1-(Trifluoromethyl)ethenyl Phenyl Selenide and 1-(Trifluoromethyl)ethenyl Phenyl Sulfide

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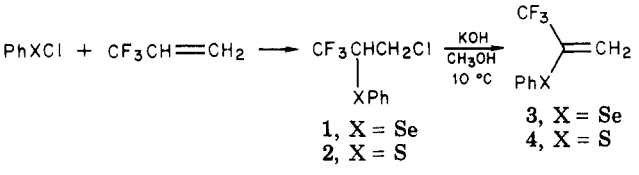
The title compounds were prepared by addition of phenylselenenyl chloride or phenylsulfenyl chloride to 3,3,3-trifluoropropene, followed by elimination of HCl. Both compounds react readily with nucleophiles, giving with ethyl acetoacetate novel 2-fluoro-4*H*-pyran derivatives. The selenium-substituted olefin reacted with *n*-butyllithium at selenium to give phenyl *n*-butyl selenide, while the corresponding sulfur-containing species underwent exclusive attack at the methylene terminus of the olefin.

In a continuation of work[1] on the chemistry of partially fluorinated vinyl selenides,[2] it seems that the previously unknown 1-(trifluoromethyl)ethenyl phenyl selenide (**3**) might have interesting properties. In this paper the synthesis and some reactions of this compound with nucleophiles are described. In addition, the corresponding vinyl sulfide (**4**) has been prepared to compare its chemistry with the selenide derivative.

Results

Phenylselenenyl chloride and phenylsulfenyl chloride reacted cleanly with 3,3,3-trifluoropropene at 60 °C to give the stable adducts **1** and **2**, respectively, in high yield. A



1, X = Se
2, X = S

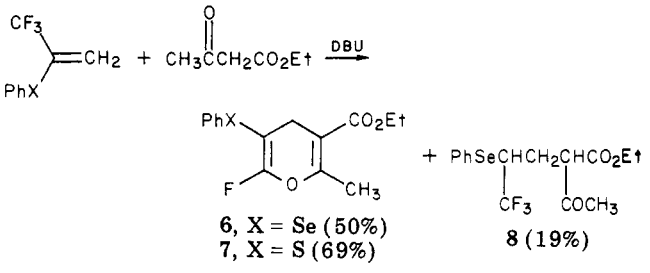
3, X = Se
4, X = S

single regioisomer was formed in both cases. Brief treatment of the adducts with methanolic potassium hydroxide at 10 °C gave the corresponding olefins **3** and **4** as stable distillable liquids.

The first indication that these olefins were reactive toward nucleophiles came when a mixture of **1** and methanolic potassium hydroxide was allowed to warm to room temperature. The major product in this case was the methyl ether **5**, formed by addition of methanol to the

$$\mathbf{1} \xrightarrow[\substack{CH_3OH\\25\ ^\circ C}]{KOH} \underset{\mathbf{5}}{PhSeCH(CF_3)CH_2OCH_3}$$

double bond. This observation suggested the possibility of carbon–carbon bond formation by reaction of **3** or **4** with carbon nucleophiles. Thus, reaction of **3** or **4** with ethyl acetoacetate in refluxing toluene containing DBU as a proton acceptor gave the corresponding 2-fluoro-4*H*-pyran derivatives **6** and **7** as the major products. With the selenium-containing substrate, the primary adduct **8** was also isolated as a minor product. In the sulfur case, the presence of the primary adduct corresponding to **8** was detected by ^{19}F NMR of the crude reaction mixture, but the compound was not isolated in pure form. The selenium-substituted olefin **3** reacted with diethyl malonate to give



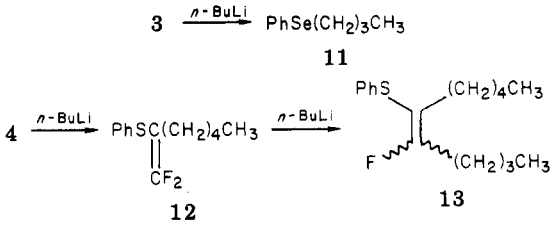
6, X = Se (50%)
7, X = S (69%)

8 (19%)

a mixture of the adduct **9** plus a smaller amount of the difluoro olefin **10**.

$$\mathbf{3} + CH_2(CO_2Et)_2 \xrightarrow{DBU} \underset{\mathbf{9}\ (41\%)}{CF_3CH(SePh)CH_2CH(CO_2Et)_2} + \underset{\mathbf{10}\ (13\%)}{CF_2{=}C(SePh)CH_2CH(CO_2Et)_2}$$

Although **3** and **4** reacted similarly with stabilized carbanion nucleophiles, their behavior on treatment with *n*-butyllithium differed significantly. The selenium-substituted olefin **3** reacted with *n*-butyllithium at −70 °C to give phenyl *n*-butyl selenide (**11**) as the only detectable product. In contrast, the sulfur-substituted olefin **4** re-



11

12

13

acted cleanly at −70 °C with *n*-butyllithium to give the difluoromethylene compound **12** in 79% yield. At somewhat higher temperatures, **12** reacted with additional *n*-butyllithium, giving 5-fluoro-6-(phenylsulfenyl)undec-5-ene (**13**), isolated as about a 1:1 mixture of the *E* and *Z* isomers.

Discussion

The formation of **1** and **2** constitutes an example of the well-known[3] addition of PhSeCl or PhSCl to olefins. The facility of this addition in the present case is somewhat surprising since 3,3,3-trifluoropropene is generally rather unreactive towards electrophilic attack.[4] The formation

(1) A. E. Feiring, *J. Org. Chem.*, preceding paper in this issue.
(2) S. Raucher and G. A. Koolpe, *J. Org. Chem.*, **43**, 4252 (1978); M. Sevrin, W. Dumont, and A. Krief, *Tetrahedron Lett.*, 3835 (1977); *Angew. Chem., Int. Ed. Engl.*, **16**, 541 (1977); M. Sevrin, J. N. Denis, and A. Krief, *Angew. Chem., Int. Ed. Engl.*, **17**, 526 (1978); S. Raucher, *J. Org. Chem.*, **42**, 2950 (1977); T. Kauffmann, R. Joussen, and A. Woltermann, *Angew. Chem., Int. Ed. Engl.*, **16**, 709 (1977); J. V. Comasseto and N. Petragnani, *J. Organomet. Chem.*, **152**, 295 (1978).
(3) E. G. Kataev, T. G. Mannofov, E. A. Berdnikov, and O. A. Komarovskaya, *J. Org. Chem. USSR (Engl. Transl.)*, 1998 (1973); D. Liotta and G. Zima, *Tetrahedron Lett.*, 4977 (1978); D. G. Garrett and G. H. Schmid, *J. Org. Chem.*, **42**, 1776 (1977); W. H. Mueller and P. E. Butler, *J. Am. Chem. Soc.*, **90**, 2075 (1968).
(4) P. C. Myhre and G. D. Andrews, *J. Am. Chem. Soc.*, **92**, 7596 (1970).

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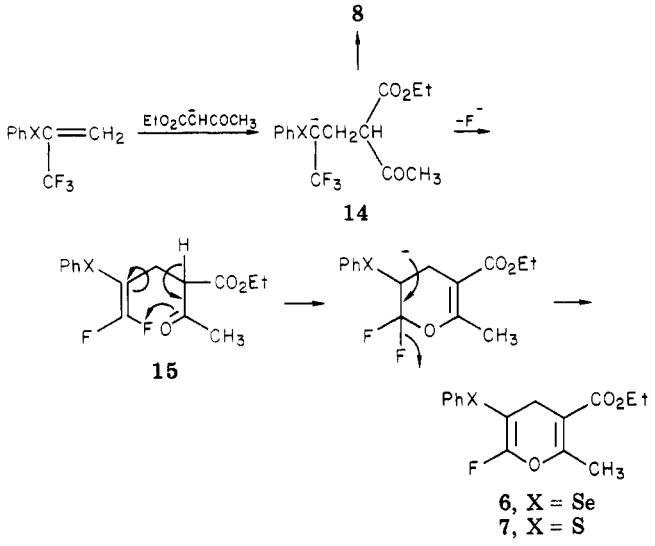
Scheme I



of a single isomer in both cases was apparent from the appearance of a single peak in the ^{19}F NMR spectra of the crude products. A definitive assignment of regiochemistry of these products could not be made solely on the basis of their spectra. However, both gave a single olefin on elimination of HCl. Since the olefin structures could be assigned on the basis of their spectroscopic properties (J_{HH} in the NMR of the olefinic protons was less than 2 Hz) and subsequent chemical transformations, the structures of the initial adducts could be assigned as **1** and **2**.

A mechanism for the formation of the novel 4*H*-pyran derivatives **6** and **7** is shown in Scheme I. Addition of ethyl acetoacetate anion to the starting olefin would give the anion **14** which is stabilized by the adjacent CF_3 and PhX groups. Protonation of this intermediate would give **8**. Alternatively, loss of fluoride ion would generate the difluoromethylene derivative **15** which could undergo ring closure and loss of fluoride ion as shown to give the final products. The formations of **6**, **7**, **8**, **9**, and **10** are apparently the first examples of Michael-type additions by stabilized anions[5a] to vinyl sulfides or selenides although examples with vinyl sulfoxides are known.[5b]

Vinyl selenides can react[2] with alkyllithium reagents by α-deprotonation, by attack at the β position, or by carbon–selenium bond cleavage. In the present case, only the latter two pathways are possible and, in fact, only the carbon–selenium bond cleavage has been observed with **3**. The products with *n*-butyllithium are phenyl *n*-butyl selenide and presumably difluoroallene.[6] The corresponding sulfur compound **4** reacts only by attack at the β position with loss of fluoride ion, giving **12** which can react further with *n*-butyllithium by addition–elimination to give the monofluoro olefin **13**.[7] A distinctive difference in behavior between sulfur and selenium compounds along these lines has been described.[8] Since vinyl sulfides are known[9] to be useful compounds, this process of stepwise addition of alkyllithiums to **4** may have utility in the construction of complex molecules.

Experimental Section

Phenylselenenyl chloride was a commercial sample (Aldrich), used as received. Phenylsulfenyl chloride was prepared as described[10] and used immediately after distillation. 3,3,3-Trifluoropropene was prepared as described[11] or purchased from PCR, Inc.

1-(Trifluoromethyl)-2-chloroethyl Phenyl Selenide (1). A 200-mL Hastelloy pressure vessel was charged with 19.1 g (0.10 mol) of phenylselenenyl chloride and 80 mL of methylene chloride. The vessel was closed, cooled in dry ice/acetone, evacuated, and charged with 15 g (0.16 mol) of 3,3,3-trifluoropropene. The mixture was agitated overnight at 60 °C. The vessel was cooled to room temperature and vented to atmospheric pressure. The vessel contents was concentrated on a rotary evaporator to a dark oil. Distillation through a short-path still gave 27.4 g (95%) of **1**: bp 69–70 °C (0.4 mm); ^1H NMR ($CDCl_3$) δ 3.3–4.0 (3 H, m), 7.1–7.7 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –66.8; exact mass, *m/e* calcd for $C_9H_8ClF_3Se$ 287.9431, found 287.9407.

1-(Trifluoromethyl)-2-chloroethyl Phenyl Sulfide (2). Following the above procedure and using 25 g (0.173 mol) of freshly distilled phenylsulfenyl chloride, 30 g (0.313 mol) of 3,3,3-trifluoropropene, and 75 mL of methylene chloride gave 35.7 g (86%) of **2**: bp 63–65 °C (0.4 mm); ^1H NMR ($CDCl_3$) δ 3.3–4.0 (3 H, m), 7.1–7.7 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –69.0 (d, J = 8 Hz); exact mass, *m/e* calcd for $C_9H_8ClF_3S$ 239.9987, found 239.9982.

1-(Trifluoromethyl)ethenyl Phenyl Selenide (3). A mixture of 6.7 g (0.12 mol) of potassium hydroxide pellets and 150 mL of methanol was stirred until the KOH dissolved. The mixture was cooled in an ice bath to 10 °C. To this vigorously stirred solution was added 17.3 g (0.06 mol) of **1** in one portion. The resulting mixture was stirred for 10 min at 10 °C and then poured into 600 mL of ice water containing 10 mL of concentrated HCl. The aqueous mixture was extracted with methylene chloride (3 × 150 mL). The combined extracts were washed with water, dried ($MgSO_4$), and concentrated on a rotary evaporator to 14.9 g of yellow oil. Distillation through a short-path still gave 14.3 g (95%) of colorless **3**: bp 43–44 °C (0.6 mm); ^1H NMR ($CDCl_3$) δ 5.58 (1 H, m), 6.32 (1 H, m), 7.1–7.7 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –65.6; exact mass, *m/e* calcd for $C_9H_7F_3Se$ 251.9665, found 251.9647.

1-(Trifluoromethyl)ethenyl Phenyl Sulfide (4). Following the above procedure and using 14 g (0.25 mol) of potassium hydroxide pellets, 200 mL of methanol, and 32.5 g (0.135 mol) of **2** gave 24.2 g (88%) of colorless **4**: bp 41–43 °C (0.5 mm); ^1H NMR ($CDCl_3$) δ 5.38 (1 H, m), 5.98 (1 H, m), 7.2–7.6 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –66.4; exact mass, *m/e* calcd for $C_9H_7F_3S$ 204.0220, found 204.0214.

2-Methoxy-1-(trifluoromethyl)ethyl Phenyl Selenide (5). A solution of 11.2 g (0.2 mol) of potassium hydroxide pellets, 80 mL of methanol, and 23 g (0.08 mol) of **1** was stirred for 2 h at room temperature. The mixture was poured into 400 mL of ice water containing 15 mL of concentrated HCl and extracted with methylene chloride (3 × 100 mL). The combined extracts were washed with water, dried ($MgSO_4$), and concentrated on a rotary evaporator to 22 g of yellow oil. The oil was distilled through a 1-ft spinning-band column of Teflon TFE-fluorocarbon resin, giving 0.66 g (3%) of **3**, bp 38–40 °C (0.5 mm), and 14.7 g (65%) of **5**: bp 68–70 °C (0.5 mm); ^1H NMR ($CDCl_3$) δ 3.33 (3 H, s), 3.4–3.9 (3 H, m), 7.1–7.7 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –66.9; exact mass, *m/e* calcd for $C_{10}H_{11}F_3OSe$ 283.9927, found 283.9903.

Reaction of 3 with Ethyl Acetoacetate. A solution of 12.5 g (0.05 mol) of **3**, 19.5 g (0.15 mol) of ethyl acetoacetate, 7.5 g (0.05 mol) of 1,5-diazabicyclo[5.4.0]undec-5-ene, and 100 mL of toluene was refluxed overnight under N_2. The cooled solution was washed with 5% HCl (2 × 100 mL), dried ($MgSO_4$), and concentrated on a rotary evaporator to 27.5 g of dark oil. Short-path distillation gave 4.85 g of unreacted ethyl acetoacetate, bp 38–40 °C (0.6 mm),

(5) (a) Organolithium reagents have been shown to add to vinyl sulfides (W. E. Parham and R. F. Motter, *J. Am. Chem. Soc.*, **81**, 2146 (1959)); (b) G. Tsuchihashi, S. Mitramura, S. Inoue, and K. Ogura, *Tetrahedron Lett.*, 323 (1973); G. A. Koppel and M. D. Kinnick, *J. Chem. Soc., Chem. Commun.*, 473 (1975); T. Hori and T. Oishi, *Tetrahedron Lett.*, 4087 (1979).

(6) The likely first product, 3,3,3-trifluoroisopropenyllithium, is known to decompose above –90 °C to the allene (F. G. Drakesmith, O. J. Steward, and P. Tarrant, *J. Org. Chem.*, **33**, 280 (1968)).

(7) Difluoroketene thioacetals undergo similar addition-elimination processes: K. Tanaka, T. Nakai, and N. Ishikawa, *Chem. Lett.*, 175 (1979).

(8) H. J. Riech, *Acc. Chem. Res.*, **12**, 22 (1979).

(9) S. Murahashi, M. Yamamura, K. Yanagisawa, N. Mita, and K. Kondo, *J. Org. Chem.*, **44**, 2408 (1979); D. Seebach and H. Neumann, *Chem. Ber.*, **107**, 847 (1974), and references contained therein.

(10) D. H. Harpp, B. T. Friedlander, and R. A. Smith, *Synthesis*, 181 (1979).

(11) A. E. Feiring, *J. Fluorine Chem.*, **12**, 471 (1978).

followed by 14.7 g of light yellow oil, bp 150–160 °C (0.6 mm). A 4-g portion of the oil was separated by high-performance LC on silica gel using 40% chloroform in cyclopentane into 2.3 g (50%) of the colorless 4*H*-pyran **6** [^{1}H NMR δ 1.20 (3 H, t), 2.27 (3 H, s), 3.20 (2 H, dq), 4.15 (2 H, q), 7.1–7.7 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –87.5 (t, J_{HF} = 5 Hz); exact mass, *m/e* calcd for $C_{15}H_{15}FO_3Se$ 342.0170, found 342.0169] and 0.96 g (19%) of **8** [^{1}H NMR 1.20 and 1.25 (3 H, 2 t), 1.7–2.9 (m), 2.18 and 2.25 (s) (5 H), 3.1–3.8 (1 H, m), 3.9–4.4 (3 H, m), 7.1–7.7 (5 H, m); ^{19}F NMR δ –68.99 and –69.20 (2 d, J_{HF} = 9 Hz); exact mass, *m/e* calcd for $C_{15}H_{17}F_3O_3Se$ 382.0294, found 382.0311].

Reaction of 4 with Ethyl Acetoacetate. A mixture of 4.08 g (0.02 mol) of **4**, 5.2 g (0.04 mol) of ethyl acetoacetate, 3.04 g (0.02 mol) of DBU, and 30 mL of toluene was refluxed overnight under N_2. After being cooled to room temperature, the solution was washed with 50 mL of 5% HCl and 50 mL of H_2O, dried ($MgSO_4$), and concentrated on a rotary evaporator to 6.7 g of dark liquid. Kugelrohr distillation of the liquid at 0.11 mm gave 5.0 g of faintly yellow liquid which distilled at a pot temperature of 140–150 °C. The oil was chromatographed on 100 g of silica gel packed in petroleum ether and eluted in 50-mL fractions with 5% ether in petroleum ether. Fractions 8–10 contained 4.07 g (69%) of the colorless 4*H*-pyran **7**: ^{1}H NMR ($CDCl_3$) δ 1.20 (3 H, t), 2.30 (3 H, s), 3.13 (2 H, dq), 4.15 (2 H, q), 7.1–7.5 (5 H, m); ^{19}F NMR δ –91.2 (t, J_{HF} = 5 Hz); exact mass, *m/e* calcd for $C_{15}H_{15}FO_3S$ 294.0723, found 294.0721.

Reaction of 3 with Diethyl Malonate. A solution of 10 g (0.04 mol) of **3**, 16 g (0.1 mol) of diethyl malonate, 7.5 g (0.05 mol) of 1,5-diazabicyclo[5.4.0]undec-5-ene, and 100 mL of toluene was refluxed for 1.5 h. The dark solution was concentrated on a rotary evaporator to 21.7 g of oil. Distillation of the oil through a short-path still gave 8.1 g of recovered diethyl malonate, bp 43–45 °C (0.6 mm), followed by 9.94 g of golden liquid, bp 147–159 °C (0.5 mm). A 4-g portion of this liquid was separated by high-performance LC on silica gel using 30% methylene chloride in cyclopentane into 2.6 g (41%) of **9** [^{1}H NMR ($CDCl_3$) δ 1.20 (3 H, t), 1.25 (3 H, t), 2.33 (2 H, m), 3.45 (1 H, m), 4.15 (2 H, q), 4.20 (2 H, q), 3.8–4.4 (1 H, m), 7.1–7.7 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –69.3 (d, J_{HF} = 9 Hz); exact mass, *m/e* calcd for $C_{16}H_{19}F_3O_4Se$ 412.0400, found 412.0384] and 0.84 g (13%) of **10** [^{1}H NMR ($CDCl_3$) δ 1.20 (6 H, t), 2.81 (2 H, dt), 3.77 (1 H, t), 4.13 (4 H, q), 7.1–7.5 (5 H, m); ^{19}F NMR ($CDCl_3$) δ –76.10 (1 F, dt, J_{FF} = 24 Hz), –80.06 (dt); exact mass, *m/e* calcd for $C_{16}H_{18}F_2O_4Se$ 392.0337, found 392.0327].

Reaction of 3 with *n*-Butyllithium. A solution of 5.02 g (0.02 mol) of **3** in 100 mL of ether was cooled under N_2 to –70 °C. A solution of *n*-butyllithium in hexane (1.6 M, 16 mL, 0.025 mol) was added over 10 min. After being stirred for 1 h at –72 °C, the solution was quenched by pouring it into 300 mL of ice water containing 10 mL of concentrated HCl. The ether layer was dried ($MgSO_4$) and concentrated on a rotary evaporator to give 4.15 g of oil. Short-path distillation gave 3.4 g (80%) of phenyl butyl selenide, bp 67–71 °C (0.5 mm).

Reaction of 4 with *n*-Butyllithium. A solution of 120 mL of ether and 40 mL of 1.6 M *n*-butyllithium in hexane (0.064 mol) was cooled to –70 °C. A solution of 8.2 g (0.04 mol) of **4** in 40 mL of ether was added dropwise over 15 min. The resulting colorless solution was stirred for 1 h at –70 °C. The solution was quenched by pouring it into 200 mL of ice water containing 10 mL of concentrated HCl. The ether layer was dried ($MgSO_4$) and concentrated on a rotary evaporator to 10 g of yellow oil. Short-path distillation gave 9.6 g (79%) of **12**: bp 82–85 °C (0.4 mm); ^{1}H NMR ($CDCl_3$) δ 0.70–2.30 (11 H, m), 7.1–7.5 (5 H, m); ^{19}F NMR δ –83.07, –82.15 (AB q, J_{FF} = 27 Hz); exact mass, *m/e* calcd for $C_{13}H_{16}F_2S$ 242.0941, found 242.0928.

Reaction of 12 with *n*-Butyllithium. A solution of 200 mL of ether and 70 mL of 1.6 M *n*-butyllithium in hexane (0.112 mol) was cooled to –70 °C. A solution of 8.4 g (0.035 mol) of **12** in 40 mL of ether was added over 10 min. The resulting colorless solution was stirred for 0.5 h at –70 °C and for 1 h at –40 °C. The solution was quenched by pouring it into 400 mL of ice water containing 20 mL of concentrated HCl. The ether solution was dried ($MgSO_4$) and concentrated on a rotary evaporator to 9.8 g of faintly yellow liquid. Short-path distillation gave 9.44 g (97%) of colorless liquid: bp 127–134 °C (0.6 mm); exact mass, *m/e* calcd for $C_{17}H_{25}FS$ 280.1659, found 280.1661. GLPC analysis of the liquid on a 10 ft × 0.25 in. 10% SE-30 column at 200 °C showed two peaks, A (57%, retention time 15.2 min) and B (43%, retention time 27.2 min). Samples of A and B were obtained by preparative GLPC and identified as (*Z*)-**13** [^{1}H NMR ($CDCl_3$) δ 0.70–2.6 (20 H, m), 7.23 (5 H, s); ^{19}F NMR ($CDCl_3$) δ –92.78 (t, t, J_{HF} = 23 Hz, 3.5 Hz)] and (*E*)-**13** [^{1}H NMR ($CDCl_3$) δ 0.70–2.70 (20 H, m), 7.27 (5 H, s); ^{19}F NMR ($CDCl_3$) δ –90.75 (t, J_{HF} = 23 Hz)].

Registry No. 1, 73194-30-6; **2**, 73194-31-7; **3**, 73194-32-8; **4**, 73194-33-9; **5**, 73194-34-0; **6**, 73194-35-1; **7**, 73194-36-2; **8**, 73194-37-3; **9**, 73194-38-4; **10**, 73194-39-5; 11, 28622-61-9; **12**, 73194-40-8; (*E*)-**13**, 73194-41-9; (*Z*)-**13**, 73194-42-0; phenylselenenyl chloride, 5707-04-0; 3,3,3-trifluoropropene, 677-21-4; phenylsulfenyl chloride, 931-59-9; ethyl acetoacetate, 141-97-9; diethyl malonate, 105-53-3; butyllithium, 109-72-8.

Heterocyclic Systems. 8.[1] Condensation Reactions of 4-Oxo-4*H*-[1]benzopyran-3-carbonitrile

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Condensation reactions of 4-oxo-4*H*-[1]benzopyran-3-carbonitriles (1; X = H, CH_3, Cl, and Br) with 1,2-diamines, acetylglycine, and themselves have been investigated. The compounds **1** on being refluxed with ethylenediamine in ethanol give initially 1,4-addition products that undergo further transformation to 2-amino-3-formylchromones **2** (45–75%) and 1,3,4,5-tetrahydro-2-[(2-hydroxybenzoyl)methylene]imidazoles **3** (7–15%). On the contrary, *o*-phenylenediamine undergoes 1,2-addition to the nitrile functions of compounds **1** to form intermediate amidines, which on further cyclization and subsequent air oxidation afford 6-amino-7-oxo-7*H*-[1]benzopyrano[2,3-*b*]-[1,5]benzodiazepines **12** (22–36%). The nitriles **1** condense with acetylglycine to afford 2-methyl[1]benzopyrano[2,3-*b*]pyridino[3,2-*d*]oxazol-5(5*H*)-ones **15** (47–54%). When refluxed with ammonium acetate in acetic acid, compounds **1** undergo self-condensation, giving 2-(4-oxo-4*H*-[1]benzopyran-3-yl)[1]benzopyrano[3,2-*e*]pyrimidin-5(5*H*)-ones **17** in 13–27% yield. **15** and **17** are also obtained by condensation of **2** with acetylglycine and **1**, respectively.

The condensation reactions of 4-oxo-4*H*-[1]benzopyran-3-carbonitrile (henceforth called chromone-3-nitrile) are little known.[2] In its reaction with sodium azide, it behaves as a simple arylnitrile to form 3-(1*H*-tetrazol-5-

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