H. J. Slater for expert technical assistance, and Drs. R. K. Blackwood and E. B. Whipple for stimulating discussions.

Registry No.—**1a,** 6342-56-9; **1b,** 5774-26-5; **1c,** 19358-00-0; **1d,** 59044-05-2; **1e,** 19255-82-4; **2a,** 19358-03-3; **2c,** 59044-06-3; **3a,** 10374-97-7; **3b,** 38167-23-6; **3c,** 59044-07-4; **4a,** 59044-08-5; **4b,** 59043-78-6; **4c,** 59044-09-6; **5,** 59044-10-9; **11,** 59044-11-0; **14,** 59044-12-1; DHA, 96-26-4; methanol, 67-56-1; ethanol, 64-17-5; 1-propanol, 71-23-8; isopropyl alcohol, 67-63-0; 1-butanol, 71-36-3; ethylene glycol, 107-21-1; 1,2-propanediol, 57-55-6; *meso*-2,3-butanediol, 5341-95-7; 1,3-propanediol, 504-63-2; glycerol, 56-81-5; 4-ethoxy-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane, 59044-13-2; 4-isopropoxy-5-methyl-3,6,8-trioxabicyclo[3.2.1]octane, 59044-14-3.

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(17) Structure **12** was eliminated on the basis of larger (0.1–0.2 ppm) anticipated shift for axial–equatorial oriented 4-CH_3 substituent. Structure **13** should reveal only a single resonance for 4-CH_3 group irrespective of the orientation of the methoxyl substituent.
(18) For an alternate synthesis of trioxa-3,6,8-bicyclo[3.2.1]octanes, see J. Gelas, *Bull. Soc. Chim. Fr.,* 3722, 4046 (1970).
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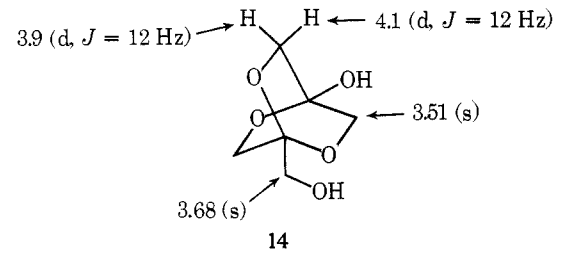
(20) Commercially available DHA (Wallerstein, Aldrich) was used in this study. DHA imparts tanning effect on skin. In addition to known monomeric and several dimeric forms,[22] we have NMR (D_2O solution) evidence for yet another possible dimer structure **14** for this compound. DHA (monomer) shows a singlet at δ 4.36 (D_2O).



14

(21) Amberlyst-15 is a sulfonated cation-exchange resin (H^+ form) marketed by Rohm and Haas, Inc. In our work we have used several brands of strongly acidic, sulfonated ion-exchange resins (H^+ form) with equally effective results.
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Novel One-Pot Synthesis of 4-Aminoquinazolines

Charles H. Foster* and Edward U. Elam

Research Laboratories, Tennessee Eastman Company, Division of Eastman Kodak Company, Kingsport, Tennessee 37662

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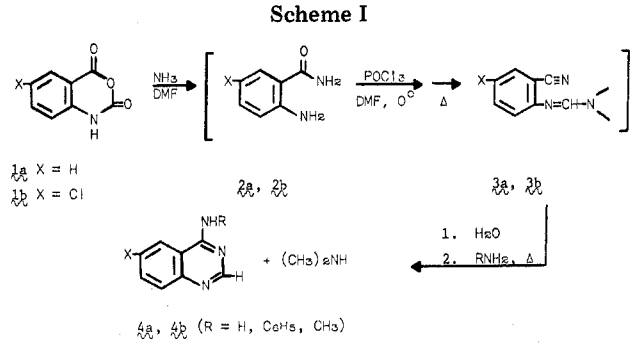
The biological activity of 4-aminoquinazolines has prompted development of many syntheses,[1] most of which are based on conversion of a quinazolone to a 4-chloroquinazoline that affords the desired product on treatment with an amine. However, several workers have reported syntheses based on conversion of *o*-aminonitriles or amides to amidines that cyclize to give the 4-aminoquinazoline directly.[2–5] We wish to report a general synthesis of this type (Scheme I) that can be carried out in one vessel starting with the readily available isatoic anhydrides (**1**, Scheme I). The intermediates in Scheme I need not be isolated.

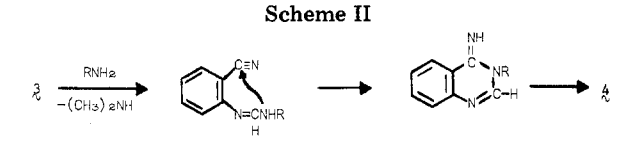
Scheme I



The reaction of isatoic anhydride with ammonia has been reported to give good yields of anthranilamide only in dilute aqueous solution,[6] and 5-chloroisatoic anhydride (**1b**) gives only about 50% yields of **2b**.[7,8] We have found that treatment of **1a** or **1b** with NH_3 in DMF gives very high yields of **2a** or **2b**. Conversion of **2** to **3** is a modification of the work of Jones and Cragoe.[9] It was found that excellent yields of **3** can be obtained if the $POCl_3$ addition is carried out at 0–15 °C, followed by heating briefly at 40–60 °C. The intermediate, **3**, may be isolated, if desired, in ~80% yield, based on **1**, by dilution of the mixture with H_2O and neutralization with NaOH to cause **3** to precipitate.

In the final step a primary aliphatic or aromatic amine undergoes amidine interchange with **3** followed by cyclization and rearrangement to give the desired 4-aminoquinazoline **4** (Scheme II). Although **4** is produced by heating the final acidic DMF solution, much better yields were obtained when the mixture was made basic before heating. (See Experimental Section.)

Scheme II



This method appears to be a general, one-pot method for synthesis of 4-aminoquinazolines in high yields and is much less time consuming than previous methods.

Experimental Section

Melting points are uncorrected. Infrared spectra were recorded using a Perkin-Elmer Model 137 instrument; NMR spectra were obtained with Varian EM-360 and Jeolco MH-100 spectrometers. Mass spectra were taken with a Consolidated Electrodynamics Corp. Model 21-110B spectrometer system.

Preparation of 4-Aminoquinazolines. General Procedure. Ammonia was bubbled into a mixture of an isatoic anhydride (0.05 mol) in DMF (50 ml) at room temperature. The reaction was monitored by ir spectra of aliquots, and when complete conversion was indicated (~15–30 min) the mixture was degassed with N_2 to remove $(NH_4)_2CO_3$. $POCl_3$ (8.5 ml) was then added dropwise at 0–15 °C. The resulting mixture was heated for 30 min at 40–60 °C, then cooled to room temperature, and H_2O (15–20 ml) was added. A primary amine or ammonia was then added until the mixture was basic,[10] and the resulting solution was heated at 100 °C until TLC indicated conversion to the desired product. On cooling, the product crystallized and was isolated by filtration. In some cases addition of H_2O was necessary to cause crystallization.

The following compounds were prepared as described:[11] **4a**, R = H (47%, mp 268–269 °C[1]); **4a**, R = CH_3 (63%, mp 196–197 °C); **4a**, R = C_6H_5 (44%, mp 218–220 °C[2]); **4b**, R = H (79%, mp >310 °C[12]); **4b**, R = CH_3 (66%, mp 256–257 °C[13]); **4b**, R = C_6H_5 (51%, mp 229–230 °C).

Acknowledgments. We wish to thank Professor E. C. Taylor for helpful discussions.

Registry No.—**1a**, 118-48-9; **1b**, 4743-17-3; **4a** (R = H), 15018-66-3; **4a** (R = CH_3), 7154-47-4; **4a** (R = C_6H_5), 34923-95-0; **4b** (R = H), 19808-35-6; **4b** (R = CH_3), 32084-63-2; **4b** (R = C_6H_5), 59169-66-3; ammonia, 7664-41-7; methylamine, 74-89-5; phenylamine, 62-53-3.

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An Unusual Addition–Fragmentation Reaction between Bisulfite and a Methallyl Ether

Gary Wentworth*

Monsanto Triangle Park Development Center, Inc., Research Triangle Park, North Carolina 27709

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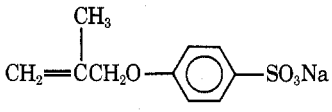
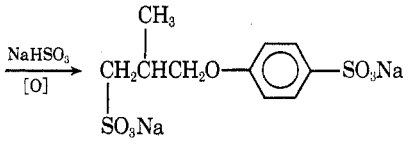
The formation of organic sulfonates by the addition of bisulfite to nonconjugated olefins appears to be a radical process accelerated by oxygen or other oxidizing agents.[1,2] Thus, isobutylene and sodium bisulfite give a good yield of sodium 2-methylpropanesulfonate.[1] While investigating radical reactions of polymerizable olefins, we have discovered a novel variant of the bisulfite–olefin reaction.

The reaction of sodium *p*-sulfophenyl methallyl ether (**1**) with a slight excess of sodium bisulfite gave the expected addition product, disodium *p*-sulfophenyl 2-methyl-3-sulfopropyl ether (**3**), in good yield when the aqueous reaction



1



3

medium was about 1 M in bisulfite. The structure of **3** was confirmed by elemental analysis and NMR spectrum. Analysis of mixtures of **1** and **3** was possible using high-pressure liquid chromatography (HPLC, see Experimental Section).

When **1** was combined with a dilute solution of bisulfite (ca. 10^{-3} M) only trace amounts of **3** were formed; after separation from unreacted **1** by column chromatography, the new products were identified as sodium phenolsulfonate (**6**) and sodium methallylsulfonate (**5**) by comparison of NMR spectra with spectra of the known compounds. The presence of **6** was fur-

Chart I