Experimental Procedures and Notebook Entries

The following is a description of the information that should be included in experimental procedures describing the synthesis of compounds and a representative experimental procedure. These guidelines are adapted from *Organic Synthesis* and are to be followed in writing notebook entries, quarterly reports, written reports for the advancement to candidacy ("orals"), doctoral dissertations, and experimental procedures for publication. The objective in writing preparative procedures is to provide a "recipe" by which others who are less experienced than yourself (e.g., students with a good laboratory course backgrounds who are just beginning research) could reproduce your synthesis. The following details should be included:

a concise description of the apparatus used.
quantities of reagents and solvents used.
a description of how quickly the key reactants was added.
a description of the times and temperatures used.
a description of how the crude product was isolated an its weight. (Including volumes of solvents/solutions used in workup.)
a description of how the product was purified.
the yield (mass and percent).
a description of the purified material color, phase (oil, solid, etc).
characterization of the material.

3-Methyloxetan-2-one-4-spirocyclohexane (12). A 250-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, rubber septum, and thermometer was charged with 100 mL of THF and diisopropylamine (3.1 mL, 22 mmol), and then cooled in an ice bath while *n*-butyllithium solution (1.67 M in hexanes, 12.4 mL, 20.7 mmol) was added via syringe over 2 min. After 15 min, the ice bath was replaced with a dry ice-acetone bath (-78 °C), and S-phenyl propanethioate **2** (3.340 g, 20.1 mmol) was added dropwise via syringe over 2 min. After 30 min, cyclohexanone (2.085 mL, 20.1 mmol) was added dropwise via syringe over 1 min. The reaction mixture was stirred at -78 °C for 30 minutes and then allowed to warm to 0 °C over 1.5 h. Half-saturated NH_4Cl solution (100 mL) was then added, and the resulting mixture was partitioned between 150 mL of water and 150 mL of diethyl ether. The organic phase was extracted with two 250-mL portions of 10% K_2CO_3 solution, 250 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford 3.095 g of a pale yellow oil. Kugelrohr distillation (oven temperature 50 °C, 0.03 mmHg) followed by low temperature (-78 °C) recrystallization from pentane afforded 2.860 g (92%) of **12** as a low-melting (ca. 25 °C) white solid: IR (film) 2936, 2860, 1816, 1450, 1377, 1364, 1348, 1323, 1286, 1262, 1205, 1186, 1153, 1141, 1108, 1070, 1054, 1019, 966, 957, 907, 877, 846, 837, 800, 773, 688, and 644 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.22 (q, J = 7.7 Hz, 1 H), 1.33-1.95 (m, 10 H), and 1.29 (d, J = 7.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 81.9, 52.3, 37.0, 30.9, 24.6, 22.9, 22.3, and 8.2; Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.20; H, 9.34.

<u>In order that this information can be included in written reports, it must be included in your notebook.</u> In addition to all of the details described above, a good notebook entry should include:

a heading (e.g., an equation)
the date
a table of chemicals and reagents (MW, weight, equivalents, density, volume, and source/sample number)
relevant references to other notebook pages and the published literature
detailed observations
drawings of TLC plates
weights of flasks (in the margin)
^1H NMR and IR spectra of crude products
sample number assigned to product (e.g., JSN-III-38)
spectrum numbers assigned to spectra (e.g., ^1H NMR -III-38A, IR-III-38A)
concise description of spectra (e.g., ^1H NMR shows desired product contaminated with 5% starting material)
conclusions and suggestions for future experiments

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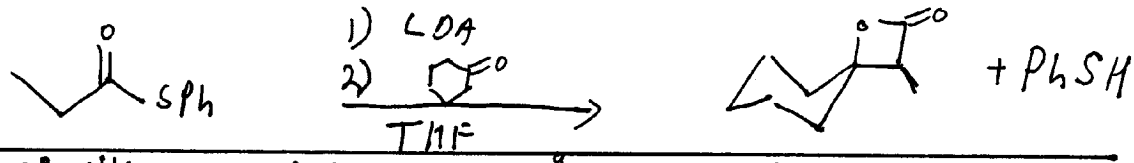
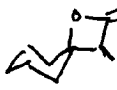
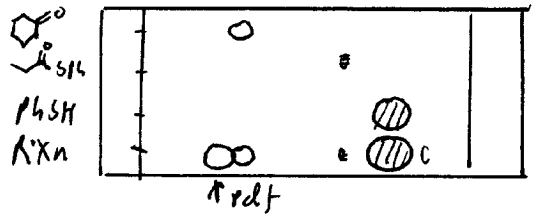


	iPr_2NH	n-BuLi	SPh		THF
MW	101.19	1.67 M	166.24	98.15	
g	2.24		3.340	1.974	
mmol	22.0	20.7	20.1	20.1	
eq	1.10	1.04	1.00	1.00	
d	0.722			0.947	
Vol	3.10 mL	12.4 mL		20.85 mL	100 mL
phase	liquid	soln	liquid	liquid	liquid
mp or bp	84 °C	—	?	155 °C	66 °C
special precaution		PYROPHORIC			
source	Aldrich distilled from CaH_2	Aldrich in Hexanes	J&N-II-175	Aldrich distilled	distilled from Ph_2CO/Na

references	J. Org. Chem 1991, 56, 1176 also Notebook V, pp 176, 177
Objective	To scale up prep of  to 20 mmol scale
6/7/89	A 250-mL, 3N RB fl. s/b equipped with a thermometer, Ar inlet adapter, septum, and stir-bar was charged with 100 mL THF and 3.10 mL iPr_2NH. The fl. s/b was cooled in an ice bath for 5 min. (Thermometer reads 0°C).
	12.4 mL n-BuLi solution was added over the course of 2 min and the fl. s/b was allowed to stir at 0°C for 15 min. Soln colorless
	Fl. s/b cooled in dry ice-acetone bath for 5 min. Temp reads −78°C.
12:05	Thiol ester was added dropwise over 2 min soln is pale yellow.
12:35	cyclohexanone added over 1 min
1:05	Begin slow warming by removing solid dry ice from bath
1:30	~ 50°
1:45	−30° Soln turning darker yellow
2:10	−10°. An aliquot was removed for TLC by inserting capillary through needle inserted through septum.

TLC run (EtOAc-Hexanes, 1:10) and viewed by UV (hashed) and PMA (Circled)



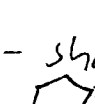
Rxn looks like it's almost done. Shows a little unreacted s.m., the desired pdt, lots of PhSH by product

2:35 0°C Rxn turning darker yellow! Quenched by adding 100 mL of half-satd aq NH_4Cl soln.

Workup: poured into 150 mL Et_2O, extracted with 150 mL H_2O, 2x 250 mL 10% K_2CO_3 soln, 250 mL brine, dried over $MgSO_4$, filtered, concentrated on rotovap to give 3.095 g light yellow oil. JSW-V-275A

42.8803
45.9757
3.0954

Theoretical yield = 0.0201 x 154.21 = 3.10 g

^1H NMR run (300 MHz, $CDCl_3$) - shows  minor impurities, 2 mol%  . ^1H NMR-V-275A

Kugelrohr distillation was performed (50°, 0.03 mm) to afford 2.963 g white low-melting solid + colorless oil

27.9235
25.0639
2.8596

Low temperature recrystallization was performed (-78°C) in a 25 mL pear flask with a septum. Solvent was removed by cannula. (15 mL pentane was used). The crystals were washed with 5 mL pentane (-78°) Crystals dried on vacuum pump to afford 2.8596 g (92%) low melting solid / colorless oil (mp at r.t. ~25°C) JSW-V-275B

2.8596 / 3.10 = 0.922

^1H NMR-V-275B ($CDCl_3$, 300 mHz) - shows one minor impurity (~1.2 mol%) and  (0.4 mol%) Estimated purity of pdt ~ 98%!

IR-V-275B (neat film on NaCl) - Strong band at 1816 cm^{-1}

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27.4326
27.3294
0.1032

Mother liquor stripped to 103.2 mg colorless oil on rotovap. JSW-V-276.
^1H NMR - V - 276. - shows much garbage.
~33 mol %

Conclusion

The scale-up worked! The 92% yield from hexanes + recrystallization is probably more representative than the 95% yield (hexanes only) - pp 177-178. Rxn works great!