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for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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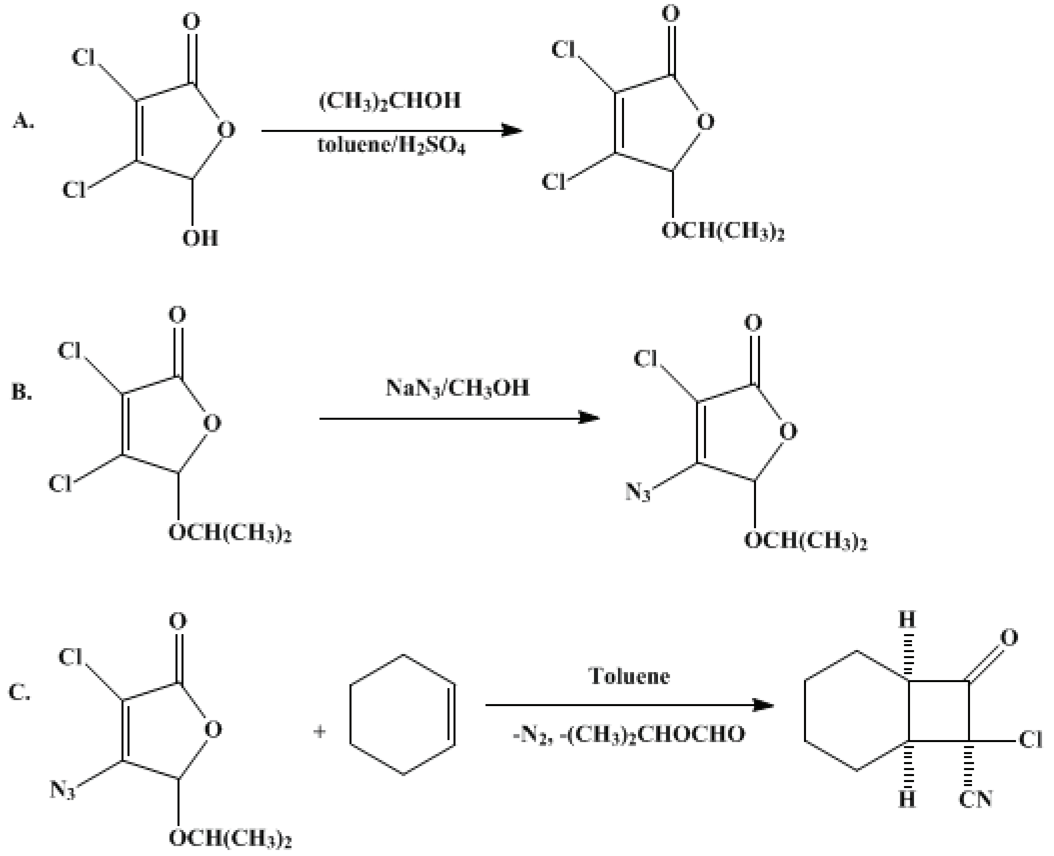
7-CHLORO-7-CYANOBICYCLO[4.2.0]OCTAN-8-ONE

[(Prepared from Chlorocyanoketene) (Bicyclo[4.2.0]octane-7-carbonitrile, 7-chloro-8-oxo-, (1α,6α,7β)-)]



Submitted by Paul L. Fishbein and Harold W. Moore[1].
Checked by Steven Wolff and David L. Coffen.

1. Procedure

A. *3,4-Dichloro-5-isopropoxy-2(5H)-furanone.*[2] A 1-L, round-bottomed flask equipped with a Dean–Stark trap, a condenser, an argon bubbler, and a magnetic stirrer is charged with 50.7 g (0.30 mol) of mucochloric acid (Note 1), 46 mL (0.60 mol) of isopropyl alcohol, 300 mL of toluene, and 20 drops of concentrated sulfuric acid. The mixture is heated to reflux with stirring overnight (~18 hr) with separation of water. The solution is cooled, washed with saturated sodium bicarbonate solution and brine, and dried with magnesium sulfate. After removal of the solvent under reduced pressure, the residue is distilled to give 60.88 g (96%) of the furanone as a clear colorless liquid (bp 90–91°C, 1.5-mm; lit.[2] mp 23–24°C, bp 109–111°C, 6 mm).

B. *7-Chloro-7-cyanobicyclo[4.2.0]octan-8-one.* To a 250-mL Erlenmeyer flask is added 20.0 g (94.8 mmol) of 3,4-dichloro-5-isopropoxy-2(5*H*)-furanone and 120 mL of methanol. The flask is cooled in an ice bath with stirring and 7.5 g (115.4 mmol) of sodium azide is added. The ice bath is removed after 15 min and the mixture is stirred for an additional 50 min. After dilution with 600 mL of water, the reaction mixture is extracted with one 100-mL and two 50-mL portions of toluene. The combined organic layers are washed with water (2 × 100 mL) and with 100 mL of brine and are dried with magnesium sulfate. TLC analysis (1 : 1 ether:hexane, SiO_2) indicates only one component ($R_f = 0.38$) and no remaining dichlorofuranone ($R_f = 0.45$) (Note 3).

A 2-L, three-necked flask fitted with condenser, argon bubbler, thermometer, and addition funnel is charged with 700 mL of toluene (freshly distilled and dried over Linde 4A molecular sieves) and 20 mL (Note 4) of cyclohexene (freshly distilled). With magnetic stirring, the mixture is heated to 105°C and the azidofuranone solution prepared above is added over a period of 20 min (Note 5). On completion, the reaction mixture is heated for an additional 1.25 hr at 105°C. The solution is cooled and concentrated under reduced pressure to yield a yellow-brown residue that is distilled using a short-path apparatus to give 13.3 g (76%) (bp 85–90°C, 0.5 mm) of the cyclobutanone as a very pale-yellow oil that solidifies (mp 34–35°C) on standing at 4°C (Note 6) and (Note 7).

2. Notes

1. Practical-guide mucochloric acid obtained from Aldrich Chemical Company, Inc. (mp 125–128°C) was used. Unless otherwise stated, all reagents and solvents were of commercial grade. The checkers used mucochloric acid obtained from Eastman Organic Chemicals.
2. The spectral properties are as follows: IR (CCl_4) cm^{-1}: 1795, 1652; ^1H NMR ($CDCl_3$) δ: 1.31 (d, 6 H, $J = 6.2$), 4.14 (heptet, 1 H, $J = 6.2$), 5.87 (s, 1 H); MS (EI): 195 (39), 151 (100), 95 (25); MS (Cl): 211 ($M^+ + 1$), 100. Anal. calcd. for $C_7H_8Cl_2O_3$: C, 39.84; H, 3.82. Found: C, 39.55; H, 3.84.
3. The submitters isolated and characterized the azidofuranone as a white crystalline solid after recrystallization from petroleum ether (bp 35–60°C), with mp 51.5–52.5°C. The spectral properties are as follows: IR (CCl_4) cm^{-1}: 2130, 1814, 1664; ^1H NMR ($CDCl_3$) δ: 1.33 (d, 6 H, $J = 6.2$), 4.17 (heptet, 1 H, $J = 6.2$), 5.99 (s, 1 H); MS (EI): 217 (M^+, 6), 158 (34), 119 (28, $C_3ClNO + H_2O$), 101 (77), 73 (100); MS (Cl): 218 ($M^+ + 1$, 55), 120 (10, $C_3HClNO + H_2O$), 102 (100). Anal. calcd. for $C_7H_8ClN_3O_3$: C, 38.64; H, 3.71. Found: C, 38.67; H, 3.65. The azidofuranone decomposes at about 80°C, so caution must be exercised when working with it.
4. If an alkene less volatile than toluene is used, 1.1–1.2 equiv of the alkene are satisfactory.
5. The ketene must be generated in situ since it is exceptionally reactive and will undergo self-condensation if permitted.
6. Recrystallization from petroleum ether (35–60°C) in a dry ice/acetone bath afforded colorless crystals with mp 39.5–40.5°C. The spectral properties are as follows: IR (CCl_4) cm^{-1}: 2340, 1838: ^1H NMR ($CDCl_3$) δ: 1.66 (m, 8 H), 3.03 (m, 1 H), 3.96 (m, 1 H); ^{13}C NMR ($CDCl_3$): 20.72, 21.20, 21.41, 24.25, 36.26, 55.33, 64.17, 115.90, 189.91; MS (EI): 183 (M^+, 6), 148 (46), 119 (13), 109 (33), 81 (100); MS (Cl): 184 ($M^+ + 1$, 84), 156 (100). Anal. calcd. for $C_9H_{10}ClNO$: C, 58.87; H, 5.49. Found: C, 58.58; H, 5.71.
7. Since chlorocyanocyclobutanones are readily hydrolyzed, protic recrystallization solvents and silica gel chromatography should be avoided. Short-path distillation is the method of choice for the purification of most of the cyclobutanones.

3. Discussion

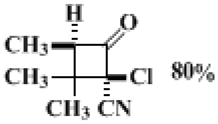
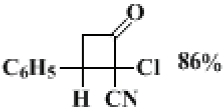
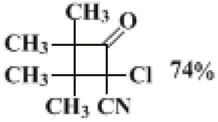
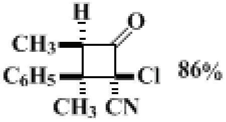
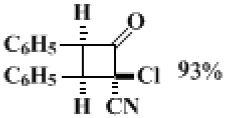
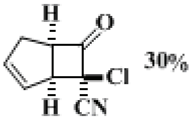
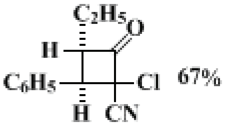
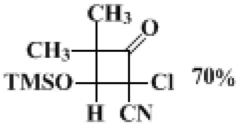
Chlorocyanoketene has been prepared previously by the thermal decomposition of the pseudomethyl ester of the azidofuranone.[3] [4] [5] This azide has been used extensively without complication. However, all azides are capable of detonation. The ratio (C + O/N) has been suggested as a threshold value for detonation, which may occur when this ratio is lower than 3:1.[6] The ratio for the previously used azide is 2.7, while that for the isopropyl analog is 3.3:1.

The synthesis of chlorocyanoketene presented here has advantages over other routes such as dehydrohalogenation of the appropriate acid chloride.[7] The most obvious advantage is that the ketene is generated slowly during thermolysis. Thus, its concentration is always low. In addition, since it is generated by pyrolytic means, the presence of *tert*-amines and/or metals is avoided. No other method for the synthesis of chlorocyanoketene has been reported. However, we have found that it can be prepared with difficulty from chlorocyanoacetyl chloride.

Chlorocyanoacetyl chloride can be made from the extremely hygroscopic acid. It is quite unstable, with 1 g decomposing in 1 hr at room temperature. If a mixture of an imine and triethylamine is treated with the acyl chloride, only a dark tar is obtained. However, if the acyl chloride is first treated with the imine, the reaction allowed to subside, and the mixture then treated with triethylamine, the resulting 2-azetidinone is formed in 63% yield. This is in comparison with the 96% yield obtained by using the azidofuranone.

Other cyclobutanones that can be made with chlorocyanoketene and their respective yields are shown in Table I.

TABLE I
Other Cyclobutanones from Chlorocyanoketene[4c]

	80%
	86%
	74%
	86%
	93%
	30%
	67%
	70%

References and Notes

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

petroleum ether

brine

SiO_2

Bicyclo[4.2.0]octane-7-carbonitrile, 7-chloro-8-oxo-, (1α,6α,7β)-)

sulfuric acid (7664-93-9)

methanol (67-56-1)

ether (60-29-7)

sodium bicarbonate (144-55-8)

Cyclohexene (110-83-8)

toluene (108-88-3)

isopropyl alcohol (67-63-0)

sodium azide (26628-22-8)

magnesium sulfate (7487-88-9)

hexane (110-54-3)

triethylamine (121-44-8)

2-azetidinone (930-21-2)

7-Chloro-7-cyanobicyclo[4.2.0]octan-8-one (89937-15-5)

Chlorocyanoketene

mucochloric acid

azidofuranone

chlorocyanoacetyl chloride

3,4-Dichloro-5-isopropoxy-2(5H)-furanone (29814-12-8)