Direct Lithiation of Chalcogenachromones, -flavones, and -pyranones. The Interconversion and Electrophilic Capture of Ring-Opened and Ring-Closed Anions

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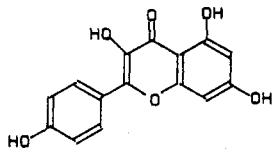
Received July 10, 1987

The metalation of chalcogenapyranones, -chromones, and -flavones with lithium diisopropylamide generates 3-lithio derivatives which interconvert with their ring-opened anions. Through appropriate choices of electrophiles, both ring-opened and ring-closed products can be isolated. 3-Lithiochalcogenapyranones are captured in the ring-closed form by carbon dioxide, benzaldehyde, dimethyl disulfide, diphenyl diselenide, diphenyl ditelluride, and iodine. Ring-opened, acetylenic products are captured with methyl triflate. 3-Lithioflavone and 3-lithiothiaflavone can be methylated with methyl triflate. Chromone, thiachromone, and tellurachromones with hydrogens at both C-2 and C-3 react with 2 equiv of lithium diisopropylamide to give ring-opened heteroatom acetylenide dianions. The addition of MeOD to these dianions gives deuterium incorporation at C-2 and C-3 while the addition of other electrophiles gives addition twice in the ring-opened form. Lithiated flavone, thiaflavone, and 2,6-di-*tert*-butylthiapyranone react with chromium hexacarbonyl followed by methyl triflate to give novel chromium carbene complexes. Lithiated 2,6-di-*tert*-butylselenapyranone loses *tert*-butylacetylenide, which then reacts with chromium hexacarbonyl to give an acetylenic carbene complex.

The chromones, flavones, pyrones, and related compounds are ubiquitous in the plant kingdom from conifers[1] to algae.[2] Many of the naturally occurring chromones and flavones such as kaempferol (**1**)[3] and hormothamnione[2] (**2**) bear a non-hydrogen substituent at C-3. One approach



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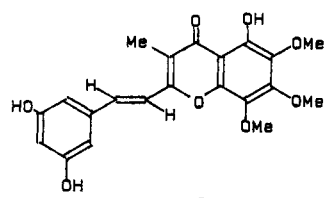

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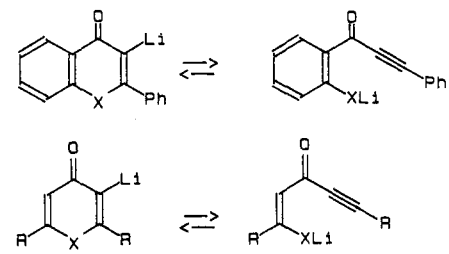
that has successfully introduced substituents to the flavone system has utilized lithiation at C-3 with lithium diisopropylamide (LDA) followed by capture of the anion with an electrophile.[4] Recently, the 3-lithioflavone system has been produced by the base-induced intramolecular cyclization of *o*-hydroxyaryl phenylethynyl ketones.[5] Although only ring-closed products have been reported in the literature for the capture of 3-lithioflavones by electrophiles, an equilibrium should exist between the ring-closed anion and the ring-opened form as depicted in Scheme I where an appropriate choice of electrophile should allow capture of either. Ring-opening has been observed in chromones bearing a 2-carboxyl substituent.[4]

Metalation of the heavier chalcogen analogues of flavone has not been explored, while alkylation of 3-lithioflavone with iodomethane has been unsuccessful.[4] Our interest in the total synthesis of natural and "unnatural" chromone and flavone products requires the metalation and functionalization at C-3 of flavone, chromones, and pyranones

Scheme I



and their S, Se, and Te analogues. Herein, we report our initial studies directed at C-3 functionalization.

Lithiation of Chalcogenachromones and -flavones. The chromones **3**–**6**[6] were each treated with 1 equiv of LDA (both normal and inverse addition) in tetrahydrofuran at −78 °C followed after 15 min with an excess of MeOD. The chromones were recovered by chromatography (SiO_2, 5% EtOAc–CH_2Cl_2) and analyzed by ^1H NMR and mass spectroscopy. Both techniques showed a 1:1 mixture of 2,3-diprotonated and 2,3-dideuteriated chromones for each substrate. The use of 2 equiv of LDA followed by quenching with MeOD gave only the 2,3-dideuteriated chromones.

The lithiation results suggest that the monolithiated species is more acidic than the starting chromone, which might suggest a 2,3-dilithiated chromone (**7**) as an intermediate. Alternatively, ring opening of the lithiated chromone could generate a species more acidic than the chromone.

As shown in Scheme II, ring opening of the 3-lithiated chromones would lead to a terminal acetylene which would be more acidic than the starting chromone. The ring-opened dilithiated materials could be intercepted by the use of suitable electrophiles. Thus, the addition of chlorotrimethylsilane to dilithiated chromone **3** gave **8** in 60% isolated yield while the addition of iodomethane to dilithiated tellurachromone **5** gave **9** in 31% isolated yield. With MeOD, the dilithiated, ring-opened forms would quench initially at the acetylenide anion, followed by cyclization to the ring-closed anion where the second quench

(1) (a) Dean, F. M. *Naturally Occurring Oxygen Ring Compounds*; Butterworths: London, 1963. (b) *Heterocyclic Compounds: Chromenes, Chromanones and Chromones*; Ellis, G. P., Ed.; Wiley: New York, 1977. (c) Swain, T. In *Chemistry and Biochemistry of Plant Pigments*, Goodwin, T. W., Ed.; Academic: London, 1976.

(2) Gerwick, W. H.; Lopez, A.; Van Duyne, G. D.; Clardy, J.; Ortiz, W.; Baez, A. *Tetrahedron Lett.* **1986**, *27*, 1979.

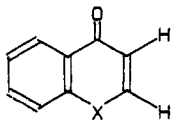
(3) Thiman, K. V. *Plant Physiology*; Steward, F. C., Ed.; Academic: New York, 1972; Vol. ViB.

(4) Costa, A. M. B. S. R. C. S.; Dean, F. M.; Jones, M. A.; Varma, R. S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 799.

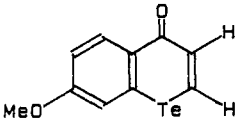
(5) Garcia, H.; Iborra, S.; Primo, J.; Miranda, M. A. *J. Org. Chem.* **1986**, *51*, 4432.

(6) Compounds **5** and **6** were prepared according to: Detty, M. R.; Murray, B. J. *J. Am. Chem. Soc.* **1983**, *105*, 883.

0022-3263/88/1953-1203$01.50/0



3, X=O
4, X=S



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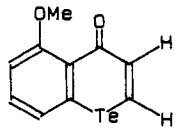

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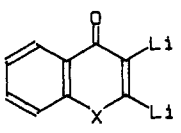

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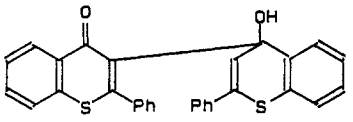

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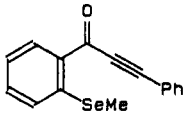
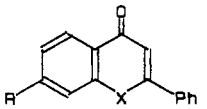


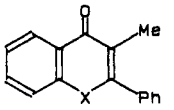
18

would occur at C-3. These results suggest that dianion **7** is not an intermediate in these reactions.

Chromones bearing a carbomethoxy substituent have been observed to give ring-opened products upon treatment with LDA.[4] However, electrophilic capture of either the ring-opened or ring-closed form in these systems has only been observed with proton as the electrophile.

Although alkylation of 3-lithioflavone with iodomethane reportedly fails,[4] the reaction of **10** with 1 equiv of LDA followed by the addition of methyl triflate gave 3-methylflavone (**14**) in 58% isolated yield. Similarly,





10, R = H; X = O
11, R = H; X = S
12, R = H; X = Se
13, R = OMe; X = Te

14, X = O
15, X = S
17, X = Se

thiaflavone (**11**) gave 3-methylthiaflavone (**15**) in 49% isolated yield. No ring-opened products were detected from either system, although **16**, isolated in 25% yield, was produced during the reaction of **11**.

The metalation of selenaflavone (**12**) followed by the addition of methyl triflate gave products from electrophilic capture of both the ring-opened and ring-closed anions. In addition to 3-methylselenaflavone (**17**), which was isolated in 11% yield, the acetylenic ketone **18** was isolated in 2% yield.

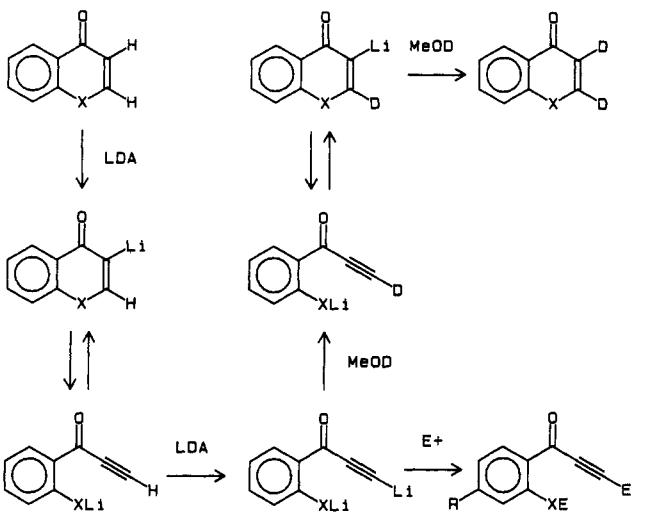
Telluraflavone **13**,[7] following reaction with 1 equiv of LDA and excess methyl triflate, gave unreacted starting material as the only characterized product in about 30% recovered yield. No alkylated materials were isolated or identified.

The ring-opened and ring-closed anions shown in Scheme I appear to interconvert in solution at −78 °C, since products from both anions can be isolated following electrophilic capture. Both the electrophile and the chalcogen atom in the ring influence the products formed.

Lithiation of the Chalcogenapyranones. The 2,6-di-*tert*-butylchalcogenapyranones **19–22**[8] were lithiated

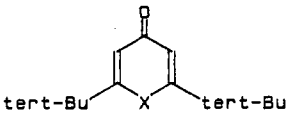
(7) Telluraflavone **13** was prepared according to ref 6.

Scheme II

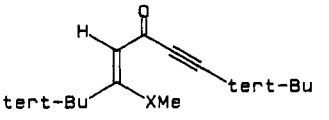


8; R=H, X=O, E=TMS
9; R=OMe, X=Te, E=Me

with 1 equiv of lithium diisopropylamide (LDA) in tetrahydrofuran at −78 °C, and the resulting anions were quenched with methyl triflate. In every case, alkylation products from only the ring-opened anions were isolated (ethers **23–26**) although products from other reaction pathways were isolated as well.

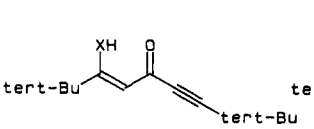


19, X = O
20, X = S
21, X = Se
22, X = Te

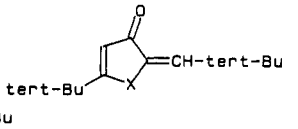


23, X = O
24, X = S
25, X = Se
26, X = Te

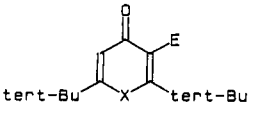
Pyranone **19** gave methyl ether **23** in 79% yield and β-diketone **27** in 16% yield. Upon standing, **27** cyclized to regenerate pyranone **19**, quantitatively.



27, X=O
30, X=S



28, X=S
31, X=Se
34, X=Te



29; X=S, E=SMe
32; X=Se, E=SeMe
33; X=Se, E=SePh
35; X=Te, E=TePh
36; X=S, E=CHOHPh
37; X=Se, E=CHOHPh
38; X=Te, E=CHOHPh
39; X=S, E=COOH
40; X=Se, E=COOH
41; X=Te, E=COOH
42; X=S, E=I

(8) Chalcogenapyranones **19–22** were prepared according to: Detty, M. R.; Hassett, J. W.; Murray, B. J.; Reynolds, G. A. *Tetrahedron* **1985**, *41*, 4853.

Thiapyranone **20** gave, in addition to methylthio ether **24**, which was isolated in 21% yield, two other products. The second product, isolated in 40% yield, was identified as **28**, an isomer of thiapyranone **20**. The third product, isolated in 16% yield, was identified as 3-(methylthio)-thiapyranone **29**.

Compound **29** presumably arises from either the formation, during lithiation, of elemental sulfur, which reacts at C-3 (with the resulting anion methylated by the triflate), or the formation of dimethyl disulfide during the addition of methyl triflate (with thiomethylation of the anion at C-3). The addition of dimethyl disulfide to metalated **20** gave **29** in 91% isolated yield, demonstrating that the ring-closed anion can be captured by an appropriate electrophile.

Compound **28** was formed from lithiated **20** by the addition of methanol. The ratio of **20** to **28** produced was approximately 3:2 by ^{1}H NMR. Protonation of the ring-opened anion would generate **30**. Intermediates similar to **30** are known to cyclize to give mixtures of five- and six-membered-ring products.[9]

Selenapyranone **21**, following lithiation with LDA and anion quench with methyl triflate, gave methylseleno ether **25** in 73% isolated yield and the starting material isomer, **31**, in 15% yield. A third product, isolated in only 2% yield, was identified as **32** on the basis of ^{1}H NMR and field-desorption mass spectroscopy ($C_{14}H_{22}OSe_2$ ion cluster). The addition of diphenyl diselenide to lithiated **21** gave 3-(phenylseleno)selenapyranone **33** in 44% yield, demonstrating electrophilic capture of the ring-closed anion. The spectral properties of **33** were quite similar to those of **32**.

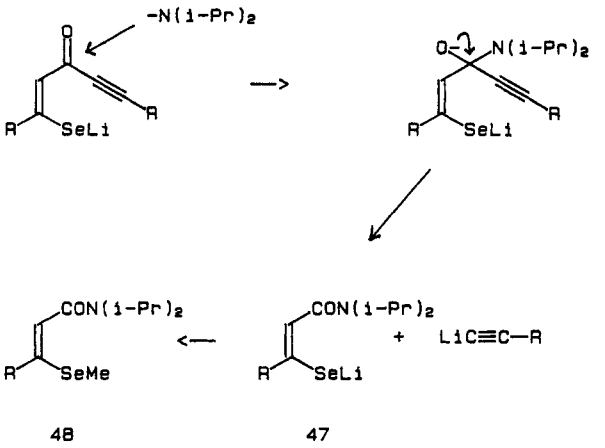
Lithiation of tellurapyranone **22** with LDA, followed by quenching the resulting anion with methyl triflate, gave methyltelluro ether **26** in 93% yield and trace amounts of **34**, an isomer of **22**. The ring-closed form of the anion was captured with diphenyl ditelluride producing **35** in 18% yield.

We were unsuccessful in our attempts to capture the ring-closed anion from pyranone **19** with various electrophiles including dimethyl disulfide, benzaldehyde, CO_2, I_2, and $Cr(CO)_6$. Compound **27** was isolated in good yield from these reactions in addition to recovered **19**.

Other electrophiles, upon addition to metalated pyranones **20–22**, gave ring-closed products. Benzaldehyde gave alcohols **36–38** in 68%, 74%, and 80% isolated yields, respectively. The use of CO_2 as an electrophile gave acids **39** and **40** in 28% and 75% isolated yields, respectively, although these materials could not be obtained analytically pure. None of the carboxylic acid **41** was isolated from metalated **22** although the anion was quite reactive to CO_2. Iodine gave **42** in 18% yield from metalated **20**, while metalated **21** and **22** did not react with iodine under these conditions.

Preparation of Fischer Carbene Complexes of Flavones and Pyranones. We were interested in applying the metalation of both the flavones and the pyranones to the preparation of Fischer carbene complexes. Fischer carbene complexes, prepared from aromatic heterocyclic anions, have been used as important intermediates in several syntheses,[10] while the preparation of carbene complexes from quinone bisketals offers similarities to the chemistry one might expect from the preparation of metal carbenes from metalated flavones and pyranones.[11] The addition of $Cr(CO)_6$ to lithiated flavone (**10**) followed by the addition of methyl triflate gave chromium carbene complex **43** in 74% isolated yield while lithiated thiaflavone (**11**) gave chromium carbene complex **44** in only 1% isolated yield. Lithiated thiapyranone **20** gave chromium carbene complex **45** in 15% isolated yield. Lithiated **21** in the presence of $Cr(CO)_6$ lost *tert*-butylacetylenide, which reacted with $Cr(CO)_6$ and methyl triflate to give chromium carbene complex **46** in 38% yield. Lithiated tellurapyranone **22** did not react with $Cr(CO)_6$ under the same reaction conditions.

Scheme III



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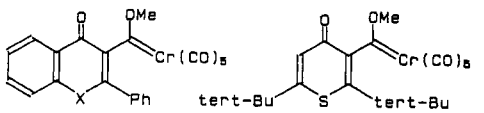
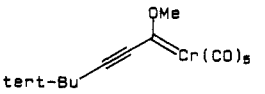


43, X=O
44, X=S

45



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The loss of *tert*-butylacetylenide from lithiated **21** can be rationalized by the addition of LDA to the ring-opened anion of **21** as shown in Scheme III. Collapse of the tetrahedral intermediate would give *tert*-butylacetylenide and amide **47**. Methylation of **47** with methyl triflate would give amide **48**, which was isolated in 30% yield in addition to carbene complex **46**.

The carbene complexes **43–45** are highly functionalized, benchtop-stable complexes that are easily prepared by the chemistry described here. We are currently investigating the chemistry of these and related structures as it applies to the synthesis of natural and unnatural products.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are corrected. ^{1}H NMR spectra were recorded on a GE NMR QE-300 instrument. Infrared spectra were recorded on a Beckman IR 4250 instrument. Solvents were dried over 3A molecular sieves before use. Tetrahydrofuran (THF) was distilled

(9) Tolmachev, A. I.; Kudinova, M. A. *Khim. Geterotsikl. Soedin.* **1966**, 183. Metter, T.; Uchida, A.; Miller, S. I. *Tetrahedron* **1968**, *24*, 4285. Migliorese, K. G.; Miller, S. I. *J. Org. Chem.* **1974**, *39*, 843. Detty, M. R.; Murray, B. J.; Seidler, M. D. *J. Org. Chem.* **1982**, *47*, 1968.

(10) Yamashita, A. *J. Am. Chem. Soc.* **1985**, *107*, 5823. Yamashita, A.; Scahill, T. A.; Chidester, C. G. *Tetrahedron Lett.* **1985**, *26*, 1159. Dötz, K. H.; Dietz, R. *Chem. Ber.* **1978**, *48*, 38.

(11) Dötz, K. H.; Popall, M.; Müller, G.; Ackermann, K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 911.

from benzophenone sodium ketyl prior to use. Microanalyses were obtained with a Perkin-Elmer C, H, and N analyzer.

General Procedures for Metalation of Chromones, Flavones, and Pyranones and Their S, Se, and Te Analogues. One equivalent of *n*-butyllithium was added to 1 equiv of diisopropylamine in dry THF (5 mL/mmol) cooled to −78 °C under an argon atmosphere. The reaction mixture was warmed to 0 °C for 0.5 h and was recooled to −78 °C. The pyranone, chromone, or flavone in tetrahydrofuran (5 mL/mmol) was added dropwise via syringe. The resulting solution was stirred for 1 h before the addition of the electrophile.

Silylation of the Dianion of 3. Preparation of 8. The dianion was generated from **3** as described by using 2 equiv of LDA. The dianion was quenched by the addition of 3 equiv of trimethylsilyl chloride. The reaction mixture was poured into water, and the products were extracted with ether. The combined ether extracts were washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by chromatography on silica gel eluted with dichloromethane to give **8** in 60% yield as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.77 (d, 1 H), 7.51 (t, 1 H), 7.04 (d, 1 H), 6.91 (t, 1 H), 0.28 (s, 9 H), 0.20 (s, 9 H); IR (film) 2160 cm^{-1}.

Preparation of Methyl Telluride 9. The dianion of **5** was prepared with 2 equiv of LDA as described. The dianion was quenched by the addition of 5 equiv of iodomethane. The reaction mixture was diluted with water, and the products were extracted with dichloromethane. The combined organic extracts were dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel eluted with dichloromethane to give **9** in 31% yield: ^{1}H NMR ($CDCl_3$) δ 8.28 (d, 1 H), 7.08 (d, 1 H), 6.83 (d × d, 1 H), 3.88 (s, 3 H), 2.14 (s, 3 H), 1.94 (s, 3 H); IR (film) 2203 cm^{-1}; FDMS, m^+/e 318 ($C_{12}H_{12}O_2{}^{130}Te$).

Preparation of 3-Methylflavones 14, 15, and 17, Flavone Dimer 16, and Methyl Selenide 18. The anions were prepared on a 5-mmol scale as described and were quenched by the slow, dropwise addition of methyl triflate via syringe. When the reaction mixture turned pale yellow, the methyl triflate addition was stopped. The resulting mixture was poured into brine, and the products were extracted with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by chromatography on silica gel eluted with dichloromethane, and the flavones were recrystallized from acetonitrile.

For **14**: 58%; mp 72–75 °C; ^{1}H NMR ($CDCl_3$) δ 8.28 (d, 1 H), 7.7–7.55 (m, 3 H), 7.48 (m, 3 H), 7.40 (d, 1 H), 7.35 (t, 1 H), 2.15 (s, 3 H); IR (KBr) 1635 cm^{-1}; FDMS, m^+/e 236 ($C_{16}H_{12}O_2$). Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.3; H, 5.1. Found: C, 80.9; H, 5.3.

For **15**: 49%; mp 78.5–80.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.57 (d, 1 H), 7.6–7.4 (m, 8 H), 2.13 (s, 3 H); IR (KBr) 1610 cm^{-1}; FDMS, m^+/e 252 ($C_{16}H_{12}OS$). Anal. Calcd for $C_{16}H_{12}OS$: C, 76.2; H, 4.8. Found: C, 76.1; H, 5.0.

For **16**: 25%; oil; ^{1}H NMR ($CDCl_3$) δ 8.51 (d, 1 H, J = 9 Hz), 7.8–7.55 (m, 4 H), 7.45–7.0 (m, 14 H), 5.75 (s, 1 H), 4.75 (br s, 1 H); FDMS, m^+/e 476 ($C_{30}H_{24}O_2S_2$).

For **17**: ^{1}H NMR δ 8.68 (d, 1 H), 7.8–7.0 (m, 8 H), 2.05 (s, 3 H); IR (KBr) 1580 cm^{-1}; FDMS, m^+/e 300 ($C_{16}H_{12}O^{80}Se$).

For **18**: ^{1}H NMR ($CDCl_3$) δ 8.57 (d, 1 H), 7.7–7.0 (m, 8 H), 2.36 (s, 3 H); IR (KBr) 2310, 1595 cm^{-1}; FDMS, m^+/e 300 ($C_{16}H_{12}O^{80}Se$).

Methylation of Lithiated Chalcogenapyranones. The 2,6-di-*tert*-butylchalcogenapyranones **19–22** were lithiated with 1 equiv of LDA in THF at −78 °C as described. The resulting anions were quenched by the addition of 1.2 equiv of methyl triflate, which was added dropwise via syringe. The reaction mixtures were poured into water, and the products were extracted with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated. The residues were purified by chromatography on silica gel eluted with dichloromethane.

For **23**: 79%; oil; ^{1}H NMR ($CDCl_3$) δ 5.80 (s, 1 H), 3.90 (s, 3 H), 1.33 (s, 9 H), 1.15 (s, 9 H); IR (film) 2215, 1670 cm^{-1}; FDMS, m^+/e 222 ($C_{14}H_{22}O_2$). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.6; H, 10.0. Found: C, 75.5; H, 10.1.

For **24**: 21%; oil; ^{1}H NMR δ 6.49 (s, 1 H), 2.36 (s, 3 H), 1.31 (s, 9 H), 1.28 (s, 9 H); IR (film) 2210, 1635 cm^{-1}; FDMS, m^+/e 238 ($C_{14}H_{22}OS$). Anal. Calcd for $C_{14}H_{22}OS$: C, 70.5; H, 9.3. Found: C, 70.5; H, 9.3.

For **25**: 73%; oil; ^{1}H NMR δ 6.62 (s, 1 H), 2.19 (s, 3 H), 1.24 (s, 9 H), 1.22 (s, 9 H); IR (film) 2210, 2190, 1640 cm^{-1}; FDMS, m^+/e 286 ($C_{14}H_{22}O^{80}Se$). Anal. Calcd for $C_{14}H_{22}OSe$: C, 58.9; H, 7.8. Found: C, 58.8; H, 7.9.

For **26**: 93%; oil; ^{1}H NMR δ 7.12 (s, 1 H), 2.14 (s, 3 H), 1.32 (s, 9 H), 1.28 (s, 9 H); IR (film) 2215, 2190, 1640 cm^{-1}; FDMS, m^+/e 336 ($C_{14}H_{22}O^{130}Te$). Anal. Calcd for $C_{14}H_{22}OTe$: C, 50.3; H, 6.6. Found: C, 50.1; H, 6.6.

For **27**: 16%; oil; ^{1}H NMR δ 5.83 (s, 1 H), 1.33 (s, 9 H), 1.26 (s, 9 H); IR (film) 2210, 1590 cm^{-1}; FDMS, m^+/e 208 ($C_{13}H_{20}O_2$).

For **28**: 40%; mp 62–65 °C; ^{1}H NMR δ 7.03 (s, 1 H), 6.13 (s, 1 H), 1.31 (s, 9 H), 1.24 (s, 9 H); IR (KBr) 1670, 1602 cm^{-1}; FDMS, m^+/e 224 ($C_{13}H_{20}OS$). Anal. Calcd for $C_{13}H_{20}OS$: C, 69.6; H, 9.0. Found: C, 69.8; H, 9.1.

For **29**: 16%; mp 120–123 °C; ^{1}H NMR δ 6.97 (s, 1 H), 2.35 (s, 3 H), 1.64 (s, 9 H), 1.37 (s, 9 H); IR (KBr) 1602 cm^{-1}; FDMS, m^+/e 270 ($C_{14}H_{22}OS_2$). Anal. Calcd for $C_{14}H_{22}OS_2$: C, 62.2; H, 8.2; S, 23.7. Found: C, 62.1; H, 7.9; S, 24.1.

For **31**: mp 60–62 °C; ^{1}H NMR δ 7.26 (s, 1 H), 6.41 (s, 1 H), 1.32 (s, 9 H), 1.22 (s, 9 H); IR (KBr) 1663, 1601 cm^{-1}; FDMS, m^+/e 272 ($C_{13}H_{20}O^{80}Se$).

For **32**: ^{1}H NMR ($CDCl_3$) δ 6.99 (s, 1 H), 2.27 (s, 3 H), 1.40 (s, 9 H), 1.22 (s, 9 H); FDMS, m^+/e 366 ($C_{14}H_{22}O^{80}Se_2$).

For **34**: ^{1}H NMR δ 7.55 (s, 1 H), 6.75 (s, 1 H), 1.28 (s, 9 H), 1.17 (s, 9 H); IR (KBr) 1660 cm^{-1}; FDMS, m^+/e 322 ($C_{13}H_{20}O^{130}Te$).

Preparation of Methylthio Adduct 29. Thiapyranone **20** (5 mmol) was lithiated with LDA as described. Dimethyl disulfide (10 mmol) was added via syringe. The reaction mixture was stirred for 30 min at −78 °C following addition. The reaction mixture was poured into water, and the products were extracted with dichloromethane. The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated. The residue was purified by chromatography on silica gel eluted with 5% ethyl acetate–dichloromethane to give a 91% yield of **29**.

For **29**: 91%; mp 120–123 °C; ^{1}H NMR δ 6.97 (s, 1 H), 2.35 (s, 3 H), 1.64 (s, 9 H), 1.37 (s, 9 H); IR (KBr) 1602 cm^{-1}; FDMS, m^+/e 270 ($C_{14}H_{22}OS_2$). Anal. Calcd for $C_{14}H_{22}OS_2$: C, 62.2; H, 8.2; S, 23.7. Found: C, 62.1; H, 7.9; S, 24.1.

Preparation of Phenylseleno Adduct 33. The procedure described for the preparation of **29** was followed with lithiated **21**. The addition of a THF solution of 2 equiv of diphenyl diselenide followed by workup and chromatography gave **33** in 44% isolated yield. For **33**: mp 133–134 °C; ^{1}H NMR δ 7.29–7.17 (m, 5 H), 6.99 (s, 1 H), 1.67 (s, 9 H), 1.35 (s, 9 H); IR (KBr) 1600 cm^{-1}; FDMS, m^+/e 428 ($C_{19}H_{24}O^{80}Se_2$). Anal. Calcd for $C_{19}H_{24}OSe_2$: C, 53.5; H, 5.7. Found: C, 53.5; H, 5.6.

Preparation of Phenyltelluro Adduct 35. The procedure described for the preparation of **29** and **33** was followed with lithiated tellurapyranone **22**. The addition of a THF solution of 2 equiv of diphenyl ditelluride gave **35** in 18% yield. For **35**: mp 110–111 °C; ^{1}H NMR δ 7.74 (d × d, 2 H), 7.22 (m, 3 H), 6.98 (s, 1 H), 1.62 (s, 9 H), 1.29 (s, 9 H); IR (KBr) 1587, 1575 cm^{-1}. Anal. Calcd for $C_{19}H_{24}OTe_2$: C, 43.6; H, 4.6. Found: C, 43.6; H, 4.5.

Preparation of Benzaldehyde Adducts 36–38. Chalcogenapyranones **20–22** were lithiated as described on a 5-mmol scale. Freshly distilled benzaldehyde (0.55 g, 5.2 mmol) in 5 mL of THF was added dropwise at −78 °C. The resulting mixtures were warmed to ambient temperature where stirring was continued for 15 h for **20** and **21** and for 6 h for **22**. The reaction mixtures were poured into 100 mL of water, and the products were extracted with dichloromethane (3 × 50 mL). The combined organic extracts were washed with brine, dried over sodium sulfate, and concentrated. The residues were purified by chromatography on silica gel eluted with 5% ethyl acetate–dichloromethane. The products were recrystallized from hexanes–ether.

For **36**: 68%; mp 135 °C; ^{1}H NMR δ 7.35–7.20 (m, 5 H), 6.88 (s, 1 H), 6.25 (d, 1 H, O*H*), 5.64 (d, 1 H), 1.54 (s, 9 H), 1.38 (s, 9 H); IR (KBr) 3350 (br), 1590, 1550 cm^{-1}; FDMS, m^+/e 330 ($C_{20}H_{26}O_2S$). Anal. Calcd for $C_{20}H_{26}O_2S$: C, 72.7; H, 7.9. Found: C, 72.6; H, 7.8.

For **37**: 74%; mp 163–164 °C; ^{1}H NMR δ 7.31 (m, 5 H), 6.94 (s, 1 H), 6.27 (d, 1 H, O*H*), 5.49 (d, 1 H), 1.56 (s, 9 H), 1.36 (s, 9 H); IR (KBr) 3400 (br), 1595, 1550 cm^{-1}; FDMS, m^+/e 378 ($C_{20}H_{26}O_2{}^{80}Se$). Anal. Calcd for $C_{20}H_{26}O_2Se$: C, 63.7; H, 6.9. Found: C, 64.0; H, 7.1.

For **38**: 80%; mp 178–179 °C; ^{1}H NMR δ 7.27 (m, 5 H), 7.06 (s, 1 H), 6.34 (d, 1 H, O*H*), 5.41 (d, 1 H), 1.55 (s, 9 H), 1.32 (s, 9 H); IR (KBr) 3400 (br), 1595 cm^{-1}; FDMS, m^+/e 428 ($C_{20}H_{26}O_2{}^{130}Te$). Anal. Calcd for $C_{20}H_{26}O_2Te$: C, 56.4; H, 6.2. Found: C, 56.8; H, 6.1.

Preparation of Carboxylic Acid Derivatives 39 and 40. Lithiated **20** and **21** were prepared on a 5-mmol scale as described. Carbon dioxide was bubbled into the reaction mixtures at −78 °C until the color of the reaction mixture faded. The reaction mixtures were poured into 100 mL of 0.1 M NaOH solution. The aqueous layer was extracted with dichloromethane (3 × 25 mL). The aqueous layer was acidified with cold 10% HCl. The acid layer was extracted with dichloromethane (3 × 50 mL). The combined extracts of the acidic layer were washed with brine, dried over sodium sulfate, and concentrated. The oily, white solids were recrystallized from acetonitrile.

For **39**: mp 165 °C dec; ^{1}H NMR δ 8.2 (br s, 1 H), 7.10 (s, 1 H), 1.55 (s, 9 H), 1.39 (s, 9 H); IR (KBr) 3000 (br), 1740, 1607, 1590 cm^{-1}; FDMS, m^+/e 268 ($C_{14}H_{20}O_3S$).

For **40**: mp 165 °C dec; ^{1}H NMR δ 8.96 (br s, 1 H), 7.15 (s, 1 H), 1.52 (s, 9 H), 1.36 (s, 9 H); IR (KBr) 2900 (br), 1730, 1580 cm^{-1}; FDMS, m^+/e 316 ($C_{14}H_{20}O_3{}^{80}Se$) and 360 (dicarboxylic acid, $C_{15}H_{20}O_5{}^{80}Se$). Anal. Calcd for $C_{14}H_{20}O_3Se$: C, 53.3; H, 6.4. Calcd for $C_{15}H_{20}O_5Se$: C, 50.1; H, 5.6. Found: C, 52.7; H, 6.2.

Preparation of Iodothiapyranone 42. Compound **20** was lithiated on a 5-mmol scale as described. Iodine (1.75 g, 6.90 mmol) was dissolved in 10 mL of a 2:1 mixture of hexanes and THF. The resulting solution was added dropwise via syringe to lithiated **20**. The resulting mixture was stirred for 2 h at −78 °C and was then warmed to ambient temperature. The reaction mixture was poured into 150 mL of ether. The resulting mixture was washed with brine, 5% sodium bisulfite solution (2 × 50 mL), and brine, was dried over sodium sulfate, and was concentrated. The residue was purified by chromatography on silica gel eluted with dichloromethane to give 0.20 g (17%) of the iodide.

For **42**: mp 108–111 °C; ^{1}H NMR δ 6.96 (s, 1 H), 1.70 (s, 9 H), 1.39 (s, 9 H). Anal. Calcd for $C_{13}H_{19}IOS$: C, 44.6; H, 5.5. Found: C, 44.7; H, 5.5.

Preparation of Chromium Carbene Complexes 43–46. The lithiated pyranones or flavones were transferred via cannula to a −78 °C slurry of chromium hexacarbonyl (equimolar with pyranone or flavone) in tetrahydrofuran (5 mL/mmol). The resulting mixture was stirred at −78 °C for 1 h, was warmed to −40 °C for 1 h, and was then warmed to 0 °C until the chromium hexacarbonyl was consumed (1–5 h). The reaction mixture was recooled to −78 °C, and a 50% molar excess of methyl triflate was added via syringe. The carbene reactions were concentrated under vacuum at room temperature or below. The residue was dissolved in a minimal amount of dichloromethane. Pentane was then added, precipitating an orange solid. The precipitate was collected and then purified by chromatography on silica gel using 2:1 dichloromethane–pentane as eluent.

For **43**: mp 101–104 °C dec; ^{1}H NMR δ 8.26 (d × d, 1 H), 7.75 (t × d, 1 H), 7.58 (d, 1 H), 7.54 (m, 5 H), 7.46 (t, 1 H), 4.57 (br s, 3 H); IR (KBr) 2060 (sharp), 1950 (br), 1620, 1610, 1550 cm^{-1}; FDMS, m^+/e 456 ($C_{22}H_{12}CrO_8$). Anal. Calcd for $C_{22}H_{12}CrO_8$: C, 57.9; H, 2.7. Found: C, 57.7; H, 3.0.

For **44**: mp 104–107 °C dec; ^{1}H NMR δ 8.58 (d, 1 H), 7.68 (t × d, 1 H), 7.57 (m, 5 H), 7.52 (d, 1 H), 7.44 (t, 1 H), 4.55 (br s, 3 H); IR (KBr) 2030 (sharp), 1990, 1935 (br), 1610, 1590 cm^{-1}; FDMS, m^+/e 472 ($C_{22}H_{12}CrO_7S$).

For **45**: mp 93 °C dec; ^{1}H NMR δ 6.89 (s, 1 H), 4.30 (br s, 3 H), 1.45 (s, 9 H), 1.37 (s, 9 H); IR (KBr) 2030 (sharp), 1990, 1925 (br), 1600 cm^{-1}; FDMS, m^+/e 458 ($C_{20}H_{22}CrO_7S$). Anal. Calcd for $C_{20}H_{22}CrO_7S$: C, 52.4; H, 4.8. Found: C, 52.6; H, 4.9.

For **46**: ^{1}H NMR δ 4.30 (s, 3 H), 1.39 (s, 9 H); IR (KBr) 2160, 2060, 1930 cm^{-1}.

For **48**: ^{1}H NMR ($CDCl_3$) δ 6.39 (s, 1 H), 4.02 (heptet, 1 H, J = 6.8 Hz), 3.46 (heptet, 1 H, J = 6.8 Hz), 2.22 (s, 3 H), 1.44 (d, 6 H, J = 6.8 Hz), 1.19 (s, 9 H), 1.16 (d, 6 H, J = 6.8 Hz); IR (KBr) 2960, 2920, 2865, 1628, 1435, 1328 cm^{-1}; FDMS, m^+/e 305 ($C_{14}H_{27}SeNO$).

Registry No. **3**, 491-38-3; **3** (2,3-dideuterated deriv), 112763-63-0; **4**, 491-39-4; **4** (2,3-dideuterated deriv), 112763-64-1; **5**, 84144-56-9; **5** (2,3-dideuterated deriv), 112763-65-2; **6**, 112763-66-3; **6** (2,3-dideuterated deriv), 112763-67-4; **8**, 112763-68-5; **9**, 112763-69-6; **10**, 525-82-6; **11**, 784-62-3; **12**, 4512-97-4; **13**, 80697-47-8; **14**, 71972-66-2; **15**, 33928-00-6; **16**, 112763-70-9; **17**, 112763-71-0; **18**, 112763-72-1; **19**, 55107-13-6; **20**, 76874-66-3; **21**, 104698-68-2; **22**, 86029-92-7; **23**, 112763-73-2; **24**, 112763-74-3; **25**, 112763-75-4; **26**, 112763-76-5; **27**, 112763-77-6; **28**, 112763-78-7; **29**, 112763-79-8; **30**, 112763-80-1; **31**, 112763-81-2; **32**, 112763-82-3; **33**, 112763-83-4; **34**, 112763-84-5; **35**, 112763-85-6; **36**, 112763-86-7; **37**, 112763-87-8; **38**, 112763-88-9; **39**, 112763-89-0; **40**, 112763-90-3; **42**, 112763-91-4; **43**, 112763-93-6; **44**, 112763-94-7; **45**, 112763-95-8; **46**, 112763-96-9; **48**, 112763-92-5; $Cr(CO)_6$, 13007-92-6.

Trisubstituted (Stannylmethyl)lithium as a Methylene Double Anion Equivalent. Reaction with Esters[1]

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Received August 10, 1987

Trisubstituted (stannylmethyl)lithium reacts with electrophiles as a methylene double anion equivalent to produce enolates from esters. The reaction mechanism is discussed.

Inspired by the established reputation of organosilicon chemistry in the field of organic synthesis,[2] a growing interest in the chemistry of group IV organometal compounds other than silicon has emerged in recent years. Among them, an increasing number of studies have been reported on the application of organotin compounds as a synthetic tool.[3] Generally it has been believed that the silyl and stannyl compounds behave similarly; both metals stabilize the neighboring carbanion due to the participation

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0022-3263/88/1953-1207$01.50/0