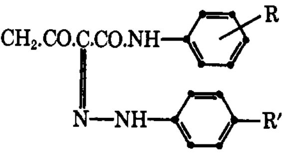
Table IV. α-Arylazo—γ-Iodoacetoacetanilides[a]



	R	R′	Yield, %	Mp,[b] °C	Formula	
VIa	H	H	48	160	$C_{16}H_{14}IN_3O_2$	(407.2)
b	*o*-CH_3	CH_3	55	150	$C_{18}H_{18}IN_3O_2$	(435.2)
c	*p*-CH_3	H	56	169	$C_{17}H_{16}IN_3O_2$	(421.2)
d	*p*-CH_3	CH_3	45	167	$C_{18}H_{18}IN_3O_2$	(435.2)
e	*p*-OCH_3	H	60	185	$C_{17}H_{16}IN_3O_3$	(437.2)
f	*p*-OCH_3	CH_3	55	181	$C_{18}H_{18}IN_3O_3$	(451.2)
g	*p*-Cl	CH_3	50	164	$C_{17}H_{15}ClIN_3O_2$	(455.7)

[a] Elemental analyses (C, H, I) in agreement with theoretical values have been obtained and were submitted for review. [b] Crystallized from acetic acid.

and left overnight. The product that separated was collected and recrystallized from ethanol (9.5 grams), mp 137° dec (see Table I).

2-Aminothiazole—4-Acetic Acid Anilide (IIa). Compound Ia (2.6 grams) and thiourea (0.8 gram; 1 mole) were refluxed in ethanol (ca. 40 ml) for 3 hr. The solution was concentrated, made alkaline with ammonium hydroxide, and evaporated. The residue was collected and crystallized from aqueous methanol (charcoal) to give 1.2 grams (50%) of IIIa, mp 152–4°. Nmr (TFA): O 4.03 (s, 2, CH_2). Found: C, 56.80; H, 4.99; N, 17.73; S, 13.59%. $C_{11}H_{11}N_3OS$ (233.3) required: C, 56.63; H, 4.75; N, 18.01; S, 13.74%.

2-Methylthiazole—4-Acetic Acid Anilide (IIb). Compound Ia (2.6 grams) and thioacetamide (0.8 gram) were refluxed in ethanol (30 ml) for 3 hr, then poured into cold water. The precipitate (1.6 grams; 65%) was collected and crystallized from water, mp 126–7°C. Found: C, 62.03; H, 5.14; N, 11.98; S, 13.69%. $C_{12}H_{12}N_2OS$ (232.3) required C, 62.04; H, 5.20; N, 12.06; S, 13.80%.

Action of Sodium Iodide on γ-Bromoacetoacetanilide—General Procedure. The bromo compound (4 grams) was dissolved in 50 ml of a 10% solution of anhydrous sodium iodide in acetone (or both constituents were separately dissolved in acetone, then mixed) at room temperature. After 1–2 hr, the brown solution was filtered (from sodium bromide) and evaporated. The residue was triturated with water and crystallized from ethanol, mp 127°C (depressed when mixed with α-iodoacetoacetanilide). When its ethanolic solution was treated with ferric chloride, a deep violet color appeared immediately. The γ-iodoacetoacetanilides obtained are listed in Table II.

The ir spectrum of IIIa (KBr) was similar to that of Ia; showing bands at 3290 (NH), 1720 (CO), and 1650 cm^{-1} (CONH)- It was different from that of α-iodoacetoacetanilide, which showed absorption at 1360 (CH_3CO), and 875 cm^{-1} (CH_3) (bands which were absent from the spectra of Ia and IIIa).

The nmr spectrum of IIIa ($CDCl_3$) showed 2-methylene groups at δ 3.85 and 4.02 ppm. In contrast, the nmr spectrum ($CDCl_3$) of α-iodoacetoacetanilide showed a methyl group at δ 2.50 ppm.

Cyclization of γ-Iodoacetoacetanilide (IV). Two grams of IIIa were dissolved in ca. 5 ml of cold concentrated sulfuric acid and left at room temperature for 2–3 hr (heating on the water bath caused decomposition as evidenced by the evolution of violet vapors). The solution was then poured onto ice and the product was collected, washed with water, and crystallized from ethanol as colorless crystals, mp 240°C. Nmr spectrum (TFA): shows a methylene group at δ 4.90 ppm similar to that of 4-bromomethyl-2-quinolone at δ 4.92; and different from 4-methyl-2-quinolone which shows a methyl group at δ 2.97 ppm. Found: C, 42.41; H, 2.87; I, 44.25; N, 4.72%. $C_{10}H_8INO$ (285.1) required: C, 42.13; H, 2.83; I, 44.51; N, 4.91%.

α-Arylazo—γ-Halogenoacetoacetanilides—General Procedure. A cold solution of the appropriate diazonium salt (prepared from 0.01 mole of the aromatic amine dissolved in 5 ml of concentrated HCl and 10 ml of water, and treated with 2 grams of sodium nitrite in 5 ml of water) was added gradually with stirring to 0.01 mole of the γ-halogenoacetoacetanilide in ca. 20 ml of ethanol containing 3 grams of sodium acetate. After complete addition, the mixture was left for 1 hr in the ice bath. The yellow to orange solid that separated was collected, washed thoroughly with water and crystallized from acetic acid (cf. Tables IV).

The nmr spectrum of Va (TFA) showed a methylene group at δ 4.72 ppm in contrast with α-phenylazo-acetoacetanilide which showed ($CDCl_3$), a methyl group at δ 2.55 ppm.

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Synthesis of Cyclobutanone

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Several procedures are available for the preparation of cyclobutanone (*1*, *5*), but all suffer from one or more drawbacks when large quantities (100 grams) of cyclobutanone are desired. Explosive materials (e.g., diazomethane), rigorously dry conditions, large quantities of solvents, expensive reagents, low yields, and lengthy procedures are some of these drawbacks. We describe here the preparation of large quantities of IV relatively free of such limitations.

During the course of other work (*6*), we developed a synthesis which easily produced large quantities (500 grams/run) of

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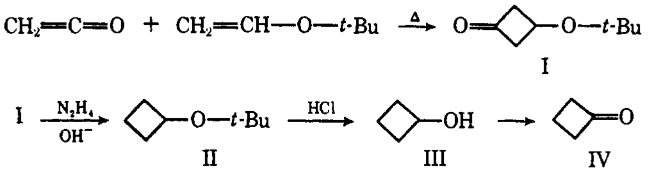
Cyclobutanone was prepared in large quantity in four steps from ketene and *tert*-butyl vinyl ether. The oxidation of cyclobutanol to cyclobutanone was effected in good yield with 1-chlorobenzotriazole.

3-*tert*-butoxycyclobutanone. This was converted to II in 66% yield under standard Wolff-Kishner reduction conditions. Treatment of neat II with gaseous hydrogen chloride at $\leqslant 32°C$ gave III in 94% yield with no rearrangement.



The oxidation of III to IV usually proceeds in low yield and is plagued with rearrangements (*1*). The oxidation of III was effected in 72% yield using 1-chlorobenzotriazole (*3*, *4*). Although we have used up to 1200-gram quantities of this oxidant without incident, a recent letter to the editor (*2*) cautions users about the possibility of spontaneous ignition. Because of this problem, the material is no longer commercially available, and it is advisable to use it immediately after its preparation.

The use of *N*-chlorosuccinimide as the oxidant gave higher boiling materials, presumably chlorinated cyclobutanones. The success of 1-chlorobenzotriazole is probably due to the removal of hydrogen chloride by the benzotriazole reduction product.

EXPERIMENTAL

***t*-Butyl Cyclobutyl Ether** (II). To a solution of 392 grams (7.8 moles) of hydrazine hydrate in 1 liter of diethylene glycol were added 556 grams (3.92 moles) of 3-*t*-butoxycyclobutanone over the period of 1 hr. The temperature of the solution rose to 55°C and when it had dropped to 37°C (3 hr after addition), 454 grams (8.1 moles) of potassium hydroxide were added. The temperature of the mixture rose to 72°C on complete dissolution of the base. Heat was applied to the mixture and the product began to distill at a pot temperature of 105°C and a head temperature of 93°C. Approximately 1 hr after distillation began, the head temperature dropped to 76°C and distillation ceased. More heat was applied until the pot temperature reached 140°C and the head temperature reached 115°C. The lower layer of the distillate was discarded, and the upper layer was washed with water until neutral and then dried. This material was sufficiently pure to be used in the next step. Distillation gave 334 grams (2.6 moles, 66%) of II, bp 62°C/95 mm, $\eta^{25}D$ 1.4141; ir (neat) 3.34, 3.38, 3.45, 7.19, 7.34, 8.76 μ; nmr (neat) δ 4.02 (m, 1H, methine), 1.3–2.3 (m, 6H, CH_2), 1.10 (s, 9H, CH_3). *Anal.* Calcd for $C_8H_{16}O$: C, 74.95; H, 12.58. Found: C, 74.51, 74.54; H, 12.28· 12.49.

Cyclobutanol (III). *t*-Butyl cyclobutyl ether (316 grams, 2.46 moles) was cooled to 15°C, and dry hydrogen chloride was bubbled through the material for about 0.75 hr. The ice bath was removed, and the solution temperature rose to 32°C (higher temperatures resulted in rearrangement). This temperature was self-maintained while more hydrogen chloride was added, and after 4 hr conversion was complete by gas-liquid partition chromatography (glpc). The *t*-butyl chloride was removed at 25 mm for 4 hr at 25°C. Solid sodium bicarbonate (70 grams) was added in portions until carbon dioxide was no longer evolved, and salts were filtered oft and placed in a desiccator. The filtrate was vaporized at 25°/0.25 mm into a cold trap (−78°C) through a column (20 × 4 cm) of 3A moleculer Sieves (Linde, $^1/_{16}$-in. pellets). The desiccator containing the salts was subjected to 0.25 mm, and additional product was collected in the same trap. The crude III was sufficiently pure to be used in the next step. A total of 166 grams (2.3 moles, 94%) of III was obtained, bp 60°C/50 mm, $\eta^{25}D$ 1.4339; ir (neat) 3.02, 3.36, 3.41, 9 μ; nmr (CCl_4) δ 5.25 (s, 1H, OH), 4.18 (m, 1H, methine), 1.2–2.5 (m, 6H, CH_2). *Anal.* Calcd for C_4H_8O: C, 66.63; H, 11.19. Found: C, 66.70; H, 11.39

Cyclobutanone (IV). A solution of 144 grams (2 moles) of cyclobutanol in 600 ml of *o*-dichlorobenzene was held at 25–30°C while 307 grams (2 moles) of 1-chlorobenzotriazole were added in teaspoonful portions over 2.5 hr. The yellow color produced on addition of the oxidant was allowed to disappear before more reagent was added. The salts were filtered off and put into a vacuum desiccator. The filtrate was refluxed for 4 hr (40°C head, 63°C pot, ~0.1 mm) in a spinning-band column with a closed takeoff. The cyclobutanone vaporized through the condenser and condensed in a cold trap (−78°C). The desiccator containing the salts was subjected to 0.1-mm pressure overnight, and additional product was collected in the same cold trap. About 15 grams of powdered calcium carbonate were added to the crude cyclobutanone to remove last traces of hydrogen chloride. The mixture was refluxed (head 40°C, pot 63°C, ~0.1 mm) for 2 hr in a spinning-band column with a closed takeoff. The cyclobutanone vaporized through the condenser and two drying towers (22 × 2.5 cm) filled with 3A Molecular Sieves (Linde, $^1/_{16}$-in. pellets) and condensed in a cold trap (−78°C). The volatiles were redistilled to give 101 grams (1.44 moles, 72%) of IV, bp 98°C/1 atm, $\eta^{25}D$ 1.4185; ir (neat) 5.59 μ; nmr (neat) δ 3.03 (m, 4H, α-H), 1.95 (m, 2H, β-H). The spectral data were compared with those of authentic material.

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