portions) and crystallized from ethanol to give crude **2** (4 g), which was purified by four recrystallizations from benzene: yellow crystals, mp 139–140°; yield 1.6 g (18%); nmr (DMF-d_6) δ 1.15 (t, 6, OCH_2CH_3), 2.38 (s, 3, aromatic CH_3), 3.28 (t, 2, $HNCH_2CH$), 3.6 (m, 4, OCH_2CH_3), 4.65 (t, 1, $HNCH_2CH$), 5.78 (s, 2, $-C(=NH)NH-$), 6.16 (t, 1, $NHCH_2CH$), 7.88 (s, 2, aromatic H); λ_{max} (MeOH) 218 nm (ϵ 21,000), ~240 sh (15,000), 349 (2400).

Anal. Calcd for $C_{14}H_{21}N_5O_6$: C, 47.32; H, 5.96; N, 19.71; O, 27.01. Found: C, 47.12; H. 5.95; N, 19.69; O, 27.14.

The filtrates from the ethanol and benzene crystallizations were combined and evaporated to dryness under vacuum to yield a gummy residue (7 g) which was dissolved in benzene and chromatographed on alumina. Elutions with benzene gave 1.2 g of 3,5-dinitro-4-methoxytoluene, mp 121–123° (lit.[3] mp 123–124°). Further elutions with benzene and benzene–chloroform solutions of increased polarity yielded additional pure **2** (3.8 g, mp 139–140°). Total yield was 5.4 g (61%).

2,6-Dinitro-*N*-(2-imidazolyl)-*p*-toluidine (3). Intermediate **2** (1.4 g, 4 mmol) in concentrated hydrochloric acid (6.5 ml) was heated on a steam bath for 1 hr. The reaction mixture was diluted with water (25 ml), boiled to remove hydrochloric acid, decolorized with charcoal, cooled, and neutralized with ammonium hydroxide. The precipitated red crude **3** was purified by crystallization from ethanol (mp 219–221°, yield 0.4 g, 39%). An additional recrystallization from ethanol gave pure **3**: mp 220–221.5°; nmr (DMF-d_6) δ 2.4 (s, 3, CH_3), 6.67 (s, 2, imidazole H), 8.1 (s, 2, aromatic H); λ_{max} (MeOH) 241 nm (ϵ 17,500), 411 (4000).

Anal. Calcd for $C_{10}H_9N_5O_4$: C, 45.63; H, 3.45; N, 26.61; O, 24.31. Found: C, 45.61; H, 3.45; N, 26.40; O, 24.08.

3,5-Dinitro-4-guanidinotoluene (6). Guanidine hydrochloride (4.8 g, 0.05 mol) was added to a solution of sodium hydroxide (2 g, 0.05 mol) in methanol (50 ml) at 10–12°. The mixture was stirred for 5 min, the precipitated sodium chloride was filtered off, and the methanolic guanidine so obtained was added to a solution of **1** (5.4 g, 0.025 mol) in methanol (150 ml). The reaction mixture was refluxed for 20 hr, cooled, clarified by gravity filtration, and evaporated to dryness under vacuum to give a semisolid dark residue. The residue was stirred in water (100 ml) for 15 min, filtered off, and recrystallized from acetone–methanol. The crude product obtained was refluxed in benzene (100 ml) for 1 hr, filtered off, and recrystallized from methanol to give pure **5**: mp 235–236°; yield 1.1 g (18%); nmr (DMF-d_6) δ 2.37 (s, 3, CH_3), 5.84 (s, 4, $NHC(=NH)NH_2$), 7.84 (s, 2, aromatic H); λ_{max} (MeOH) 216 nm (ϵ 19,000), ~240 sh (~ 15,000), 343 (2500).

Anal. Calcd for $C_8H_9N_5O_4$: C, 40.17; H, 3.79; N, 29.28. Found: C, 40.08; H, 3.84; N, 29.47.

The aforementioned benzene solution was concentrated and cooled to yield 3,5-dinitro-4-methoxytoluene (2.1 g) formed by the concurrent reaction of **1** with the solvent methanol, mp 123° (lit.[3] mp 123–124°).

Reaction of 4-Chloro-3,5-dinitrotoluene with 2-Aminopyrimidine. 2,6-Dinitro-*p*-toluidine (5). A solution of **1** (54.2 g, 0.25 mol) and 2-aminopyrimidine (52.3 g, 0.55 mol) in glycol (125 ml) was stirred at 195–200° for 3 hr, cooled, and filtered. The black solid obtained was dissolved in acetone (500 ml) and filtered from undissolved tar, and the filtrate was brought to dryness under vacuum to yield an orange solid. This solid was purified by crystallization from methylene chloride–ethanol, mp 167–171°, yield 19.4 g (39%). Two additional recrystallizations from chloroform–methanol and benzene gave pure **5**, mp 170–171° (lit.[12] mp 172°). The compound was identified by ir spectrum and mixture melting point with an authentic sample: λ_{max} (MeOH) 224 nm (ϵ 16,000), 252 (7300), 438 (7300).

Anal. Calcd for $C_7H_7N_3O_4$: N, 21.31. Found: N, 21.58.

Registry No.—**1**, 5264-65-3; **2**, 52225-72-6; **3**, 52225-71-5; **5**, 6393-42-6; **6**, 52322-50-6; *N*-(2,2-diethoxyethyl)guanidine sulfate, 52225-73-7; guanidine hydrochloride, 50-01-1; 2-aminopyrimidine, 109-12-6.

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Preparation of *cis*-Methyl α-(Tetrahydro-2-furylidene)acetate

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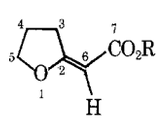
Several methods for the preparation of *trans*-α-(tetrahydro-2-furylidene)acetates **1** have been reported in the literature.[1,2] We wish now to report the successful preparation of the thermodynamically less stable *cis*-methyl α-(tetrahydro-2-furylidene)acetate (**2**) by stereospecific displace-



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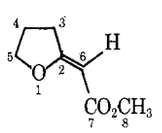

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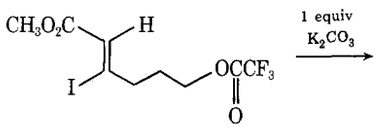
ment of iodide ion in *trans*-methyl 3-iodo-6-hydroxy-2-hexenoate (**4**).

trans-Methyl 3-iodo-6-hydroxy-2-hexenoate (**4**) was obtained by hydrolysis of *trans*-methyl 3-iodo-6-trifluoroacetoxy-2-hexenoate (**3**)[3] with 1 equiv of potassium carbonate in water–methanol–THF (10:1:2). Treatment of **4** with sil-



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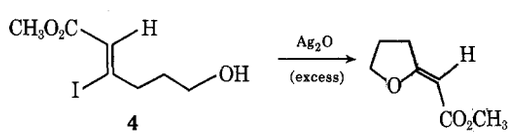

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2

ver oxide (excess) in ethyl ether gave a 1:1 mixture of the cis isomer **2** and the starting alcohol which could be separated by rapid partial distillation at reduced pressure. However, slow distillation at reduced pressure converts the cis isomer quantitatively into the trans isomer (**1**).[4] At room temperature the cis isomer slowly (several days) isomerizes to **1**. This latter isomerization (**2** to **1**) limited the reaction time that could be used for the conversion of iodide **4** to furylidene **2**. The cis isomer (**2**) could be stored for up to 4 months at −10° without detectable changes in structure.

Under more vigorous cyclization conditions the iodo alcohol **4** could be completely converted to a furylidene structure; however, the products thus formed were mixtures of geometric isomers. For example, treatment of **4**

Table I
Spectral Data of *cis*- and *trans*-Methyl α-(Tetrahydro-2-furylidene)acetate

	cis-	*trans*-
Ir, λ_{max} (film)	1702, 1644 cm^{-1}	1701, 1641 cm^{-1}
Pmr, δ_{TMS} (CCl_4)	C-3 H's (2.64, m)	C-3 H's (3.03, m)
	C-4 H's (2.00, m)	C-4 H's (2.02, m)
	C-5 H's (4.30, t, J = 6.5 Hz)	C-5 H's (4.13, t, J = 7 Hz)
	C-6 H (4.64, t, J = 1.2 Hz)	C-6 H (5.11, t, J = 1.5 Hz)
	C-8 H's (3.53, s)	C-8 H's (3.54, s)
Cmr, ppm (TMS, $CDCl_3$)	C-2 (172.26)	C-2 (176.99)
	C-3 (32.18)	C-3 (30.33)
	C-4 (23.28)	C-4 (23.92)
	C-5 (74.42)	C-5 (71.90)
	C-6 (87.79)	C-6 (89.12)
	C-7 (166.41)	C-7 (168.88)
	C-8 (50.62)	C-8 (50.52)

with sodium hydride in THF or sodium methoxide in methanol resulted in the formation of a mixture of cis and trans isomers in ratios of 23:77 and 21:79, respectively. We note also that treatment of the trifluoroacetoxy compound **3** with thallous ethoxide in ethyl ether gave a similar mixture of cis and trans isomers in a ratio of 28:72.

Stereochemical assignments are based on (a) ir, pmr, and cmr data (see Table I), (b) the observed ease of conversion of the cis isomer into the trans isomer, and (c) nmr shift reagent studies using tris(dipivalomethanato)europium(III) or Eu(DPM)$_3$.[1] With Eu(DPM)$_3$ larger deshielding effects were observed for the C-3 hydrogens in the trans isomer **1**, where these allylic hydrogens are close to the carbonyl group, than in the cis isomer **2**, where the corresponding methylene hydrogens are well removed from the carbonyl group.

Experimental Section

Preparation of *trans*-Methyl 3-Iodo-6-hydroxy-2-hexenoate. To a solution of *trans*-methyl 3-iodo-6-trifluoroacetoxy-2-hexenoate (3.66 g, 10 mmol) in 2.5 ml of methanol and 5 ml of tetrahydrofuran was added a solution of potassium carbonate (1.38 g, 10 mmol) in 25 ml of water. The resulting mixture was stirred for 4 hr at room temperature and then extracted with ethyl ether (3 × 25 ml). The combined ether extracts were washed with water (25 ml) and saturated sodium chloride solution and dried (Na_2SO_4). The solvent was removed *in vacuo* to give 2.56 g of a pale yellow oil which was distilled (Kugelrohr oven, 150°, 0.9 mm) to yield 2.48 g (92%) of *trans*-methyl 3-iodo-6-hydroxy-2-hexenoate: λ_{max} (film) 3400, 1720, 1620, 1180 cm^{-1}; pmr δ_{TMS} (CCl_4) 6.37, (s, 1, C-2 H), 3.62 (m, 6, C-6, C-7 H's, OH), 2.80 (m, 2, C-4 H's), 1.78 (m, 2, C-3 H's).

Preparation of *cis*-Methyl α-(Tetrahydro-2-furylidene)acetate. To a suspension of silver oxide (0.765 g, 3.3 mmol) in ethyl ether (10 ml, distilled from sodium) was added *trans*-methyl 3-iodo-6-hydroxy-2-hexenoate (0.81 g, 3 mmol). The mixture was stirred under nitrogen at room temperature overnight and then filtered through a pad of Celite to remove the silver salts. The solvent was removed *in vacuo* to give 0.60 g of a light yellow oil which was a 1:1 mixture of starting material and desired product (determined by nmr). The oil was partially distilled[6] (Kugelrohr oven, 107°, 0.6 mm) and then partially redistilled (Kugelrohr oven, 107° 0.6 mm) to afford a sample of *cis*-methyl α-(tetrahydro-2-furylidene)acetate pure enough for spectral analysis: mass spectrum *m/e* 142 (see Table I for other spectral data).

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Registry No.—**1**, 52196-15-3; **2**, 52196-16-4; **3**, 51755-87-4; **4**, 52259-83-3.

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(5) Similar *trans*-furylidene acetates have been prepared: S. J. Danishefsky, *et al.*, private communication.
(6) Since the starting alcohol has a boiling point slightly higher than that of the desired product, partial distillation increased the percentage of lower boiling component in the mixture (**2**, estimated to be better than 85% pure by pmr).

Dissolving Metal Reductions of Benzylic Esters[1a]

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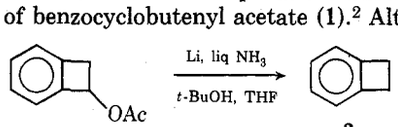
Recently we reported a convenient route to benzocyclobutene (**2**) in which the novel step was the dissolving metal reduction of benzocyclobutenyl acetate (**1**).[2] Although this



1 2

reductive cleavage was patterned after a similar reaction of allylic acetates,[3] the above reaction was to our knowledge its first application to a benzylic system. The benzyl moiety is frequently employed as a protecting or activating group because its subsequent removal can be effected by hydrogenolysis[4] or hydrostannolysis.[5] The latter procedure, however, failed to bring about the conversion of **1** to **2**.[2] In view of such a difference, it seemed desirable to define the scope of this dissolving metal reductive cleavage. In order to investigate the effect of the ester group six benzylic compounds were selected: acetate (**3**), benzoate (**4**), carbamate (**5**), formate (**6**), trifluoroacetate (**7**), and thioacetate (**8**). The choice was based on availability, ease of preparation for new applications, and possible biochemical utility.[6]

Two standardized procedures were developed. Method A involved the addition of a solution of the ester and *tert*-butyl alcohol in tetrahydrofuran (THF) to a solution of lithium in liquid ammonia. Method B involved the addition of lithium to a solution of the ester and *tert*-butyl alcohol in liquid ammonia–THF until the color of the reaction solution persisted blue. In both cases, after a standard work-up, the yield of toluene was determined by quantitative gas–liquid chromatography (glc). Since the conditions used (Li, NH_3, *t*-BuOH) can also reduce aromatic rings, it was necessary to consider product contamination by dihydro and tetrahydro derivatives of toluene. The absence of further reduced products was established by two procedures. A mixture of authentic samples of toluene, 1-methyl-1,4-cyclohexadiene, and 1-methylcyclohexene was cleanly resolved by glc analysis, and peaks corresponding to the latter two compounds were absent in the reaction mixture. Also, the hydrocarbon product from the reduction of benzyl acetate by method A was isolated by preparative glc; its nmr spectrum confirmed the presence of toluene exclusively.

The results are summarized in Table I. Method A was developed using a 20% excess of lithium based on the stoichiometry of 2 equiv of lithium per equivalent of ester. Under these conditions only the reductions of **3**, **5**, and **6** proceeded with preservation of the blue color throughout