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A novel protocol for the generation of tropothione and its trapping with electron deficient dienophiles

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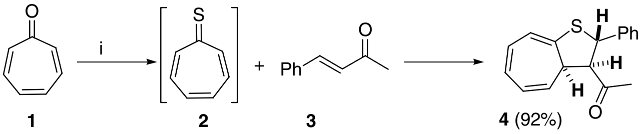
Abstract—Utilization of Lawesson's reagent for the generation of tropothione and novel cycloaddition reactions of the latter with a range of dienophiles are described.

Heptafulvenes and their heteroanalogs constitute an important class of compounds by virtue of their propensity to undergo higher-order cycloadditions.[1] Among the heteroanalogs, tropone is the most noted member which is known to react preferentially as a 6π component in cycloaddition reactions.[2] In contrast to the substantial amount of work involving tropone, its sulfur analog tropothione has received only scant attention, probably due to its inaccessibility and instability.[3] The scattered reports available on the cycloaddition chemistry of tropothione, mainly by Machiguchi et al., reveal it as a very efficient 8π partner in cycloaddition reactions.[4] The reactions with maleic anhydride,[4a,b] dimethyl acetylenedicarboxylate,[4a] cyclopentadiene,[4c] pentafulvenes,[4d] and ketenes[4e,f] are especially noteworthy. In view of this, and in the context of our continued interest in the cycloaddition chemistry of fulvenoid compounds,[5] it was decided to study the reactivity of tropothione in some detail. It was observed that even though Lawesson's reagent is well known as an efficient thionation agent,[6] surprisingly, it has never been employed for the synthesis of tropothione. Thus, we have utilized Lawesson's reagent for the generation of tropothione and the cycloaddition reactions of the latter were carried out with a range of dienophiles. The results of our investigations form the subject matter of this letter.

Our studies were initiated by treating a benzene solution of tropone **1** with Lawesson's reagent under argon at room temperature (Scheme 1). The facile generation of tropothione was inferred by the developing red color of the solution. After 30 min, benzylidene acetone was added and the solution was allowed to stir at room temperature until the red color had disappeared completely. The reaction mixture was filtered to remove the traces of solid material and the solvent was removed under reduced pressure. The crude product was purified by column chromatography to afford **4** as a colorless crystalline solid in a 92% yield.[7]

The structure of **4** was assigned on the basis of spectroscopic data. In the IR spectrum the carbonyl absorption was visible at 1703 cm^{-1}. This was further supported by the presence of the keto carbonyl signal at δ 204.8 in the ^{13}C NMR spectrum. In the ^{1}H NMR spectrum of **4**, the signal due to the methyl group was visible as a singlet at δ 2.06. The sp^{3}–CH on the cycloheptatriene appeared as a multiplet at δ 2.79–2.83. The proton adjacent to the carbonyl group exhibited a doublet of doublets at δ 3.80 and the signal due to the benzylic proton was visible as a doublet ($J = 11.2$ Hz) at δ 5.08. Other ^{1}H and ^{13}C resonance signals assignable to the phenyl and cycloheptatriene moieties were also observed.



Scheme 1. Generation and trapping of tropothione. Reagents and conditions: (i) Lawesson's reagent, benzene, rt.

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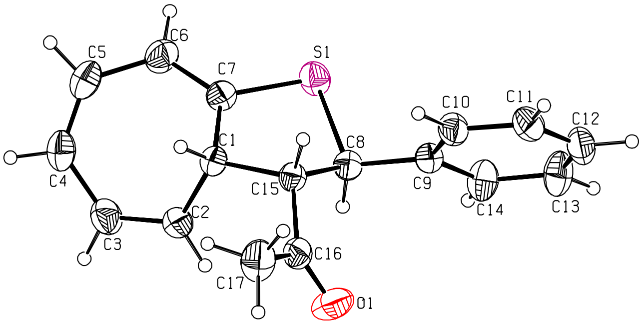
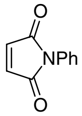
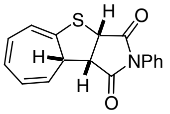
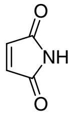
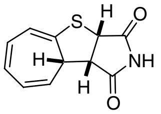
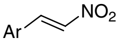
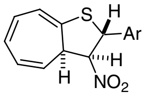
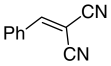
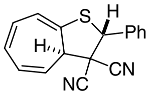
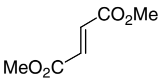
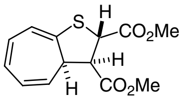
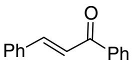
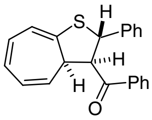
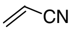
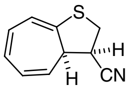
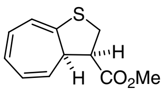


Figure 1. Single crystal X-ray structure of compound **4**.

The structure and stereochemistry of compound **4** was confirmed by single crystal X-ray analysis (Fig. 1).[7]

The reaction was also found to work well with other electron deficient dienophiles; the results are summarized in Table 1. Interestingly, mono-activated alkenes such as chalcones, acrylates, also underwent efficient cycloadditions to the tropothione generated in situ. It may be mentioned that the reported method for the synthesis of tropothione involves the treatment of tropone with tetraphosphorus decasulfide in the presence of excess triethylamine at 0 °C.[3] In the present protocol, there is no need to use a base and the reactions take place at room temperature. Also, Lawesson's reagent being an organic compound, offers better solubility in common organic solvents.

Table 1. Cycloaddition products

Entry	Dienophile	Product	Yield (%)
1			90
2			86
3[a]			47
4			56
5			82
6			76
7			24
8			67

[a] Ar = 4-methoxyphenyl.

In conclusion, we have devised an easy protocol for the generation of tropothione utilizing Lawesson's reagent. It was observed that tropothione thus generated underwent efficient [8+2] cycloadditions to a variety of electron-deficient dienophiles.

Acknowledgments

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7. *General procedure*. Tropone (106 mg, 1 mmol) was taken in 15 mL of dry benzene under argon at room temperature.

To this, Lawesson's reagent (242 mg, 0.6 mmol) was added and the mixture was allowed to stir for 30 min. Benzylidene acetone (175 mg, 1.2 mmol) was added and the solution was stirred overnight at room temperature. The reaction mixture was filtered to remove the small amounts of insoluble material and the solvent was removed under reduced pressure. The residue, on column chromatography, (100–200 mesh silica gel and 90:10 hexane–ethyl acetate solvent mixture) afforded product **4** (247 mg, 92%) as a colorless crystalline solid, which was recrystallized from hot ethanol. Data for compound **4**: mp: 96–98 °C. IR (KBr) $\nu_{\max}$: 3012, 2914, 2832, 1703, 1601, 1363, 1129, 769, 716, 618 cm^{-1}. ^{1}H NMR: δ 2.06 (s, 3H), 2.79–2.83 (m, 1H), 3.80 (dd, 1H, $J_1 = 7.7$ Hz, $J_2 = 11.1$ Hz), 5.08 (d, 1H, $J = 11.2$ Hz), 5.16 (dd, 1H, $J_1 = 5.8$ Hz, $J_2 = 9.2$ Hz), 6.14 (d, 1H, $J = 6.0$ Hz), 6.18–6.25 (m, 1H), 6.47 (dd, 1H, $J_1 = 5.7$ Hz, $J_2 = 10.9$ Hz), 6.67 (dd, 1H, $J_1 = 6.0$ Hz, $J_2 = 10.9$ Hz), 7.25–7.34 (m, 3H), 7.51–7.54 (m, 2H). ^{13}C NMR: δ 30.7, 49.1, 54.5, 65.3, 113.7, 115.8, 126.9, 127.1, 128.1, 128.5, 128.6, 131.9, 134.7, 137.6, 204.8. HRMS (EI): Calcd for $C_{17}H_{16}OS$: 268.0922. Found: 268.1012. X-ray data for compound **4**: Empirical formula, $C_{34}H_{32}O_2S_2$, formula weight = 536.72, monoclinic, space group = $P21/c$, $a = 17.896$ (2), $b = 8.3357$ (11), $c = 19.655$ (3) Å, $\alpha = 90°$, $\beta = 105.445$ (2)°, $\gamma = 90°$, $V = 2826.2$ (6) Å^3, $Z = 4$, $D_{\text{calcd}} = 1.261$ Mg/m^3, $\lambda = 0.71073$ Å, $\mu = 0.218$ cm^{-1}, $F(000) = 1136$, $T = 273$ (2) K, crystal size: $0.24 \times 0.14 \times 0.08$ mm. CCDC 617649 contains the supplementary crystallographic data for this compound.