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for the Preparation
of Organic Compounds

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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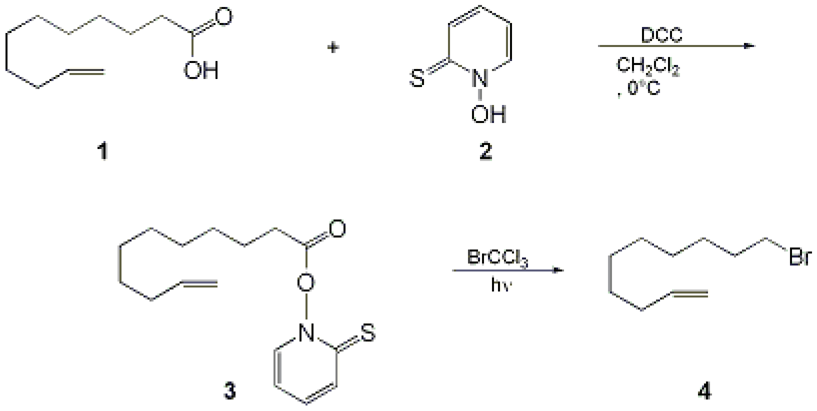
EFFICIENT SYNTHESIS OF BROMIDES FROM CARBOXYLIC ACIDS CONTAINING A SENSITIVE FUNCTIONAL GROUP: DEC-9-ENYL BROMIDE FROM 10-UNDECENOIC ACID

[1-Decene, 10-bromo-]



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Checked by Jessica E. Reed and Robert K. Boeckman, Jr..

1. Procedure

Caution! Barton esters are light sensitive; therefore all procedures should be carried out in the absence of light.

N-(10-Undecenoyloxy)pyridine-2-thione **(3)** . To an oven-dried, one-necked, 250-mL, round-bottomed flask equipped with a nitrogen inlet with gas bubbler, a magnetic stirrer, and a dropping funnel are added 3.61 g (28.4 mmol) of N-hydroxythiopyridone **(2)** (Note 1), 6.20 g (30.0 mmol) of dicyclohexylcarbodiimide (Note 2), and 40 mL of methylene chloride (Note 3). The resulting homogeneous solution is cooled to 0°C and 4.99 g (27.1 mmol) of 10-undecenoic acid **(1)** is added dropwise (Note 4). Following the addition of the undecenoic acid, the ice bath is removed and the reaction mixture is allowed to warm to room temperature and stirred for a further 8 hr. The bright yellow suspension that results is filtered through a bed of silica gel (Note 5). The solvent is removed under reduced pressure to give 8.06 g of the crude Barton ester **(3)** (Note 6) and (Note 7).

Dec-9-enyl bromide **(4)**. To an oven-dried, one-necked, 250-mL, round-bottomed flask equipped with a nitrogen inlet with gas bubbler, magnetic stirrer and a condenser are added 8.06 g (27.1 mmol) of the Barton ester **(3)** , 100 mL of methylene chloride (Note 3), and 3 mL (30.0 mmol) of bromotrichloromethane (Note 8). The reaction mixture is photolyzed with a 250W tungsten lamp under reflux for 30 min (Note 9). The color of the reaction mixture changes from bright yellow to pale yellow. The reaction mixture is cooled to room temperature and the solvent is removed under reduced pressure. The crude product is purified by flash column chromatography (hexanes) until all the bromide **4** (Note 10) is eluted, affording 5.81 g of dec-9-enyl bromide (98%) (Note 11).

2. Notes

1. N-Hydroxythiopyridone is purchased from the Olin Corp. as an aqueous 40% solution of sodium 2-pyridinethiol-1-oxide (sodium omadine). Sodium omadine (1 L) is diluted with water (H_2O, 600 mL) and the solution cooled to 0°C. Hydrochloric acid (350 mL) is added dropwise over a 20-min interval

with continuous stirring and cooling for a further 20 min. The resulting suspension containing N-hydroxythiopyridone is filtered and the solid is washed with H_2O (2 L). The N-hydroxythiopyridone is dried over sodium hydroxide or potassium hydroxide under reduced pressure and recrystallized from ethanol (250-300 mL). The product is finally dried over phosphorus pentoxide and stored at all times in a refrigerator. The checkers employed N-hydroxythiopyridone obtained from Aldrich Chemical Company, Inc.

2. Dicyclohexylcarbodiimide was purchased from the Aldrich Chemical Company, Inc. , and used directly.

3. Dichloromethane is distilled from calcium hydride under argon immediately prior to use.

4. 10-Undecenoic acid was purchased from the Aldrich Chemical Company, Inc. , and used after distillation under reduced pressure (bp 87°C / 2 mm Hg).

5. Using a medium size filter funnel, add enough silica gel to the depth of about 1.5" covered with sand. Prewash the silica gel with methylene chloride (CH_2Cl_2) under suction, discarding the filtrate. Add the reaction mixture and flush with CH_2Cl_2. Dicyclohexylurea remains at the top of the silica gel bed.

6. Spectral data for **3** are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22-1.45 (m, 10 H), 1.75-1.85 (m, 2 H), 1.99-2.06 (ddd, 2 H, J = 7.2, 6.9, 6.6), 2.70 (t, 2 H, J = 7.5) 4.89-5.02 (m, 2 H), 5.75-5.84 (m, 1 H), 6.62 (ddd, 1 H, J = 7.0, 6.5, 1.6), 7.19 (ddd, 1 H, J = 8.8, 7.0, 1.3), 7.53 (dd, 1 H, J = 6.5, 1.3), 7.68 (dd, 1 H, J = 8.8, 1.6) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 24.21, 28.78, 28.86, 28.93, 28.99, 29.13, 31.50, 33.68, 112.46, 114.10, 133.42, 137.36, 137.57, 139.07, 168.99, 175.86 ; IR (film) cm^{-1}: 3074, 1807, 1639, 1608, 1525, 1447, 1410, 1283 .

7. The purity is estimated to be 98% by NMR. Crude material is obtained with a mass balance in excess of theoretical. Minor impurities can be detected by ^{13}C NMR having signals at δ: 24.61, 25.36, and 34.84 which may be due to the presence of a small amount of internal olefin in the 10-undecenoic acid.

8. Bromotrichloromethane was purchased from Aldrich Chemical Company, Inc. , and used as received.

9. The 250W tungsten lamp generates a sufficient amount of heat to reflux the solution. The submitters used a 300W lamp. No other external source is required. The checkers observed the reaction to be complete in less than 30 min, although irradiation was carried out for the specified amount of time.

10. Spectral data for **4** are as follows: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.32-1.46 (m, 10 H), 1.82-1.91 (m, 2 H), 1.96-2.09 (m, 2 H), 3.41 (t, 2 H, J = 6.8), 4.93-5.04 (m, 2 H), 5.81 (m, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.15, 28.71, 28.86, 28.99, 29.27, 32.82, 33.75, 33.82, 114.16, 138.99 ; IR (film) cm^{-1}: 3075, 1640, 1463, 1438, 993, 791 . The purity is estimated to be >98% by NMR.

11. This procedure is also suitable for large scale preparation.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

The procedure described here allows for a convenient and efficient preparation in very high yields of large quantities of bromides from carboxylic acids containing an olefinic functionality. The Hunsdiecker reaction is traditionally accomplished by treating anhydrous silver carboxylates with bromine or iodine .[2] Heavy metal salts such as mercury,[3] lead,[4] and thallium [5] have also been used successfully as well as tert-butyl hypoiodite .[6] The major disadvantages associated with the above methods, such as use of heavy metal salts and non-tolerance towards olefins, has led to the development of a more versatile method using O-acyl thiohydroxamates.[7,8] The O-acyl thiohydroxamates are neither strongly oxidizing nor strongly electrophilic species and have therefore a greater potential within organic synthesis.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

Dec-9-enyl bromide:
1-Decene, 10-bromo- (10); (62871-09-4)

Undecenoic acid:
10-Undecenoic acid (8,9); (112-38-9)

N-(10-Undecenoyloxy)pyridine-2-thione:
2(1H)-Pyridinethione, 1-[(1-oxo-10-undecenyl)oxy]- (12); (114050-28-1)

N-Hydroxythiopyridone:
2(1H)-Pyridinethione, 1-hydroxy- (8,9); (1121-30-8)

Dicyclohexylcarbodiimide: HIGHLY TOXIC.
Carbodiimide, dicyclohexyl- (8);
Cyclohexanamine, N,N'-methanetetraylbis- (9); (538-75-0)

Bromotrichloromethane:
Methane, bromotrichloro (8,9); (75-62-7)