared from 1-methylimidazole and 2-thiophenecarboxaldehyde (55%): mp. 96-98°; ^{1}H NMR ($CDCl_3$): δ 7.22 (d, 1H), 6.90 (br t, 1H), 6.77 (d, 1H), 6.71 (d, 1H), 6.68 (br d, 1H), 6.04 (s, 1H), 3.50 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 148.5, 145.7, 126.6, 126.0, 124.8, 123.8, 122.2, 65.9, 33.3; IR (halocarbon oil): 3084 cm^{-1}.

Anal. Calcd for $C_9H_{10}N_2OS$: C, 55.65; H, 5.19; N, 14.42; S, 16.51
Found: C, 55.57; H, 5.18; N, 14.38; S, 16.54

2-(1-Methylimidazolyl)-2-furylmethanol was analogously prepared from 1-methylimidazole and 2-furaldehyde (52%): mp. 100-102°; ^{1}H NMR ($CDCl_3$): δ 7.33 (s, 1H), 6.77 (d, 1H), 6.74 (d, 1H), 6.29 (dd, 1H), 6.18 (d, 1H), 5.86 (s, 1H), 3.58 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 153.6, 146.9, 142.2, 126.2, 122.1, 110.2, 107.0, 63.7, 33.1; IR (halocarbon oil): 3041 cm^{-1}.

Anal. Calcd for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.58; H, 5.66; N, 15.54

2-Benzothiazolyl-2-thiazolyl-2-thienylmethanol was analogously prepared from thiazole and 2-benzothiazolyl 2-thienyl ketone (31%): mp. 120-122°; ^{1}H NMR ($CDCl_3$): δ 8.03 (d, 1H), 7.85 (d, 1H), 7.81 (d, 1H), 7.47 (td, 1H), 7.40-7.35 (m, 2H), 7.32-7.29 (m, 2H), 6.96 (dd, 1H), 6.36 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 174.2, 173.2, 151.9, 147.2, 142.3, 136.2, 126.9, 126.5, 126.4, 126.2, 125.5, 123.4, 121.8, 121.0, 77.9; IR (halocarbon oil): 3225 cm^{-1}.

Anal. Calcd for $C_{15}H_{10}N_2OS_3$: C, 54.52; H, 3.05; N, 8.48; S, 29.11
Found: C, 54.53; H, 3.07; N, 8.49; S, 28.98

2-Benzothiazolyl-2-thienylmethanol was analogously prepared from benzothiazole and thiophene-2-carboxaldehyde (65%): mp. 90-92°; ^{1}H NMR ($CDCl_3$): δ 7.91 (d, 1H), 7.80 (d, 1H), 7.41 (t, 1H), 7.33 (t, 1H), 7.26 (dd, 1H), 7.09 (d, 1H), 6.92 (dd, 1H), 6.38 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 174.7, 152.4, 144.3, 135.0, 126.8, 126.2, 126.1, 125.8, 125.2, 123.0, 121.7, 70.1; IR (halocarbon oil): 3217 cm^{-1}.

Anal. Calcd for $C_{12}H_9NOS_2$: C, 58.27; H, 3.67; N, 5.66; S, 25.93

Found: C, 58.19; H, 3.66; N, 5.62; S, 25.83

Preparation of 2-Benzothiazolyl 2-Thienyl Ketone.- A mixture of 2-benzothiazolyl-2-thienylmethanol (1.14 g, 4.63 mmol) and manganese dioxide (2.01 g, 23.1 mmol) in methylene chloride (25 mL) was magnetically stirred at 25° under nitrogen for 3 days. The excess manganese dioxide was removed by vacuum filtration and the filter cake was washed with acetone (50 mL). The filtrate was concentrated *in vacuo* and adsorbed onto silica gel; flash chromatography (3:1 hexanes/ether) gave 2-benzothiazolyl 2-thienyl ketone (0.94 g, 83%) as a fluffy, pale yellow solid: mp. 107-108°; ^{1}H NMR ($CDCl_3$): δ 8.76 (d, 1H), 8.24 (br d, 1H), 7.99 (br d, 1H), 7.82 (dd, 1H), 7.61-7.50 (m, 2H), 7.26 (t, 1H); ^{13}C NMR ($CDCl_3$): δ 176.9, 166.6, 153.7, 139.7, 137.4, 137.0, 136.8, 128.4, 127.5, 126.9, 125.5, 122.2; IR (nujol): 1615 cm^{-1}.

Anal. Calcd for $C_{12}H_7NOS_2$: C, 58.75; H, 2.88; N, 5.71; S, 26.14

Found: C, 58.57; H, 2.88; N, 5.65; S, 26.24

General Reduction Procedure. Preparation of α-(2-Thiazolyl)diphenylmethane.- To trifluoroacetic acid (25 mL) at 25° was added over 5 min sodium borohydride (4 pellets, 1.6 g, 42 mmol) and the resulting mixture was magnetically stirred at 25° for 20 min. A solution of α-(2-thiazolyl)diphenylmethanol (0.44 g, 1.6 mmol) in methylene chloride (10 mL) was added in portions over 1 hr and the resulting mixture was magnetically stirred at 25° for 20 hrs. The reaction mixture was carefully poured into 25% aqueous sodium hydroxide/ice (50 mL) to basify to pH 11 and extracted with ether (2 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate, filtered, and concentrated *in vacuo* to afford a yellow oil. Flash chromatography (3:1 hexanes/ether) gave α-(2-thiazolyl)diphenylmethane as a pale yellow solid (0.30 g, 73%): mp. 46-48°; ^{1}H NMR ($CDCl_3$): δ 7.78 (d, 1H), 7.34-7.24 (m, 11H), 5.58 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 173.5, 142.9, 141.9, 128.9, 128.6, 127.1, 119.1, 54.9.

Anal. Calcd for $C_{16}H_{13}NS$: C, 76.46; H, 5.21; N, 5.57; S, 12.76

Found: C, 76.45; H, 5.22; N, 5.55; S, 12.66

α-(2-Benzothiazolyl)diphenylmethane was analogously prepared from α-(2-benzothiazolyl)-diphenylmethanol (58%): mp. 87-89°; lit.[5] mp. 89-91°; ^{1}H NMR ($CDCl_3$): δ 8.01 (d, 1H), 7.79 (d, 1H), 7.47 (td, 1H), 7.36-7.27 (m, 11H), 5.95 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 174.2, 153.4, 141.3, 135.6, 129.0, 128.6, 127.3, 126.0, 124.9, 123.2, 121.4, 55.8.

α-(2-Benzoxazolyl)diphenylmethane was analogously prepared from α-(2-benzoxazolyl)diphenylmethanol (55%): mp. 64-65°; ^{1}H NMR ($CDCl_3$): δ 7.74-7.71 (m, 1H), 7.48-7.43 (m, 1H), 7.36-7.21 (m, 12H), 5.77 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 166.6, 150.9, 141.2, 139.2, 128.7, 128.6, 127.4, 124.8, 124.2, 120.2, 110.6, 51.5.

Anal. Calcd for $C_{20}H_{15}NO$: C, 84.19; H, 5.30; N, 4.91. Found: C, 84.14; H, 5.36; N, 4.92

α-(2-(1-Methylimidazolyl))-α-(2-thienyl)toluene was analogously prepared from α-(2-(1-methylimidazolyl))-α-(2-thienyl)benzyl alcohol (73%): mp. 156-158°; ^{1}H NMR ($CDCl_3$): δ 7.35-7.24 (m, 5H), 7.21 (dd, 1H), 7.03 (s, 1H), 6.92 (dd, 1H), 6.82 (s, 1H), 6.78 (dd, 1H), 5.69 (s, 1H), 3.46 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 148.0, 144.2, 140.6, 128.6, 128.3, 127.5, 127.2, 126.5, 126.1, 125.0, 121.1, 44.6, 32.9.

Anal. Calcd for $C_{15}H_{14}N_2S$: C, 70.83; H, 5.55; N, 11.01; S, 12.61
Found: C, 70.85; H, 5.58; N, 10.98; S, 12.56

α-(2-Benzo[b]furyl)-α-(2-benzothiazolyl)toluene was analogously prepared from α-(2-benzo[b]furyl)-α-(2-benzothiazolyl)benzyl alcohol (53%): mp. 77-79°; ^{1}H NMR ($CDCl_3$): δ 8.03 (d, 1H), 7.81 (d, 1H), 7.52-7.32 (m, 9H), 7.27-7.17 (m, 2H), 6.61 (s, 1H), 6.06 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 170.6, 156.3, 155.1, 153.1, 138.3, 135.5, 128.9, 128.7, 128.2, 128.0, 126.1, 125.1, 124.2, 123.3, 122.8, 121.5, 121.0, 111.2, 105.9, 50.5.

Anal. Calcd for $C_{22}H_{15}NOS$: C, 77.39; H, 4.43; N, 4.10; S, 9.39
Found: C, 77.13; H, 4.58; N, 4.04; S, 9.23

2-Benzothiazolyl-*bis*-2-thienylmethane was analogously prepared from 2-benzothiazolyl-*bis*-2-thienylmethanol (46%): mp. 70-72°; ^{1}H NMR ($CDCl_3$): δ 8.03 (d, 1H), 7.81 (d, 1H), 7.46 (t, 1H), 7.36 (t, 1H), 7.26 (d, 2H), 7.06 (d, 2H), 6.97 (dd, 2H), 6.37 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 172.8, 153.0, 143.7, 135.6, 126.8, 126.1, 125.6, 125.2, 123.3, 121.6, 46.3.

Anal. Calcd for $C_{16}H_{11}NS_3$: C, 61.31; H, 3.54; N, 4.47; S, 30.69
Found: C, 61.18; H, 3.60; N, 4.40; S, 30.76

2-Benzothiazolyl-2-benzothienyl-2-thienylmethane was analogously prepared from 2-benzothiazolyl-2-benzothienyl-2-thienylmethanol (39%): mp. 85-86°; ^{1}H NMR ($CDCl_3$): δ 8.05 (d, 1H), 7.82 (d, 1H), 7.75 (br d, 1H), 7.68 (br d, 1H), 7.47 (t, 1H), 7.37 (td, 1H), 7.32-7.26 (m, 4H), 7.13 (br d, 1H), 7.00 (dd, 1H), 6.42 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 171.9, 153.0, 144.5, 142.8, 140.0, 139.3, 135.6, 127.2, 126.9, 126.2, 125.9, 125.3, 124.5, 124.4, 123.7, 123.5, 123.4, 122.2, 121.6, 40.0.

Anal. Calcd for $C_{20}H_{13}NS_3$: C, 66.08; H, 3.60; N, 3.85; S, 26.46
Found: C, 66.02; H, 3.61; N, 3.85; S, 26.50

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ELECTROPHILIC SUBSTITUTION OF 7-*tert*-BUTYL-1-SUBSTITUTED PYRENES. A NEW ROUTE FOR THE PREPARATION OF 1,3-DISUBSTITUTED PYRENES†

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Pyrenes belong to the class of polycyclic aromatic hydrocarbons (PAHs), and are reported to cause cancer or mutations in living organisms,[1] thus making them the largest class of chemical carcinogens today. Pyrenes are formed when organic materials are burned or strongly heated. They are produced in larger amounts under inefficient combustion conditions. Analysis of the complicated mixtures of polycyclic aromatic compounds in the environment is possible only when pure and well-characterized reference materials are available.[2] Reference materials are essential also for the study of the biological effects of polycyclic aromatic compounds and for the establishment of structure-activity relationships. The preparation of 1,3-disubstituted pyrene using the regioselective electrophilic disubstitution is quite difficult in spite of the fact that electrophilic substitution of pyrene itself occurs at 1, 3, 6, and 8 positions.[3-7] For example, Harvey *et al* [7a] reported that the acetylation of pyrene afforded 1,8-diacetylpyrene as a major product along with 1,6- and 1,3-analogues. Therefore, the selective