ditions with $Cl_2$ instead of $Br_2$ only traces (<2%) of **6f** were observed.

**Hydrolysis of the Dibromocyclohexadienone 7.** Procedure A at room temperature allows the separation of the dibromocyclohexadienone **7** in 10% yield by flash chromatography on silica gel (hexane–ethyl acetate, 3:1) as a crystalline product: mp 127 °C (lit.[16] mp 127–128 °C); IR 1660 $cm^{-1}$; $^1H$ NMR $\delta$ 1.2 (s, t-Bu, 18 H), 7.08 (s, CH of quinone, 2 H); MS, $m/z$ 306 ($M^+$), 284, 269, 253, 242, 252, 189.

**Hydrolysis of 7 in the Presence of $H_2O_2$.** The hydrolysis of **7** was performed under the same conditions of procedure A in the absence of $Br_2$. A quantitative yield of 2,6-di-*tert*-butyl-*p*-benzoquinone was obtained.

**Hydrolysis of 7 in the Absence of $H_2O_2$.** The hydrolysis was performed under the same conditions of procedure A by using 10 mL of $H_2O$ instead of $H_2O_2$ and in the absence of $Br_2$. A 47% yield of 2,6-di-*tert*-butyl-*p*-benzoquinone was obtained.

**Oxidation of 2,6-Di-*tert*-butylphenol by Stoichiometric $Br_2$.** Procedure A was utilized by using a stoichiometric amount of $Br_2$ and in the absence of $H_2O_2$. A 37% yield of 2,6-di-*tert*-butyl-*p*-benzoquinone was obtained.

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**Registry No.** **1a**, 123-31-9; **1b**, 95-71-6; **1c**, 654-42-2; **1d**, 700-13-0; **1e**, 527-18-4; **1f**, 72693-14-2; **1g**, 2444-28-2; **1h**, 88-58-4; **1i**, 13379-77-6; **2a**, 106-51-4; **2b**, 553-97-9; **2c**, 137-18-8; **2d**, 935-92-2; **2e**, 527-17-3; **2f**, 29148-36-5; **2g**, 2460-77-7; **2h**, 719-22-2; **2i**, 844-51-9; **3a**, 2785-74-2; **3b**, 98-29-3; **3c**, 1020-31-1; **4a**, 4370-50-7; **4b**, 1129-21-1; **4c**, 3383-21-9; **5a**, 576-26-1; **5b**, 2416-94-6; **5c**, 527-35-5; **5d**, 2432-11-3; **5e**, 1687-64-5; **5f**, 128-39-2; **5g**, 4096-72-4; **5h**, 1139-52-2; **5i**, 7469-77-4; **7**, 1144-36-1; 1,4-dihydroxynaphthalene, 571-60-8; 2-methyl-1,4-dihydroxynaphthalene, 481-85-6; 1,4-naphthaquinone, 130-15-4; 2-methyl-1,4-naphthaquinone, 58-27-5.

## Synthesis of 1-Alkyl-1,2,4-triazoles: A New One-Pot Regiospecific Procedure[1]

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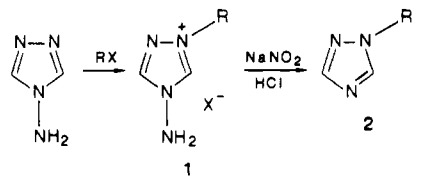
Regiospecific alkylation of 1,2,4-triazoles provides a synthetic challenge.[2] Direct alkylation of 1,2,4-triazole affords usually a mixture of mainly 1- and some 4-substituted product.[3] Ratios vary with the nature of the alkylating agent and conditions but frequently range from 70:30 to 90:10. Preparation of 1-substituted 1,2,4-triazoles has become important of late, as a number of such triazoles has been found to be very effective agricultural fungicides,[4] antimycotics,[5] and more recently aromatase inhibitors.[6]

**Scheme I**




4-Amino-1,2,4-triazole (4-AT) is an activated and blocked triazole that can be prepared directly from hydrazine and derivatives of formic acid.[7] We report a regiospecific one-pot synthesis of some 1-alkyl-1,2,4-triazoles based on the alkylation of 4-amino-1,2,4-triazole and the subsequent deamination of the so formed triazolium salt (Scheme I).

### Results and Discussion

Alkylation of 4-AT proceeded easily in polar media (isopropyl alcohol, or acetonitrile) exclusively at N-1 usually in good yield (Table I). In the case of alkylation with *sec*-butyl bromide, the yield of **1g** was only 59%, owing to the difficulty encountered in separating **1g** from remaining aminotriazole. However, a satisfactory yield of **2g** was obtained in the one-pot reaction. The aminotriazolium salts (**1a–h**) were deaminated readily with a slight excess of nitrous acid in essentially quantitative yield. Evolution of nitrous oxide was observed during deamination, as has been found in nitrous acid deamination of other 1,1-disubstituted aromatic hydrazines.[8] It should be noted that the 2,4-dichlorophenacyltriazole (**2c**) reacts with nitrous acid at ambient temperature. Therefore, it is advisable to carry out deaminations at 0–5 °C and to avoid too large an excess of nitrous acid.

We found that the alkylation and deamination reactions could be performed sequentially in one-pot in good yield without isolation of the aminotriazolium salts. Alkyltriazole isolation is facilitated by the fact that any 4-AT (starting material) or 1,2,4-triazole (a potential byproduct) remains in the aqueous phase from which the desired product is precipitated or extracted. This reaction sequence is useful for alkylating agents as unreactive as primary alkyl chlorides as well as for more reactive benzylic and phenacyl halides. Furthermore, the mild nonbasic conditions employed here are particularly suited to alkylating agents that bear base-sensitive substituents, which contrast with the strongly basic conditions frequently used in direct alkylations of triazoles. The reaction sequence has failed with trityl chloride, however, because the intermediate trityl(aminotriazolium) salt undergoes solvolysis to form trityl alcohol under the acidic deamination conditions used.

Our work provides the first example of a fairly general high-yield regiospecific one-pot synthesis of 1-substituted 1,2,4-triazoles from 4-AT,[9] although alkylation of 4-AT[10] and deamination of aminotriazoles[11] and -triazolium salts[10]

(1) Dedicated to Dr. Alan R. Katritzky on the occasion of his 60th birthday.

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Table I. Preparation of 1 and 2[a]

| R | X (/1)[b] | % yield 1 | mp, °C; lit. value | % yield 2 | mp (bp), °C; lit. value | % yield 2 (one-pot) |
|---|---|---|---|---|---|---|
| a: $PhCH_2$ | Cl (1) | 85[c] | 156–158; 160[10] | 96 | 53–55 (118/0.9 mm); 54[10] | 83 |
| b: $PhCOCH_2$ | Cl (1) | 76[d] | 214 dec | 89 | 117–118.5; 119[15] | 76 |
| c: $2,4\text{-}Cl_2C_6H_3COCH_2$ | Cl (0.95) | 82[d] | 214–215 dec | 89 | 113.5–115.5; 117[14] | 88 |
| d: $t\text{-}BuCOCH_2$ | Br (1) | 81[e] | 129–131 | 87 | 70–70.5; 69[16] | 86 |
| e: $4\text{-}ClC_6H_4OCHCO\text{-}t\text{-}Bu$ | Cl (1.05) | 86[c] | 164–165 | 81 | 74–76; 74–76[17] | 62 |
| f: $n$-Bu | Br (1) | 97[e] | 47.5–49 | 92 | (97–98/14 mm); (98/13 mm)[10] | 76 |
| g: $s$-Bu | Br (1.1) | 59[e] | 78–81 | 85 | (75–76/4 mm); (70/4 mm)[3c] | 84 |
| h: $n\text{-}C_5H_{11}$ | Cl (2) | 97[e] | 53–55 | 94 | (101–103/7 mm) | 84 |

[a] IR and NMR spectral data recorded for all compounds were consistent with the assigned structure. Satisfactory analytical data (±0.40% for C, H, N) were reported for all new compounds listed in the table. [b] Ratio of alkylating agent to 4-amino-1,2,4-triazole. [c] Reaction time 16 h. [d] Reaction time 4 h. [e] Reaction time 24 h.

have been reported before. This synthetic sequence has the advantage over others[12] in that the starting triazole is already protected, and 4-AT is readily available at low cost.[13]

## Experimental Section

Melting points were obtained in open capillary tubes in a silicon oil bath and are uncorrected. IR spectra were obtained on a Beckman Spectrophotometer IR 4230. $^1H$ NMR spectra were obtained on a Varian EM360A NMR spectrometer at 60 MHz with TMS as an internal standard. GLC analyses were performed on a Hewlett-Packard 5890 instrument utilizing a flame-ionization detector on a DB 1701 capillary column. Deaminations were followed with starch iodide paper until a continuous black/mauve color was obtained. Reagents were generally purchased and used without additional purification, with the exception of 1-bromopinacolone, which was distilled. 4-Amino-1,2,4-triazole (purity, >99%) is a product of Reilly Industries, Inc.

The following are illustrative of the procedures used.

**Alkylation Procedure. 1-(2,4-Dichlorophenyl)-2-(4-amino-4*H*-1,2,4-triazoliumyl)ethanone Chloride (1c).** 4-Amino-1,2,4-triazole[7] (4.41 g, 52.5 mmol), 2-chloro-1-(2,4-dichlorophenyl)ethanone (97%) (11.52 g, 50 mmol), and isopropyl alcohol (100 mL) were mixed together and heated at reflux with stirring for 4 h. The product in this case crystallized at reflux temperature. The reaction mixture was cooled, filtered, washed with isopropyl alcohol, and dried to yield **1c** (2.56 g, 82%): mp 214–215 °C dec; NMR (DMSO-$d_6$) $\delta$ 9.47 (s, 1), 10.64 (s, 1), 7.57 (s, 2), 6.34 (s, 2), 7.89–7.76 (m, 2), 8.22 (d, 1); IR (KBr disk) 3220 (broad), 1709 (C=O) $cm^{-1}$. Anal. Calcd for $C_{10}H_9Cl_3N_4O$: C, 39.05; H, 2.95; N, 18.22. Found: C, 38.95; H, 3.11; N, 18.42.

**Deamination Procedure. 1-(2,4-Dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone (2c).** 1-(2,4-Dichlorophenyl)-2-(4-amino-4*H*-1,2,4-triazoliumyl)ethanone chloride (6.42 g, 21 mmol) and water (50 mL) were mixed, and hydrochloric acid (3.60 g, 42 mmol, 11.6 M) was added. After this mixture was cooled to 0–5 °C, a saturated aqueous solution of sodium nitrite (1.52 g, 22 mmol) was added dropwise. Gas evolution was observed. The reaction mixture was allowed to warm to ambient temperature and neutralized with 28% w/w ammonium hydroxide solution to pH 7. The product was isolated by filtration, washed with water, and dried to give **2c** (4.76 g, 89%): mp 115–116 °C (lit.[14] mp 117 °C) (purity >99% by GLC); NMR ($CDCl_3$) $\delta$ 8.21 (s, 1), 7.92 (s, 1), 7.68–7.23 (m, 3), 5.62 (s, 2); IR (KBr disk) 2990, 1709 (C=O) $cm^{-1}$.

Liquids were isolated by dichloromethane extraction, drying (anhydrous magnesium sulfate), concentration, and distillation (see Table I).

**One-Pot Procedure. 1-(2,4-Dichlorophenyl)-2-(1*H*-1,2,4-triazol-1-yl)ethanone (2c).** A mixture of 4-amino-1,2,4-triazole (4.41 g, 52.5 mmol), 2-chloro-1-(2,4-dichlorophenyl)ethanone (97%) (11.52 g, 50 mmol), and isopropyl alcohol was heated at reflux. After 4 h the reaction mixture was concentrated by distillation, the isopropyl alcohol removed was replaced with water (100 mL), and the reaction mixture was cooled to 5 °C. Concentrated hydrochloric acid (9.1 mL, 0.11 mol) was added, followed by dropwise addition of saturated aqueous sodium nitrite solution (15 mL, 55 mmol). The reaction mixture was allowed to warm to ambient temperature, and then it was neutralized with potassium carbonate. The product was isolated by filtration, washed with water, and dried to give **2c** (11.35 g, 89%), mp 113.5–115.5 °C (lit.[14] mp 117 °C) (purity 98.8% by GLC, no 4-isomer detected).

**Registry No.** **1a**, 6085-98-9; **1b**, 118227-29-5; **1c**, 118227-30-8; **1d**, 118227-31-9; **1e**, 118227-32-0; **1f**, 118227-33-1; **1g**, 118227-34-2; **1h**, 118227-35-3; **2a**, 6085-94-5; **2b**, 58905-26-3; **2c**, 58905-16-1; **2d**, 58905-32-1; **2e**, 43121-43-3; **2f**, 6086-22-2; **2g**, 63936-01-6; **2h**, 118227-36-4; 4-AT, 584-13-4; $PhCH_2Cl$, 100-44-7; $PhCOCH_2Cl$, 532-27-4; $2,4\text{-}Cl_2C_6H_3COCH_2Cl$, 4252-78-2; $\pm\text{-}BuCOCH_2Br$, 5469-26-1; $4\text{-}ClC_6H_4OCHClCO\text{-}\pm\text{-}Bu$, 57000-78-9; BuBr, 109-65-9; $s$-BuBr, 78-76-2; $n\text{-}C_5H_{11}Cl$, 543-59-9.

**Supplementary Material Available:** Analytical, full $^1H$ NMR, and full IR data for compounds **1b–h** and **2h** (3 pages). Ordering information is given on any current masthead page.

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