

Simplified Synthesis for ¹⁴C-Labeling of Aryl Dimethylurea Herbicides

¹⁴C-labeled aryl dimethylurea herbicides can be synthesized directly from aryl isocyanates or aryl

N-carbonylimidazoles and dimethylamine-¹⁴C hydrochloride with high yields and purity.

The transfer of very small amounts of radioactive dimethylamine can be avoided by using a simple method developed to synthesize aryl dimethylurea herbicides (III), such as monuron and fenuron. These compounds are being used to study the structural characteristics in the translocation of systemic pesticides in forest timber. The study is part of an investigation of chemical insecticides being carried out by the Pacific Southwest Forest and Range Experiment Station. In our method, a mixture of the appropriate aryl isocyanate (I) or aryl *N*-carbonylimidazole (II) (Staab and Benz, 1961), dimethylamine-¹⁴C hydrochloride, potassium hydroxide, and methylene chloride were stirred in a water-free environment to form the dimethylurea herbicide in high yield and radiopurity (Figure 1). In most cases, the radioactive yields from aryl isocyanates are 85 to 98%; yields from *N*-carbonylimidazole are slightly lower. The technique generates dimethylamine *in situ*, avoids the transfer of small amounts of radioactive gas, and can be carried out in most laboratories. Because only small amounts of materials are involved, the products can be separated efficiently by preparative thin-layer chromatography.

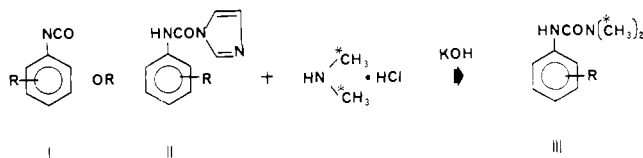


Figure 1. Synthesis of dimethylurea herbicides

Table I. Radioactive Yields and Tlc Characteristics of Four Herbicides Synthesized by Two Methods

Herbicide Synthesized ^a	Method ^b	% Radio-activity Yield	<i>R_f</i> 's Silica gel G Tlc	
			Benzene-Acetone	Benzene-MEK
Monuron	A	92	0.58	0.30
Diuron	A	85	0.67	0.36
Fenuron	A	98	0.52	0.29
Chloroxuron	B	72	0.49	0.26

^a In all cases, authenticity was established by co-chromatography with a known sample in at least two solvent systems, melting point, and infrared spectrophotometry. ^b Methods: A = using aryl isocyanates; B = using *N,N'*-carbonyldiimidazole.

MATERIALS AND METHODS

The synthetic method was developed for the preparation of radiolabeled monuron and the applicability of this method for synthesizing other urea derivatives was tested by using tracer amounts of dimethylamine-¹⁴C hydrochloride for quantitative studies (Table I). Dimethylamine-¹⁴C hydrochloride (49.5 mCi per mmole in 20% ethanol and water) was purchased from New England Nuclear Corp. (Boston, Mass.). Aryl isocyanates and amines were purchased from regular supply houses. Carbonyldiimidazole was purchased from Aldrich Chemical Co. (Milwaukee, Wis.). The normal precautions (*i.e.*, use of fumehood) of working with radioactive materials were taken, although in no case was radioactivity even detected leaking from the vessels.

Method Using Aryl Isocyanates (A). Synthesis of monuron-methyl-¹⁴C. A solution of 256 μ Ci of dimethylamine-¹⁴C hydrochloride was diluted with nonlabeled dimethylamine hydrochloride to yield a solution of a specific activity of 10 mCi per mmole. The solution was freeze-dried in a vacuum. To the dry salt (0.0256 mmole) in the original vessel was added 5 ml of methylene chloride, 50 mg of *p*-chlorophenyl isocyanate, (0.33 mmole) and 0.1 g of potassium hydroxide. The container was closed off with a drying tube of sodalime and the suspension was left standing overnight. Unreacted isocyanate shortly trimerized to insoluble white solid. The supernatant was removed and applied directly to a silica gel G plate for preparative thin-layer chromatography using benzene-acetone (2 to 1). The portion corresponding to monuron-¹⁴C as detected by the autoradiogram was removed and extracted with methylene chloride to give monuron-¹⁴C (236 μ Ci, sp. act. 10 mCi per mmole, 92%

radioactivity yield). Radioactive purity, determined by thin-layer chromatography, resolved with benzene-acetone (2 to 1) benzene-methyl ethyl ketone (2 to 1) solvent system, and measured with a Tracerlab 4 π scanner, was greater than 98% on the basis of peak area measurements. Chemical identity and purity were established by co-chromatography using two solvent systems (above) with a known sample of unlabeled monuron and chromogenic detection with 3% aqueous potassium permanganate and irradiation of sprayed plate with ultraviolet light (Look and White, 1970).

Method Using *N,N'*-Carbonyldiimidazole (B). Under anhydrous conditions, stoichiometric amounts of an arylamine and *N,N'*-carbonyldiimidazole were stirred in methylene chloride solution at room temperature for 1 hr. A tenfold excess of this solution was transferred to a flask holding freeze-dried dimethylamine-¹⁴C hydrochloride. A pellet of potassium hydroxide was added, and the mixture was allowed to sit overnight at room temperature. The workup was identical to that in the first method.

LITERATURE CITED

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