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(24) The possibility cannot be excluded that a minute amount of **3b** is in rapid (on the nmr time scale) equilibrium with **3a** in toluene, and this equilibrium produces slightly larger (but still quite small) amounts of **3b** at higher temperatures. Since **3b** should have a negative ^{31}P shift, slightly larger amounts of **3b** would produce a lower time-averaged ^{31}P shift for **3a** plus **3b**.
(25) Equilibration between certain cyclic 2,2-dihydro-1,3,2-dioxaphospholenes and their open chain forms is rapid relative to the nmr scale; the observed ^{31}P shift is a time average of the positive shift for the cyclic form and the negative shift for the open chain form.[20,21] The value of the time-averaged ^{31}P shift is solvent dependent as a result of specific solvent effects on the position of the equilibrium.[20,21]
(26) Noise levels were too high to allow integrations without proton decoupling.
(27) Melting points were taken in open capillaries with a Mel-Temp apparatus and are corrected. Ir spectra were determined with Perkin-Elmer Model 137 and Beckman IR-10 spectrometers. Nmr spectral data reported in the text were determined with a JEOL JNM-C-60HL spectrometer and with Varian T-60 and HA-100 spectrometers. Temperatures for the variable temperature ^1H nmr spectra were calibrated by comparison of measured shifts between the OH and CH_3 protons of a methanol sample with a calibrated chart supplied by JEOL Co.; indicated temperatures are probably ±2. Temperatures for the variable temperature ^{31}P nmr spectra were calibrated by means of a thermocouple inserted into a methanol sample in the ^{31}P probe; indicated temperatures are probably ±2°. A variable temperature study of the 85% H_3PO_4 standard indicated that the shift was negligible (*ca.* 0.1 ppm downfield or upfield) as the temperature was varied from −60 to +90°. Positive ^{31}P shifts are upfield from 85% H_3PO_4.

Reaction of *p*-Toluenesulfonylhydrazones with *N*-Bromosuccinimmide in Methanol. Regeneration of Carbonyl Compounds[1]

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A number of aldehydes and ketones have been regenerated in high yields from the corresponding *p*-toluenesulfonylhydrazones by reaction with *N*-bromosuccinimmide in methanol. A mechanistic pathway of the reaction is proposed.

There has been considerable interest in the development of mild techniques for the conversion of oximes,[2,3] 2,4-dinitrophenylhydrazones,[4] and semicarbazones into aldehydes and ketones. A variety of procedures have been described but only one is concerned with the conversion of *p*-toluenesulfonylhydrazones into parent carbonyl compounds.[5]

Here we wish to describe a new method for the regeneration of aldehydes and ketones from their *p*-toluenesulfonylhydrazones by treatment with *N*-bromosuccinimmide (NBS).

The method involves additions of NBS (4 mol) to a methanolic acetone solution of *p*-toluenesulfonylhydrazone (1 mol). The reaction was rapid, evolution of nitrogen was observed, and the solution quickly turned red. Then sodium hydrogen sulfite was added and the mixture refluxed for 10 min, cooled, and worked up. Some representative conversions are summarized in Table I.

From an examination of the reactions of several *p*-toluenesulfonylhydrazones with NBS under a variety of conditions, the advantages and limitations of the present method can be summarized as follows. (1) Reaction proceeds virtually instantaneously at room temperature, and yields of pure products are uniformly high. (2) The addition of sodium hydrogen sulfite when nitrogen was evolved and the presence of acetone as a solvent are sufficient to almost completely suppress reactions of molecular bromine on the substrate such as α-bromination and oxidation of secondary alcohols to ketones. (3) Treatment of *p*-toluenesulfonylhydrazone derivatives of α,β-unsaturated ketones and aldehydes does not result in a consistent regeneration of the parent carbonyl compound but leads to mixtures of products.

Table I
Conversion of *p*-Toluenesulfonylhydrazones into Aldehydes and Ketones with NBS[a] in Methanol

Ketone or aldehyde	Registry no.	Yield, %[b]
Cyclohexanone	108-94-1	81.3
3,3,5,5-Tetramethylcyclohexanone	14376-79-5	85.2
Acetophenone	98-86-2	74.3
Deoxybenzoin	451-40-1	88.7
Benzoin	119-53-9	86.8
Cholestan-3-one	15600-08-5	89.0
Androstanolone	521-18-6	78.2
Cyclohexylphenyl ketone	712-50-5	84.5
Benzophenone	119-61-9	91.0
Fluoren-9-one	486-25-9	89.4
n-Heptaldehyde	111-71-7	75.3
Benzaldehyde	100-52-7	82.0
Anisaldehyde	123-11-5	84.2
p-Chlorobenzaldehyde	104-88-1	85.3

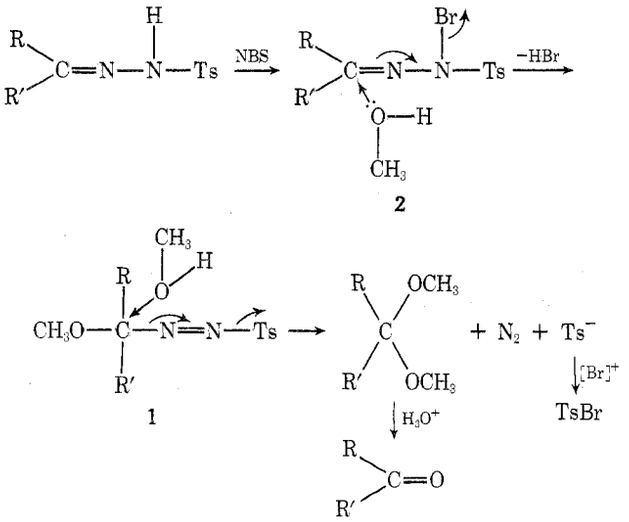
[a] Registry no. 128-08-5. [b] Calculated on pure chromatographed material.

Two moles of NBS are sufficient to regenerate aromatic ketones from the corresponding *p*-toluenesulfonylhydrazones. A nearly quantitative amount of nitrogen was evolved during such a reaction in methanol at room temperature; the solution turned red but slowly faded to yel-

low. Tlc analysis of the mixture revealed the formation of a dimethyl ketal that undergoes hydrolysis on silica gel to form ketone, and p-toluenesulfonylbromide that slowly reacts with methanol to form methyl p-toluenesulfonate.[6]

These facts can be explained assuming the formation of azo ether 1 by nucleophilic attack of methanol on the carbon atom double bonded to nitrogen of N-bromo(p-toluenesulfonyl)hydrazone 2. Azo ether 1 provides a good leaving group (the p-toluenesulfinate anion) so that nucleophilic displacement by methanol occurs easily (Scheme I).

Scheme I



Such a mechanism for the decomposition of azo ether 1 corresponds to that proposed for the reaction of benzophenone p-toluenesulfonylhydrazone with lead tetraacetate in methanol.[7]

Experimental Section

All melting points are uncorrected. Spectra were recorded on Perkin-Elmer 257, Unicam SP 800, and Jeol C60 HL spectrometers. Nmr spectra were performed using TMS as internal standard. Microanalyses were performed using C, H, N Analyzer Model 185 of Hewlett-Packard Co. Ketones, aldehydes, NBS, and p-toluenesulfonylhydrazine are commercial materials. NBS was recrystallized from benzene. The p-toluenesulfonylhydrazones were readily prepared in good yields by reaction of carbonyl compounds with equimolar quantities of p-toluenesulfonylhydrazine in methanol or ethanol at temperatures not exceeding 50° (1–2 hr). These derivatives all showed ir absorption (KBr) at approximately 3200, 1600, 1360, 1170, and 820 cm^{-1}. Thin layer chromatography (tlc) was performed with Merck fluorescent silica gel plates; compounds were visualized with 254-nm light, with iodine vapor, or by spraying with 2% 2,4-dinitrophenylhydrazine in acidic ethanol.

Conversion of p-Toluenesulfonylhydrazones into Parent Carbonyl Compounds. General Procedure. Powdered NBS (4×10^{-2} mol) was added at 0–5° to an efficiently stirred 50% acetone–methanol solution or suspension of p-toluenesulfonylhydrazone (1×10^{-2} mol). Nitrogen evolution was complete within 1–3 min and the solution quickly turned red; saturated aqueous sodium hydrogen sulfite was added to suppress the bromine formed. Then the solution was heated for 10 min while adding water; it was cooled and shaken with ether. The organic phase was washed with saturated aqueous sodium carbonate and water, dried (Na_2SO_4), and evaporated at reduced pressure. The residue was chromatographed on a silica gel column.

Deoxybenzoin. To an efficiently stirred solution of deoxybenzoin p-toluenesulfonylhydrazone (3.64 g, 1×10^{-2} mol) in 25 ml of acetone and 25 ml of methanol in a 200-ml flask was added NBS (7.12 g, 4×10^{-2} mol) at 0–5°. After complete evolution of nitrogen, saturated aqueous sodium hydrogen sulfite was added until the red color of the solution disappeared. The reaction mixture was heated at its boiling point while adding water; then it was cooled and shaken with ether. The organic phase was washed with saturated aqueous sodium carbonate and water, dried (Na_2SO_4), and evaporated at reduced pressure. The resulting mixture was chromatographed on silica gel using benzene as eluent. Deoxybenzoin[8] (1.74 g, mp 55–56°) was obtained in 88.7% yield.

Anal. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.12. Found, C, 85.43; H, 6.32.

Benzoin. To an efficiently stirred solution of benzoin p-toluenesulfonylhydrazone (3.80 g, 1×10^{-2} mol) in 50 ml of acetone and 50 ml of methanol in a 200-ml flask was added NBS (7.12 g, 4×10^{-2} mol) at 0–5°. After complete evolution of nitrogen, saturated aqueous sodium hydrogen sulfite was added until the red color of the solution disappeared. The reaction mixture was worked up as reported above and the resulting residue was chromatographed on silica gel using benzene as eluent. Benzoin[8] (1.84 g, mp 133–135°) was obtained in 86.8% yield.

Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.31; H, 5.84.

Cholestan-3-one. To an efficiently stirred solution of cholestan-3-one p-toluenesulfonylhydrazone (2.77 g, 0.5×10^{-2} mol) in 25 ml of acetone and 25 ml of methanol in a 200-ml flask was added NBS (3.56 g, 2×10^{-2} mol) at 0–5°. After complete evolution of nitrogen, saturated aqueous sodium hydrogen sulfite was added until the red color of the solution faded. The reaction mixture was treated as reported above and the resulting residue was chromatographed on silica gel, using cyclohexane–ethyl acetate 8:2 mixture as eluent. Cholestan-3-one[8] (1.7 g, mp 128–129°) was obtained in 89% yield.

Anal. Calcd for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.75; H, 12.11.

Fluoren-9-one. To an efficiently stirred suspension of fluoren-9-one p-toluenesulfonylhydrazone (1.74 g, 0.5×10^{-2} mol) in 50 ml of methanol in a 200-ml flask was added NBS (1.78 g, 1×10^{-2} mol) at room temperature. Nitrogen evolved completely during 3–4 min and the yellow solution quickly turned red-orange but slowly faded to yellow. Tlc analyses revealed the formation of dimethyl ketal that underwent hydrolysis on silica gel to form fluoren-9-one, and p-toluenesulfonyl bromide that slowly reacted with methanol giving methyl p-toluenesulfonate.[6] The solution was heated for 10 min adding water, cooled, and shaken with ether. The organic phase was washed with saturated aqueous sodium carbonate and water, dried (Na_2SO_4), and evaporated at reduced pressure. The residue was chromatographed on silica gel using cyclohexane–ethyl acetate mixture (9:1) as eluent. Fluoren-9-one[8] (0.8 g, mp 82–83°) was obtained in 89.4% yield.

Anal. Calcd for $C_{13}H_8O$: C, 86.65; H, 4.48. Found: C, 86.48; H, 4.56.

Continuing the eluition with the same eluent, methyl p-toluenesulfonate was collected; mp 26–28° (lit.[9] mp 27–28°); ir (KBr) 6.27 (m, phenyl), 7.44–8.5 (both s, sulfonyl); nmr (CCl_4) δ 7.8–7.15 (AA'BB' m, 4 h, p-substituted phenyl), 3.62 (s, 3 H, OCH_3), 2.36 (s, 3 H, $C_6H_4CH_3$).

Anal. Calcd for $C_6H_{10}O_3S$: C, 51.61; H, 5.41. Found: C, 51.45; H, 5.50.

Acknowledgment. I wish to thank Professor Luciano Caglioti for his interest in this work.

Registry No.—Cyclohexanone p-toluenesulfonylhydrazone, 4545-18-0; 3,3,5,5-tetramethylcyclohexanone p-toluenesulfonylhydrazone, 42449-09-2; acetophenone p-toluenesulfonyl hydrazone, 4545-21-5; deoxybenzoin p-toluenesulfonylhydrazone, 19816-85-4; benzoin p-toluenesulfonylhydrazone, 24854-35-7; cholestan-3-one p-toluenesulfonylhydrazone, 37826-48-5; androstanolone p-toluenesulfonylhydrazone, 52718-77-1; cyclohexylphenyl ketone p-toluenesulfonylhydrazone, 52718-78-2; benzophenone p-toluenesulfonylhydrazone, 4545-20-4; fluoren-9-one p-toluenesulfonylhydrazone, 52341-51-2; n-heptaldehyde p-toluenesulfonylhydrazone, 52718-79-3; benzaldehyde p-toluenesulfonylhydrazone, 1666-17-7; anisaldehyde p-toluenesulfonylhydrazone, 19350-72-2; p-chlorobenzaldehyde p-toluenesulfonylhydrazone, 19350-69-7.

References and Notes

(1) This work was done with financial support of the Italian National Research Council (CNR).
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Synthesis of *s*-Triazolo[3,4-*b*]benzothiazoles

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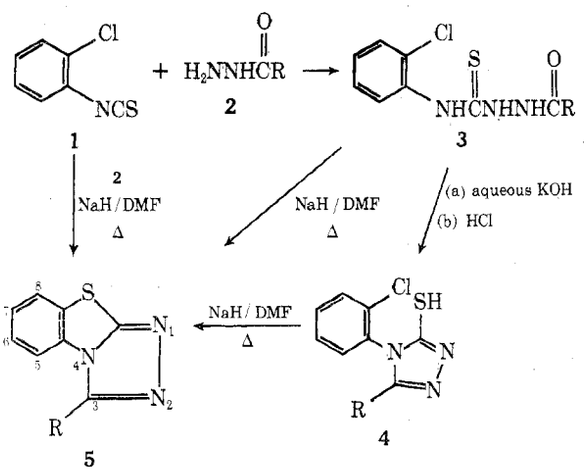
A general and convenient synthesis of *s*-triazolo[3,4-*b*]benzothiazoles is described. Treatment of 4-(2-halophenyl)-1-acyl-3-thiosemicarbazides with sodium hydride and heating to reflux in dimethylformamide yielded *s*-triazolo[3,4-*b*]benzothiazoles.

Syntheses of *s*-triazolo[3,4-*b*]benzothiazoles have been reported by Reynolds and Van Allan[1] as well as Butler, O'Sullivan and Scott.[2,3] Reynolds and Van Allan reported various cyclodehydration reactions of the 2-benzothiazoylhydrazides, while Butler, *et al.*, reported the oxidative cyclizations of the substituted benzothiazolylhydrazones. In all instances, an extended synthetic sequence is necessary to obtain various *s*-triazolo[3,4-*b*]benzothiazoles. We would like to report a novel ring-forming reaction for the synthesis of *s*-triazolo[3,4-*b*]benzothiazoles. The method allows a variety of substituted *s*-triazolo[3,4-*b*]benzothiazoles to be obtained in a series of facile reactions. This method is outlined in Scheme I.

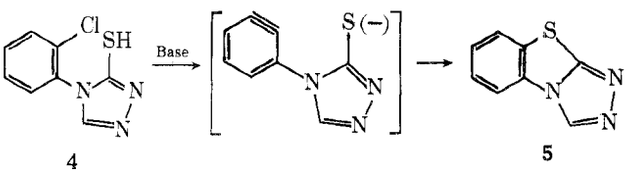
Scheme I



Compounds **3** and **4** (R = H) were readily synthesized in the manner outlined. Heating the potassium salt of **4** in refluxing dimethylformamide (DMF)[4] yielded the *s*-triazolo[3,4-*b*]benzothiazole (**5**, R = H). This compound was identical with a sample prepared by the method of Reynolds and Van Allan[1] from the reaction of 2-hydrazinobenzothiazole with triethyl orthoformate. However, simply treating compounds **4** or **3** with sodium hydride followed by heating to reflux in DMF gave compound **5** in similar yields. Thus, it is now possible to prepare *s*-triazolo[3,4-*b*]benzothiazole (**5**) in only two steps. Compound **1** can also be directly converted to compound **5** but the product from this method is difficult to purify.

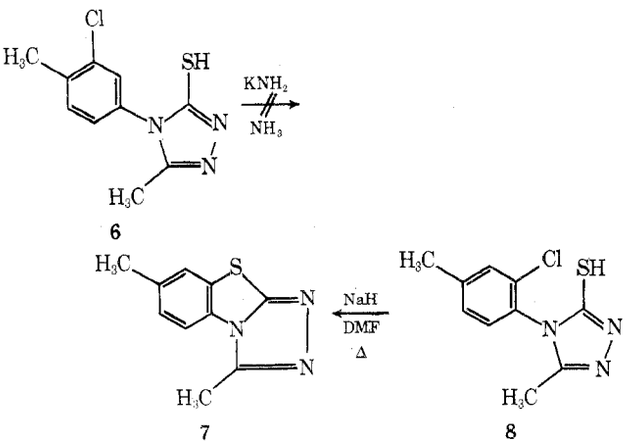
Utilization of appropriately substituted acylhydrazides (**2**) in this reaction ultimately results in substitution at the 3 position of compound **5**. Substituents may also be placed in the 5, 6, or 7 positions of compound **5** through the utilization of the appropriately substituted 2-halophenyl isothiocyanate (**1**) in this reaction. Tables I and II illustrate some of the possible variations.

A possible mechanism for the formation of *s*-triazolo[3,4-*b*]benzothiazoles from the triazole-3-thiols would be a nucleophilic displacement by the thiolate anion. Alternatively, the mechanism could involve elimination of a halogen to yield a benzyne followed by thiolate addition to close the ring.



Ogura and Itoh[5] reported the synthesis of imidazo[2,1-*b*]benzothiazoles *via* a benzyne intermediate from 1-(3-chlorophenyl)-2-mercaptoimidazole and liquid ammonia potassium amide.

In this instance a benzyne mechanism is not probable since 4-(3-chloro-4-methylphenyl)-5-methyl-1,2,4-triazole-3-thiol (**6**) did not yield 3,7-dimethyl-*s*-triazolo[3,4-*b*]benzothiazole (**7**) under their reaction conditions or under the conditions employed in the synthesis of compound **7** from compound **8**.



Experimental Section

All chemicals were reagent grade and used without further purification. The products separated were characterized by elemental analysis, nmr, and mass spectra. All isothiocyanates were commercial grade or prepared from the aniline according to the literature. All melting points were uncorrected and were determined in a capillary tube using a Mel-Temp apparatus. The acylhydrazines were of commercial quality or were prepared by standard methods.