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# Free Radical-initiated Reactions of Acetylene with Thiols and Carbon Monoxide

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3-Alkylthiopropenals (RSCH=CH—CHO) have been prepared in modest yields by the free radical-initiated reaction of an alkyl thiol, acetylene and carbon monoxide. Aryl thiols reacted similarly but in poor yield. An important concurrent reaction is the interaction of the acetylene with the thiol to give a 1,2-disulfide, a reaction which takes place in high yield in the absence of carbon monoxide.

The reaction of acetylene with thiols in the presence of alkaline catalysts[1] or of substituted acetylenes with various types of thiol derivatives in the presence of free-radical initiators[2] to give 1,2-disulfides has been described in the literature. It has now been found that acetylene itself readily reacts with thiols in the presence of a free-radical initiator to give 1,2-disulfides in yields of 63–94%. The mechanism for this synthesis may be postulated as

$$C_2H_5SH \longrightarrow C_2H_5S\cdot$$

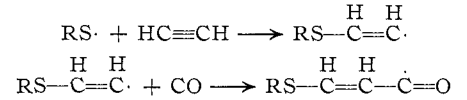
$$C_2H_5S\cdot + HC{\equiv}CH \longrightarrow C_2H_5S{-}CH{=}\dot{C}H$$

$$C_2H_5SCH{=}\dot{C}H + C_2H_5SH \longrightarrow C_2H_5SCH{=}CH_2 + C_2H_5S\cdot$$

$$C_2H_5SCH{=}CH_2 + C_2H_5S\cdot \longrightarrow C_2H_5S\dot{C}H{-}CH_2SC_2H_5$$

$$C_2H_5S\dot{C}HCH_2SC_2H_5 + C_2H_5SH \longrightarrow C_2H_5SCH_2CH_2SC_2H_5 + C_2H_5S\cdot$$

When the acetylene–thiol reaction is carried out in the presence of carbon monoxide, the latter participates in the reaction and a 3-alkylthiopropenal results, as shown by the suggested mechanism



$$RS\cdot + HC{\equiv}CH \longrightarrow RS{-}\overset{H}{C}{=}\overset{H}{C}\cdot$$

$$RS{-}\overset{H}{C}{=}\overset{H}{C}\cdot + CO \longrightarrow RS{-}\overset{H}{C}{=}\overset{H}{C}{-}\dot{C}{=}O$$

$$RS{-}\overset{H}{C}{=}\overset{H}{C}{-}\dot{C}{=}O + RSH \longrightarrow RS{-}\overset{H}{C}{=}\overset{H}{C}{-}\overset{H}{C}{=}O + RS\cdot$$

However, there is a tendency for the mercaptovinyl free radicals to combine preferentially with thiol rather than carbon monoxide. Thus, the thiopropenals have been isolated in yields up to 17%, whereas the greater part of the thiol is converted to the 1,2-disulfide. This 3-alkylthiopropenal synthesis is analogous to the recently reported formation of 3-alkylthiopropanals ($RSCH_2CH_2CHO$) from ethylene, carbon monoxide and a thiol.[3]

## Experimental

A convenient procedure for carrying out the 1,2-disulfide synthesis involved the injection of acetylene at 13–17 atm. pressure into a rocker bomb containing the thiol and initiator heated to a temperature at which the initiator is known to be active. Acetylene was repressured as required. Cylinders of acetylene containing 20 parts per million of oxygen or less were used. The acetylene was also passed through a series of solid scrubbers containing, in order, activated alumina, calcium chloride and sodium hydroxide pellets. After the bomb was cooled and excess acetylene vented, the reaction mixture was purified by distillation. The reactions involving carbon monoxide were carried out similarly except that a prescribed amount of acetylene was measured into a rocker bomb containing the thiol–initiator mixture, and carbon monoxide at pressures in the range of 1000–3000 atm. was injected at the desired temperature. Comparatively high carbon monoxide pressures appear to be necessary for the synthesis of the 3-alkylthiopropenals. Lower yields were obtained at 1000 atm. than at 3000 atm., and no 3-alkylthiopropenal was obtained at 90 atm.

**Synthesis of 3-(*n*-Butylthio)-2-propenal from 1-Butanethiol, Acetylene and Carbon Monoxide.**[4]—A stainless steel rocker bomb was swept out with oxygen-free nitrogen and was then charged with 12 g. of 1-butanethiol and 0.3 g. of di-*t*-butyl peroxide. The bomb was closed, pressure-tested with nitrogen, cooled in a mixture of solid carbon dioxide–methanol, and evacuated to 5 mm. pressure. The bomb was installed behind a heavy barricade, and all operations were controlled from the outside. Acetylene (5 g.) was introduced by allowing the gas under 100–200 lb./sq. in. pressure to flow from a previously calibrated reservoir into the bomb until the pressure drop in the reservoir indicated that the desired quantity of acetylene had been removed. The bomb was then connected to a source of carbon monoxide. The reaction mixture was heated to 122–125° for a period of 2.8 hours during which the gage pressure was maintained at 2450–2950 atm. by injection of carbon monoxide. The bomb was then cooled to room temperature, pressure released, and contents removed. The reaction mixtures from three such runs were combined and distilled. After recovering 12.9 g. of 1-butanethiol, the 3-(*n*-butylthio)-2-propenal fraction distilled at 120° (19 mm.), $n^{25}$D 1.5451 (6.2 g., 17% yield). The disulfide fraction distilled at 149–151° (17 mm.), $n^{25}$D 1.4975 (8.5 g., 32% yield).

**Synthesis of 3-(*n*-Butylthio)-2-propenal at 1000 Atmospheres.**—Somewhat lower yields of the propenal were obtained when the pressure was dropped from 3000 to 1000 atm. Using the procedure described above, 60 g. of 1-butanethiol, 2 g. of 1,1′-azodicyclohexanecarbonitrile and 26 g. of acetylene reacted at a gage pressure of 960–1000 atm. and a temperature of 110° for 14.5 hours. From the composite of three such runs there was obtained 49.1 g. of crude 3-(*n*-butylthio)-2-propenal distilling at 85–152° (23 mm.). Redistillation gave 15.5 g. (5.4% yield) of high-purity propenal distilling at 98° (3 mm.), $n^{25}$D 1.5444. An additional, undetermined amount of product was also present in other fractions of the distillation as judged by infrared spectra and carbonyl tests.

**Characterization of 3-(*n*-Butylthio)-2-propenal.**—*Anal.* Calcd. for $C_7H_{12}OS$: C, 58.4; H, 8.3; S, 22.0; mol. wt., 144; carbonyl, 19.5. Found: C, 58.3; H, 8.3; S, 22.3; mol. wt., 148; carbonyl, 19.6. The infrared spectrum showed aldehyde CH absorption at 3.55 and 3.68 μ, aldehyde carbonyl at 6.0 μ, and conjugated carbon: carbon double bond at 6.4 μ. The ultraviolet spectrum showed a single peak corresponding to $\lambda_{\max}^{\mathrm{CH_3OH}}$ 289 mμ (*E* 19,584). The reddish-brown 2,4-dinitrophenylhydrazone melted at 114° after recrystallization from alcohol and acetone. *Anal.* Calcd. for $C_{13}H_{16}O_4N_4S$: C, 48.0; H, 4.9; N, 17.3; S, 9.9. Found: C, 48.1; H, 4.9; N, 16.9; S, 9.8.

Further proof of structure consisted in an independent synthesis by the method

$$n\text{-}C_4H_9SH + HC{\equiv}C{-}CHO \longrightarrow n\text{-}C_4H_9SCH{=}CH{-}CHO$$

Propiolaldehyde[5] (16.2 g.) was added to 1-butanethiol (27.0 g.) containing 1 ml. of triethylamine at −80°. The reaction was quite vigorous. The distilled product (11 g., 26% yield) was identical in all respects to the 3-(*n*-butylthio)-2-

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(1) W. Reppe, P. B. Report 40837-T, Office of Technical Services, Department of Commerce, Washington, D. C.

(2) H. Bader, L. C. Cross, I. Heilbron and E. R. H. Jones, *J. Chem. Soc.*, 619 (1949); H. Behringer, *Ann.*, **564**, 219 (1949); L. N. Owen and M. U. S. Sultanbawva, *J. Chem. Soc.*, 3109 (1949).

(3) R. E. Foster, A. W. Larchar, R. D. Lipscomb and B. C. McKusick, This Journal, **78**, 5606 (1956).

(4) T. L. Cairns and J. C. Sauer, U. S. Patent 2,776,995 (1957).

(5) F. Wille and L. Saffer, *Ann.*, **568**, 34 (1950).

propenal prepared from acetylene, 1-butanethiol and carbon monoxide.

**3-(Benzylthio)-2-propenal.**—Using the procedure described above, there was charged into the bomb 124 g. of benzylthiol, 2.5 g. of 1,1′-azodicyclohexanecarbonitrile and 26 g. of acetylene. The reaction was carried out at 98–100° for a period of 16.7 hours while maintaining a pressure of 960–1000 atm. by carbon monoxide injection. From a composite of three such runs, there was obtained the desired propenal distilling at 107–112° (1.3 mm.), $n^{25}\text{D}$ 1,6167 (1.6 g., 0.5% yield). There was also isolated by distillation 228.4 g. of the disulfide, b.p. 175–180° (3 mm.) (79.4% yield), and 110 g. of benzylthiol was recovered.

The infrared spectrum of the propenal fraction was similar to that of 3-(*n*-butylthio)-2-propenal and in addition showed aromatic vibrations. *Anal.* Calcd. for $C_{10}H_{10}OS$: C, 67.4; H, 5.6; S, 18.0. Found: C, 69.3; H, 6.6; S, 19.6. A brown dinitrophenylhydrazone melted at 158–160° after recrystallization from acetone. *Anal.* Calcd. for $C_{16}H_{14}N_4O_4S$: C, 53.6; H, 3.9; N, 15.6; S, 8.9. Found; C, 52.8; H, 3.9; N, 15.2; S, 9.0.

**Synthesis of 3-(Phenylthio)-2-propenal.**—Using the procedure described above, 55 g. of benzenethiol, 1 g. of 1,1′-azodicyclohexanecarbonitrile and 26 g. of acetylene were heated at 100° for 16 hours under a pressure of 920–960 atmospheres maintained by carbon monoxide injection. From a composite of three such runs, there was obtained 7 g. of crude 3-(phenylthio)-2-propenal distilling at 65–144° (18–18.5 mm.) with a small flat at 157–158° (18 mm.) (1.5 g.) and 46 g. of the disulfide distilling at 155° (2 mm.) (63% yield). The recovered benzenethiol amounted to 80.1 g.

The elemental analysis of the propenal cut indicated disulfide impurity. *Anal.* Calcd. for $C_9H_8OS$: C, 66.0; H, 4.9; S, 19.6. Found: C, 66.7; H, 5.5; S, 22.4. A chocolate-brown 2,4-dinitrophenylhydrazone melted at 193–194° after recrystallization from toluene. *Anal.* Calcd. for $C_{15}H_{12}O_4N_4S$: C, 52.4; H, 3.5; N, 16.2. Found: C, 52.3; H, 3.9; N, 15.9.

**Synthesis of 1,2-Bis-(*n*-butylthio)-ethane.**—Using the procedure described above, acetylene was injected at 11–16 atm. into 1-butanethiol (100 g.) containing 3 ml. of di-*t*-butyl peroxide during 6.5 hours at 125–135°. After stripping 47.5 g. of unreacted 1-butanethiol from the reaction mixture, the residual liquid was distilled at 68–114° (1 mm.), largely at 111–114° (1 mm.) (42 g.). Redistillation of this fraction gave 38 g. (63% yield) of the disulfide distilling at 121–124° (5 mm.), $n^{25}\text{D}$ 1.4947. The disulfide (2.0 g.) was refluxed with 20 ml. of 30% hydrogen peroxide for one hour. The resulting disulfone was recrystallized from methanol and melted at 177–178°.[6]

In a "control" run (no catalyst), 1-butanethiol (68 g.) was treated with acetylene as described above at 130° for 4.5 hours at a gage pressure of 18 atm. There was recovered 58.5 g. of 1-butanethiol, and there was no evidence for the formation of disulfide.

**Synthesis of 1,2-Bis-(benzylthio)-ethane.**—A mixture of 100 g. of benzylthiol and 1.5 g. of 1,1′-azodicyclohexanecarbonitrile was treated with acetylene as described above for 5.2 hours at 100–112° at a gage pressure of 13–15 atm. From the reaction mixture there was recovered by distillation 53 g. of benzylthiol. The disulfide distilled at 175–183° (2 mm.) and melted at 38°[7] (48.8 g., 94% yield). The disulfone, prepared by oxidation with 30% hydrogen peroxide and purified by recrystallization from acetic acid, appeared to darken and sublime at temperatures slightly higher than 300°.

**Synthesis of 1,2-Bis-(ethylthio)-ethane.**—When a mixture of ethanethiol (42 g.), acetylene (26 g.) and di-*t*-butyl peroxide (2.5 ml.) was heated in the presence of carbon monoxide at a bomb gage pressure of 80–90 atm. and 100–130°, only the disulfide distilling at 112–114° (35 mm.), $n^{25}\text{D}$ 1.5094 (32.0 g., 50% yield), was isolated. *Anal.* Calcd. for $C_6H_{14}S_2$: C, 48.0; H, 9.3; S, 42.6. Found: C, 48.43; H, 9.4; S, 41.3. The disulfone, made by adding the disulfide to 30% hydrogen peroxide, melted at 131–132°.[8] *Anal.* Calcd. for $C_6H_{14}O_4S_2$: S, 29.9. Found: S, 29.9. Thus carbon monoxide at comparatively low pressure does not participate in the acetylene–thiol reaction.

**Acknowledgment.**—The author is pleased to express his gratitude for the valuable suggestions of Dr. T. L. Cairns.

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(6) T. C. Whitner, Jr., and E. E. Reid, THIS JOURNAL, **43**, 638 (1921), gave the boiling point of the disulfide as 129–130° (5 mm.), $n^{20}\text{D}$ 1.4962, and the melting point of the disulfone as 182°.

(7) E. Fromm, H. Benzinger and F. Schafer, *Ann.*, **394**, 327 (1912), report the melting point of the disulfide as 38°; these authors report that the disulfone begins to sublime at 304°.

(8) R. Otto, *J. prakt. Chem.*, [2] **36**, 437 (1887), gives the melting point of 1,2-bis-(ethylthio)-ethane as 136.5°.

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# COMMUNICATIONS TO THE EDITOR

## DIRECT MONOALKYLATION OF STEROIDS AT $C_4$

*Sir:*

It has been reported[1,2] that direct alkylation is unsuitable as a means of preparing 4-alkyl-3-keto-$\Delta^4$-steroids; however, conditions used in this laboratory have given good yields of monoalkylated products.

Testosterone (1.77 g.) in boiling *t*-butyl alcohol (35 ml.) was added to a boiling solution of potassium (0.36 g.) in the same solvent (20 ml.). A solution of methyl iodide (0.87 g.) in *t*-butyl alcohol (100 ml.) was added dropwise over a 2.5-hour period to the stirring and refluxing basic solution. After a further 0.5 hour at reflux the product was isolated. Chromatography on silica gave 3 well separated crystalline peaks. The first eluted with ethyl acetate-benzene (1:19) was identified as 17β-hydroxy-4,4-dimethylandrost-5-en-3-one (Ia) (conversion 9%[3]; m.p. 184-185.5°; $[\alpha]\text{D}$ −5° (*c* 1.04)[4]; infrared 3.03μ, 5.82μ, 6.03μ; calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 79.30, 79.41; H, 10.21, 10.21). The second, 4-methyltestosterone[2] (IIa, conversion 44%) was eluted with ethyl acetate–benzene (1:9) (m.p. 168.5-170.5°; $[\alpha]\text{D}$ +137° (*c* 1.02); $\lambda_{\text{max.}}$ 250 mμ (ε14,200), infrared 2.88μ, 6.04μ, 6.22μ). This material was identical, as shown by a mixture m.p. and comparison of the infrared spectra, with a sample of IIa

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(1) G. D. Meakins and O. R. Rodig, *J. Chem. Soc.*, 4679 (1956).

(2) F. Sondheimer and Y. Mazur, THIS JOURNAL, **79**, 2906 (1957).

(3) Conversions, yields and recoveries are based on weights of crystalline chromatography fractions which contained no more than 10% impurity as shown by physical constants or further purification.

(4) Optical rotations, spectra and analytical data determined by the Analytical Department in charge of Dr. R. T. Dillon. Optical rotations are in chloroform, ultraviolet spectra in methanol and infrared spectra in potassium bromide.