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Metal Substituted Diazo Esters as Substrates for Cross Coupling Reactions

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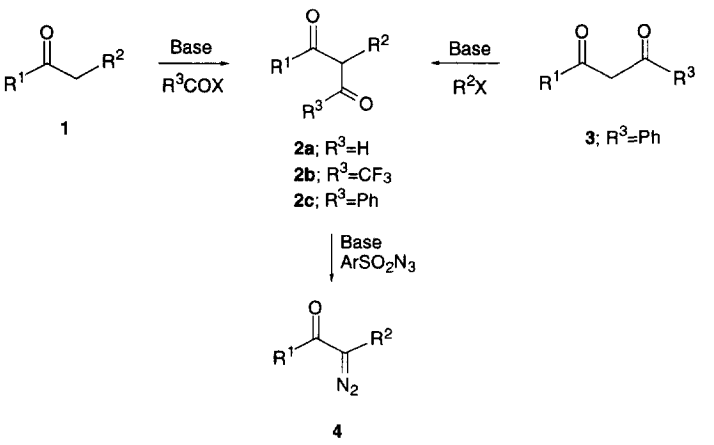
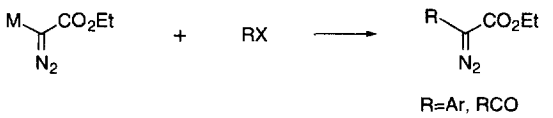
Abstract: Ethyl (trialkylstannyl)diazoacetates have been employed as substrates in the Stille reaction. The palladium(0)-catalyzed cross coupling works well with aryl iodides but not with acyl or aryl chlorides. *Bis*-[ethoxycarbonyl-diazomethyl]-mercury showed high reactivity toward bromoacetyl bromide furnishing ethyl 4-bromo-2-diazo-3-oxo-butanoate in excellent yield. This compound was used in substitution reactions with a variety of nucleophiles. The base-promoted reaction of ethyl 4-azido-2-diazo-3-oxo-butanoate with both acetaldehyde and benzaldehyde proceeded in high yield to produce mixed aldol products. The use of an equivalent amount of DABCO was found to be the best way to promote the reaction. The diastereoselectivity exhibited in the reaction is low and characteristic of condensations of α-substituted ketones with substituents other than alkyl groups at the α-position. Similar consequences were found for the reaction of ethyl 2-diazo-3-oxo-4-phenyl-butanoate with acetaldehyde and benzaldehyde.

α-Diazo carbonyl compounds are widely used in organic synthesis for the preparation of heterocyclic and carbocyclic rings.[1-13] The Arndt-Eistert sequence employs the Wolff rearrangement of an α-diazo ketone to a ketene in the one-carbon homologation of carboxylic acids.[14] Ring contraction of cyclic diazo ketones represents a general method for the preparation of highly strained small-ring compounds.[15] α-Diazo carbonyl compounds also form metallocarbenoid intermediates when exposed to various metal complexes or salts.[1,3,4,11,12,16] The high synthetic versatility of these compounds has brought diazo transfer reagents into wide usage as the most convenient method for achieving preparative diazotization.[17,18] The diazo transfer reaction, which proceeds best with azido sulfonyl compounds,[19] is quite general, but is limited by the requirement that the methylene hydrogens of the substrate be sufficiently acidic.[17] Direct diazo transfer to ketone enolates is very difficult to carry out.[20,21] Instead, an indirect deformylation strategy in which the ketone is first formylated and then treated with a sulfonyl azide reagent is often used.[22-24] Danheiser and coworkers have also utilized α-trifluoroacetyl derivatives **2b** to activate simple ketones toward the diazo transfer reaction with great success (Scheme I).[25] More recently, Taber developed an alternative method for the regioselective construction of α-diazoketones based on the acylation of benzoylacetone **3** followed by selective debenzoylation to provide the desired unsymmetrical α-diazoketone **4**.[26]

Although α-diazo esters are also extremely valuable intermediates for organic synthesis,[18,27] very few procedures for diazo transfer to the α-methylene position of an ester have been developed. Formylation of esters does not lead to successful diazo transfer,[28,29] although Taber has reported that benzoylation followed by reaction with *p*-nitrobenzenesulfonyl azide (*p*-NBSA) in the presence of DBU works well in certain cases.[28]



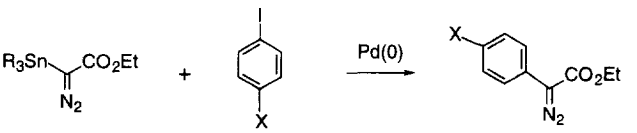
In this paper we wish to describe an alternative procedure for the preparation of a wide assortment of α-diazo esters which is based on the reaction of metalated α-diazo esters[30] with aryl and acyl halides, as depicted below.



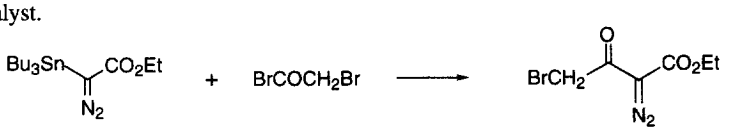
Results and Discussion

Commercially available ethyl diazoacetate (EDA) is readily lithiated at low temperature.[31] Using a related metallation reaction, ethyl tri-*n*-butylstannyl (**5**) and trimethylstannyl diazoacetate (**6**) were prepared from EDA and the respective (dialkylamino)trialkylstannanes.[32,33] The palladium-catalyzed coupling of unsaturated halides or triflates with organometallic reagents (the Stille reaction) has evolved as a powerful means of carbon-carbon bond formation.[34-36] However, there is no literature precedent for palladium(0)-catalyzed cross coupling using stannyl diazoesters such as **5** or **6**. We envisaged that the palladium-catalyzed reaction of these reagents with common coupling partners such as aryl, vinyl and acyl halides could lead to a facile synthesis of a variety of diazoesters which may not be attainable by the standard diazo transfer protocol.

Indeed, the coupling of stannyl diazoester **5** (or **6**) with iodobenzene in the presence of 5 mol % *bis*(triphenylphosphine)palladium(II) dichloride and tri-2-furylphosphine (10 mol %) proceeded in THF at reflux (4 h) and gave ethyl phenyldiazoacetate (**7**) in 30-40% yield. The coupling of **6** with 1-iodo-4-nitrobenzene afforded a much higher yield (91%) of the coupled diazoester **8**. Aryl and vinyl bromides or chlorides failed to provide the coupled products, with destannylation occurring under the reaction conditions. Thus, the palladium catalyzed coupling reaction offers no advantage over the traditional diazo transfer protocol.



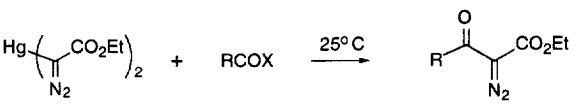
Acyl halides are widely used coupling partners in the Stille reaction and generally provide ketones in high yield.[34,37] Consequently, we investigated the reaction of **5** with several acyl and aroyl chlorides but found that only trace amounts of the cross coupled products were produced. Reaction of **5** with bromoacetyl bromide did lead to bromo diazoester **10** (41%) but this same compound was also produced in the absence of the palladium(0)-catalyst.



5 **10**

Organomercury compounds possess a number of characteristics which make them attractive intermediates in organic synthesis.[38] Their chemistry generally takes advantage of the ease with which they undergo transmetallation by a variety of transition metal reagents, particularly palladium salts, to generate the corresponding organometallic. We found that bromo diazoester **10** was formed in excellent yield (93%) by treating the diazomercurial reagent **9** with bromoacetyl bromide at 25° C in the absence of a palladium(0)-catalyst. The generality and scope of this new process was investigated using a variety of acid halides. As illustrated in Table I, the reaction can deliver a variety of substituted β-ketoesters. Acid chlorides (entries **6** and **7**) proved to be poor coupling partners and provided only moderate yields of the diazo esters. Functional groups such as iodo, ester and alkenyl are tolerated using this methodology.

Table I. Synthesis of Diazo β-ketoesters from the Reaction of Acid Halides with Mercuryl Diazoacetate **9**



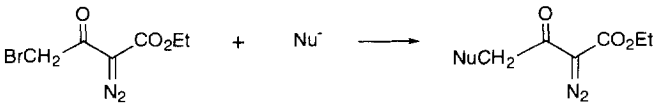
9

Entry	R	X	Product	Yield%
1	$BrCH_2$	Br	**10**	93
2	CH_3	Br	**11**	60
3	$PhCH_2$	Br	**12**	76
4	$(CH_3)_2C{=}CH$	Br	**13**	96
5	*o*-IC_6H_5	Br	**14**	76
6	$CH_3CH{=}CH$	Cl	**15**	40
7	$CH_3O_2CCH_2$	Cl	**16**	35

Ethyl 4-bromo-2-diazo-3-oxo-butanoate (**10**) was found to be a stable, pale yellow oil requiring no special precautions to prevent decomposition. The displacement of the bromide group in **10** with various

nucleophiles was used as a method to prepare a wide assortment of functionalized diazo β-ketoesters. The reaction appears to be quite general, is operationally simple and yields are high. The results of our studies are summarized in Table II. The examples selected span a wide range of different nucleophiles. In all but two

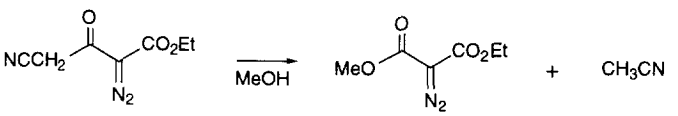
Table II. Substitution Reaction of Ethyl 4-Bromo-2-diazo-3-oxo-butanoate (**10**) with Various Nucleophilic Reagents



10

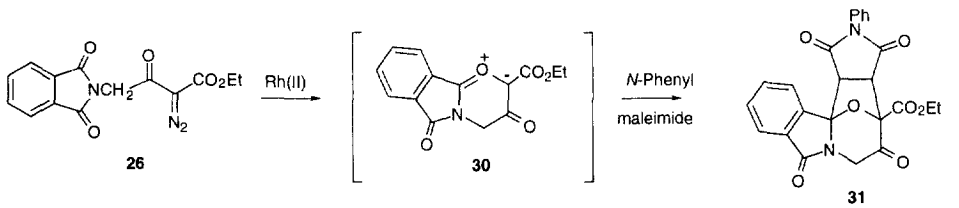
Entry	Reagent	Product	Yield%
1	NaN_3	**17**	95
2	KSCN	**18**	97
3	NaI	**19**	93
4	NaCl	**20**	86
5	p-$CH_3C_6H_4SO_2Na$	**21**	97
6	CH_3CO_2Na	**22**	96
7	HCO_2H-NEt_3	**23**	91
8	NaCN	**24**	35
9	NaSH	**25**	81
10	Phthalimide (K^+)	**26**	92
11	$NCCH(Na)CO_2Et$	**27**	74
12	C_6H_5ONa	**28**	31

cases (entries 8 and 12), the yields were good to excellent. The reaction of **10** with sodium cyanide afforded **24** in only 35% yield together with ethyl methyl 2-diazomalonate (**29**) (8%). The formation of **29** involves methanol (solvent) addition to the keto group of **24** followed by ejection of the $^-CH_2CN$ anion.



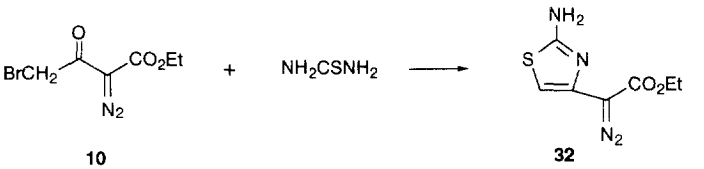
24 **29**

Several years ago our laboratory became interested in using the cycloaddition reaction of diazoimides for the construction of a variety of azapolycyclic ring systems.[39] In the context of this program, ethyl 2-diazo-3-oxo-4-(*N*-phthalimido)-butanoate (**26**) became of interest to us as a reagent for six-ring dipole formation (*i.e.*, **30**). Indeed, when **26** was treated with *N*-phenylmaleimide in the presence of $Rh_2(OAc)_4$ in benzene at reflux, cycloadduct **31** was obtained in 87% yield. Our original synthesis of **26** involved the reaction of *N*-phthalimido glycine with hydrogen ethyl malonate followed by diazo transfer (28% overall yield).[40] By comparison, the method described herein gave **26** in 51% overall yield from commercially available starting materials.



26 **30** **31**

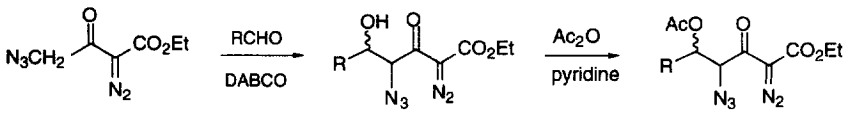
The use of thiazole containing compounds in the curative treatment of bacterial disorders has been firmly established and the development of new methods for the preparation of functionalized thiazoles is an area of active research.[41] One method that is occasionally used to prepare the thiazole ring involves the reaction of α-bromo carbonyl compounds with thiourea.[42] We have used this protocol to prepare the novel 2-amino diazothiazole **32** in one step (36%) by treating bromo diazobutanoate **10** with thiourea. The availability of **32** should allow for the synthesis of other novel thiazole derivatives, and further studies along these lines are currently underway.



10 **32**

Organo azides and diazo compounds have been extensively utilized for the synthesis of nitrogen containing heterocycles.[43] The chemistry exhibited by these two groups is often closely related. Both of these functional groups are quite common, although there are few examples in the literature where both an azido and diazo group are contained within the same molecule. As a consequence of the availability of **17** from the reaction of bromo diazobutanoate **10** with sodium azide, we decided to examine the chemical behavior of this interesting molecule. α-Azido ketones which possess α-hydrogens are highly base-sensitive and generally undergo base-promoted loss of nitrogen.[44] Recently, Hoffman and Patonay demonstrated that the base-induced reaction of α-azido ketones with aldehydes afforded α-azido-β-hydroxyketones which are useful 1,2,3-trifunctionalized synthons.[45] On the basis of this report, we examined the base-promoted reaction of **17** with both acetaldehyde and benzaldehyde and were delighted to find that the mixed aldol products **33** and **34** were obtained in 71% and 83% yield, respectively. Use of an equivalent amount of DABCO was found to efficiently promote the reaction. Further treatment of the mixed aldols with acetic anhydride furnished the

corresponding acetates **35**, **36** in excellent yield. The diastereoselectivity exhibited in the formation of **33** (or **34**) is low (*ca.* 2.5:1) and is quite characteristic for the condensations of α-substituted ketones with substituents other than alkyl groups at the α-position.[46] The assignment of *syn* and *anti* stereochemistry in **33** and **34** was made from the coupling constants of the methine protons at C-2 and C-3.[47]

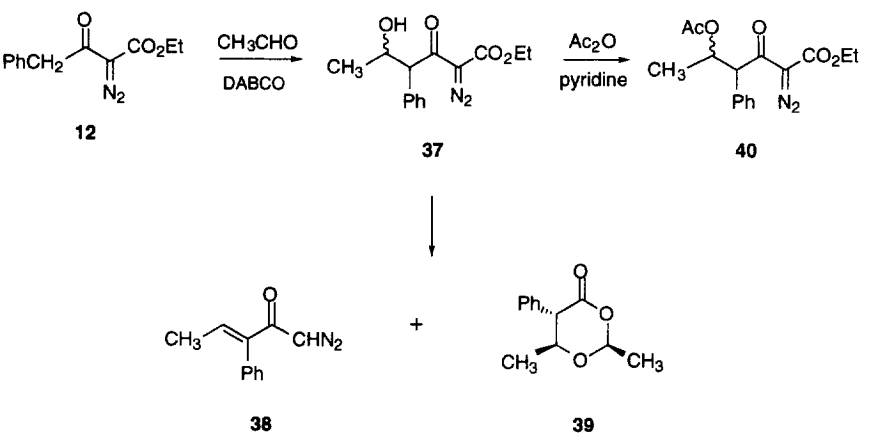


17

33; R=Me
34; R=Ph

35; R=Me
36; R=Ph

We next extended our study to include ethyl 2-diazo-3-oxo-4-phenyl-butanoate (**12**) as the enolate precursor. Reaction of **12** with acetaldehyde in the presence of 1 equiv of DABCO resulted in the isolation of aldol product **37** in 91% yield as a 1:1-diastereomeric mixture, together with two minor by-products identified as diazopentenone **38** (4%) and the known dioxanone **39** (3%).[48] The formation of **39** presumably involves reaction of **37** with excess acetaldehyde followed by cyclization and subsequent elimination of ethyl diazoacetate. The hydroxyl group present in **37** can be acylated with acetic anhydride to give acetate **40** in 99% yield.



12

37

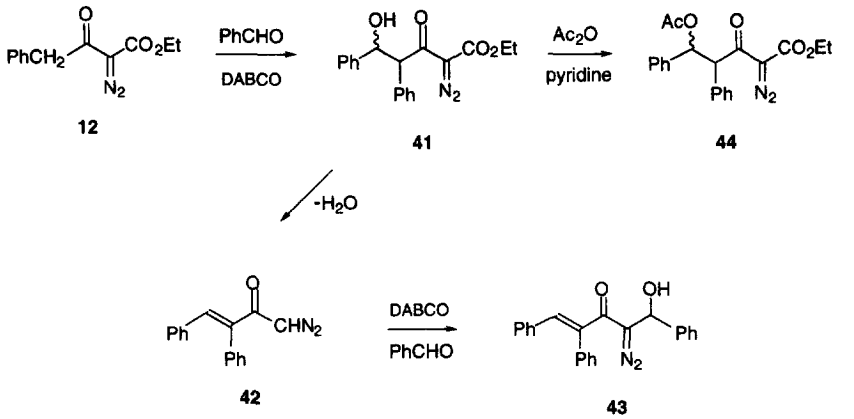
40

38

39

Similar results were found for the reaction of **12** with benzaldehyde. In this case, a 2:1-diastereomeric mixture of aldol products **41** was obtained in 74% yield and was easily converted to the corresponding acetate **44**. A minor amount of diazobutenone **42** (11%) was also isolated together with the unique diazo keto alcohol **43** (8%). Formation of **43** may be rationalized by attack of the diazo enolate derived from **42** on benzaldehyde. Indeed, treatment of a pure sample of **42** with benzaldehyde in the presence of 1 equiv. of DABCO furnished **43** in high yield (89%).

In conclusion, we have developed a new method for the synthesis of a wide assortment of α-diazo ketoesters which is based on the reaction of metallated α-diazo esters with aryl and acyl halides. Another interesting finding is the base-promoted reaction of several of the resulting α-diazo-β-ketoesters that possess α-hydrogens with aldehydes. The reaction proceeded in excellent yield producing mixed aldol products which



have great potential in synthesis. Further investigation of the reactions of these diazo ketoester anions with various other C-electrophiles is in progress and will be reported in due course.

General Experimental

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ether-hexane mixture as the eluent unless specified otherwise. As a consequence of their lability, the aryl diazoacetates reported below were characterized by HRMS rather than by elemental analyses.

Ethyl Phenyldiazoacetate (7). To a solution containing 2.4 mmol of (dimethylamino)trimethylstannane[33] in 1.5 mL of anhydrous THF under argon at rt was added 2.4 mmol of ethyl diazoacetate and the reaction was stirred for 20 min.[32] The resulting solution was added to a mixture of 1.6 mmol of iodobenzene, 5 mol% of $PdCl_2(PPh_3)_2$ and 10 mol% of tri-2-furylphosphine in 3 mL of anhydrous THF under argon at rt. The reaction was heated at reflux for 4 h, filtered through a Celite-silica gel plug using ether as the eluent and the filtrate was concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give **7** (39%)[22] as a clear oil; IR (neat) 2086, and 1700 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, J = 7.0 Hz), 4.35 (q, 2H, J = 7.0 Hz), and 7.20-7.50 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 61.1, 124.0, 125.6, 125.7, 130.1, and 164.3. A similar procedure was carried out using diethylamino-tri-*n*-butylstannane[33] which resulted in the isolation of **7** in 31% yield.

Ethyl (4-Nitrophenyl)diazoacetate (8). To a solution containing 0.4 mL (2.4 mmol) of (dimethylamino)trimethylstannane in 1.2 mL of anhydrous THF under argon at rt was added 0.26 mL (2.4 mmol) of ethyl diazoacetate and the reaction was stirred at rt for 15 min. The resulting solution was added to a mixture of 0.40 g (1.6 mmol) of 1-iodo-4-nitrobenzene, 0.055 g (0.08 mmol) of $PdCl_2(PPh_3)_2$ and 0.037 g (0.16 mmol) of tri-2-furylphosphine in 3 mL of anhydrous THF under argon at rt. The reaction mixture was stirred at rt for 6 h and filtered through a Celite-silica gel plug using ether as the eluent. The filtrate was concentrated under reduced pressure and the residue was recrystallized to give 0.34 g (91%) of **8** as an orange solid; mp 80-81°C (lit[20] mp 81-83°C); IR (neat) 2095, and 1700 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, J = 7.0 Hz), 4.35 (q, 2H, J = 7.0 Hz), 7.65 (d, 2H, J = 9.0 Hz), and 8.21 (d, 2H, J = 9.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.4, 61.6, 123.1, 124.2, 134.0, 144.9, and 163.6.

***Bis*-[Ethoxycarbonyl-diazomethyl]-mercury (9).** The synthesis of mercuryl diazoacetate **9** using the experimental conditions reported by Regitz[20] only furnished **9** in low yield. A modification of the original procedure was employed. Yellow mercuric oxide (58 g, 268 mmol) was added over a period of 4 h to 57 mL (540 mmol) of ethyl diazoacetate at -10° C with vigorous stirring. After the first portion of HgO had dissolved, 25 g (207 mmol) of anhydrous magnesium sulfate and 250 mL of ether was added to the reaction mixture. The mixture was slowly warmed to 0° C and maintained at 0-5° C for 20 h. At the end of this time, 100 mL of ether was added, the solid was filtered and washed with ether. Concentration of the filtrate under reduced pressure afforded 67 g (59%) of **9** as yellow solid; mp 102-103°C (lit[20] mp 102-104°C); IR (neat): 2078 and 1645 cm^{-1}.

General Procedure for the Preparation of the α-Diazo-β-Ketoesters (10-16). To a solution containing 2.0 g (4.7 mmol) of mercuryl diazo acetate **9** in 32 mL of CH_2Cl_2 under argon at 0°C was added dropwise 10 mmol of the appropriate acyl halide with vigorous stirring. After warming to rt, the mixture was stirred for an additional 10-30 min, the mercuric salts formed were decanted and the mixture was filtered through a silica gel plug using ether as the eluent. The filtrate was concentrated under reduced pressure and the residue was subjected to flash silica gel chromatography to give the diazo compounds specified below.

Ethyl 4-Bromo-2-diazo-3-oxo-butanoate (10) was isolated as a yellow oil (93%); IR (neat) 2140, 1715, and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.0 Hz), 4.30 (q, 2H, *J* = 7.0 Hz), and 4.40 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 31.7, 62.0, 160.6, and 184.1; HRMS Calcd for $C_6H_8N_2O_3Br$ ($M+H^+$): 234.9718. Found: 234.9724.

Ethyl 2-Diazo-3-oxo-butanoate (11)[23] was isolated as a pale yellow oil (60%); IR (neat) 2145,1720 and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.0 Hz), 2.46 (s, 3H) and 4.28 (q, 2H, *J* = 7.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 28.2, 61.4, 161.4, and 190.2.

Ethyl 2-Diazo-3-oxo-4-phenyl-butanoate (12) was isolated as a yellow oil (76%); IR (neat) 2138, 1715, and 1652 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.33 (t, 3H, *J* = 7.0 Hz), 4.19 (s, 2H), 4.31 (q, 2H, *J* = 7.0 Hz), and 7.30 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 45.8, 61.5, 127.0, 128.5, 129.7, 134.0, 161.2, and 190.2; HRMS Calcd for $C_{12}H_{13}N_2O_3$ ($M+H^+$): 233.0926. Found: 233.0923.

Ethyl 2-Diazo-5-methyl-3-oxo-4-hexenoate (13) was isolated as a yellow oil (96%); IR (neat) 2132, 1715, 1650, and 1610 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.0 Hz), 1.94 (s, 3H), 2.18 (s, 3H), 4.26 (q, 2H, *J* = 7.0 Hz), and 6.91 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 21.3, 28.0, 61.2, 120.5, 156.8, 161.5, and 182.0; HRMS Calcd for $C_9H_{13}N_2O_3$ ($M+H^+$): 197.0926. Found: 197.0924.

Ethyl 2-Diazo-3-(2-iodophenyl)-3-oxo-propionate (14) was isolated as a yellow oil (76%); IR (neat) 2145, 1715, and 1635 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.15 (t, 3H, *J* = 7.0 Hz), 4.19 (q, 2H, *J* = 7.0 Hz), 7.15 (ddd, 1H, *J* = 7.5, 7.5, and 1.5 Hz), 7.22 (dd, 1H, *J* = 7.5 and 1.5 Hz), 7.40 (ddd, 1H, *J* = 7.5, 7.5o, and 1.0 Hz), and 7.84 (dd, 1H, *J* = 7.5 and 1.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 61.7, 91.6, 127.1, 127.9, 138.8, 138.9, 143.8, 160.2, and 188.3; HRMS Calcd for $C_{11}H_{10}N_2O_3I$ ($M+H^+$): 344.9736. Found: 344.9729.

Ethyl 2-Diazo-3-oxo-4-hexenoate (15) was isolated as a yellow oil (40%); IR (neat) 2138, 1720, 1652, and 1610 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3H, *J* = 7.0 Hz), 1.92 (dd, 3H, *J* = 6.5 and 1.5 Hz), 4.28 (q, 2H, *J* = 7.0 Hz), 7.04 (dq, 1H, *J* = 15.5 and 6.5 Hz), and 7.18 (dq, 1H, *J* = 15.5 and 1.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 18.3, 61.3, 126.5, 143.3, 161.3, and 181.6; HRMS Calcd for $C_8H_{11}N_2O_3$ ($M+H^+$): 183.0770. Found: 183.0770.

Ethyl 2-Diazo-3,5-dioxo-5-methoxy-pentanoate (16) was isolated as a yellow oil (35%); IR (neat) 2145, 1745, 1720, and 1658 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3H, *J* = 7.0 Hz), 3.74 (s, 3H), 3.88 (s, 2H), and 4.30 (q, 2H, *J* = 7.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 46.2, 52.3, 61.7, 161.0, 167.6, and 184.9; HRMS Calcd for $C_8H_{11}N_2O_5$ (M+H$^+$): 215.0668. Found: 215.0677.

Ethyl 4-Azido-2-Diazo-3-Oxo-Butanoate (17). To a solution containing 5.0 g (21.3 mmol) of bromo diazobutanoate **10** in 30 mL of acetone at 0°C was added 2.12 g (32.6 mmol) of NaN_3 in 15 mL of H_2O. After the addition was complete, the reaction mixture was allowed to warm to rt and was stirred for 4 days. The resulting solution was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, and filtered. Concentration under reduced pressure furnished 3.97 g (95%) of **17** as a yellow solid. Recrystallization from isopropyl ether-petroleum ether furnished colorless needles; mp 26-27°C; IR (neat) 2145, 2105, 1715, and 1665 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.0 Hz), 4.30 (q, 2H, *J* = 7.0 Hz), and 4.38 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 56.0, 61.9, 160.8, and 186.5; Anal. Calcd for $C_6H_7N_5O_3$: C, 36.55; H, 3.58; N, 35.52; Found: C, 36.51; H, 3.63; N, 35.53.

Ethyl 2-Diazo-3-oxo-4-thiocyano-butanoate (18). To a solution containing 0.45 g (4.6 mmol) of KSCN in 5 mL of MeOH at rt was added 0.50 g (2.1 mmol) of bromo diazobutanoate **10** in 2.5 mL of MeOH. After stirring for 1 h, the mixture was diluted with ether, washed with H_2O, dried over $MgSO_4$ and filtered. Concentration under reduced pressure afforded 0.45 g (99%) of **18** as a pale orange oil; IR (neat) 2145, 1710, and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, *J* = 7.0 Hz), 4.30 (q, 2H, *J* = 7.0 Hz), and 4.31 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 41.3, 62.3, 111.3, 160.7, and 183.6; HRMS Calcd for $C_7H_8N_3O_3S$ (M+H$^+$)214.0286. Found: 214.0287.

Ethyl 2-Diazo-4-iodo-3-oxo-butanoate (19). To a solution containing 3.0 g (20 mmol) of NaI in 70 mL of MeOH at rt was added 2.22 g (9.4 mmol) of bromo diazobutanoate **10** in 30 mL of MeOH and the solution was stirred for 3.5 h. The reaction mixture was diluted with CH_2Cl_2, washed with H_2O, a saturated solution of $Na_2S_2O_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was filtered through a Celite-silica gel plug using a 1:1 mixture of hexane/ether as the eluent. The filtrate was concentrated under reduced pressure to give 2.5 g (93%) of **19** as a pale orange oil; IR (neat) 2140, 1712, and 1650 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.36 (t, 3H, *J* = 6.5 Hz), 4.34 (q, 2H, *J* = 6.5 Hz), and 4.36 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 2.6, 14.3, 61.9, 160.5, and 185.8; HRMS Calcd for $C_6H_8N_2O_3I$ (M+H$^+$): 282.9580. Found: 282.9586.

Ethyl 4-Chloro-2-diazo-3-oxo-butanoate (20). To a solution containing 0.051 g (0.87 mmol) of NaCl in 2 mL of a 1:1 mixture of MeOH/H_2O at rt was added 0.056 g (0.24 mmol) of bromo diazobutanoate **10** in 1 mL of MeOH. After stirring for 48 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered and concentrated under reduced pressure to give 0.039 g (86%) of **20** as a yellow oil; IR (neat) 2142, 1715, and 1670 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, *J* = 7.0 Hz), 4.32 (q, 2H, *J* = 7.0 Hz), and 4.62 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 46.9, 62.0, 160.8, and 184.0; HRMS Calcd for $C_6H_7N_2O_3Cl$: 190.0145. Found: 190.0151.

Ethyl 2-Diazo-3-oxo-4-(p-toluenesulfonyl)-butanoate (21). To a solution containing 6.39 g (35.8 mmol) of sodium *p*-toluenesulfinate in 90 mL of a 2:1 mixture of MeOH/H_2O at rt was added 4.0 g (17.1 mmol) of bromo diazobutanoate **10** in 40 mL of MeOH. The mixture was stirred for 4 h at rt, diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced

pressure to give 5.25 g (99%) of **21** as a pale green solid. Recrystallization from CH_2Cl_2-ethyl ether furnished pale green crystals; mp 125-126° C; IR (neat) 2145, 1710, and 1650 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, *J* = 6.5 Hz), 2.48 (s, 3H), 4.34 (q, 2H, *J* = 6.5 Hz), 4.81 (s, 2H), 7.37 (d, 2H, *J* = 8.2 Hz), and 7.81 (d, 2H, *J* = 8.2 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 21.6, 62.0, 62.6, 128.4, 129.7, 136.4, 145.1, 160.3, and 179.9; Anal. Calcd for $C_{13}H_{14}N_2O_5S$: C, 50.32; H, 4.55; N, 9.03; Found: C, 50.43; H, 4.57; N, 9.15.

Ethyl 4-Acetoxy-2-diazo-3-oxo-butanoate (22). To a solution containing 1.43 g (17.4 mmol) of anhydrous sodium acetate in 30 mL of 95% EtOH at rt was added 3.30 g (14.1 mmol) of bromo diazobutanoate **10** in 20 mL of 95% EtOH and the reaction mixture was stirred at rt for 4 days. The resulting solution was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give 2.88 g (96%) of **22** as a yellow solid. Recrystallization from hexane afforded colorless crystals; mp 40-41°C; IR (neat) 2145, 1752, 1715, and 1673 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.34 (t, 3H, *J* = 7.0 Hz), 2.19 (s, 3H), 4.31 (q, 2H, *J* = 7.0 Hz), and 5.10 (s, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 20.4, 61.8, 66.7, 161.0, 170.3, and 185.4; Anal. Calcd for $C_8H_{10}N_2O_5$: C, 44.86; H, 4.71; N, 13.08; Found: C, 44.88; H, 4.70; N, 13.19.

Ethyl 2-Diazo-4-formyloxy-3-oxo-butanoate (23). To a solution containing 2.87 g (12.2 mmol) of bromo diazobutanoate **10** in 30 mL of acetonitrile at 0° C was added 0.55 mL (14.6 mmol) of formic acid followed by 2.05 mL (14.7 mmol) of triethylamine. The mixture was stirred for 5 min at 0°C, warmed to rt, and stirred for 50 h. The solution was diluted with CH_2Cl_2, washed with H_2O, 1N HCl, saturated $NaHCO_3$, brine, H_2O, dried over $MgSO_4$, and filtered. Concentration under reduced pressure afforded 2.22 g (91%) of **23** as a clear solid. Recrystallization from isopropyl ether-petroleum ether gave pale yellow crystals; mp 43-44°C; IR (neat) 2145, 1730, 1710, and 1670 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, 3H, *J* = 7.0 Hz), 4.33 (q, 2H, *J* = 7.0 Hz), 5.21 (s, 2H), and 8.19 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 61.9, 66.0, 160.0, 160.9, and 184.5; Anal. Calcd for $C_7H_8N_2O_5$: C, 42.01; H, 4.03; N, 14.00; Found: C, 42.01; H, 4.03; N, 14.09.

Ethyl 4-Cyano-2-diazo-3-oxo-butanoate (24). To a solution containing 1.53 g (31.2 mmol) of sodium cyanide in 45 mL of a 1:1 mixture of MeOH/H_2O at -5° C was added 2.0 g (8.5 mmol) of bromo diazobutanoate **10** in 15 mL of MeOH. The reaction was stirred at -5° C for 20 min, warmed to rt, diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, and filtered. The major product isolated from the column contained 535 mg (35%) of **24**; mp 62-63° C; IR (KBr) 2260, 2165, 1710, and 1660 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3H, *J* = 6.5 Hz), 3.98 (s, 2H), and 4.31 (q, 2H, *J* = 6.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 30.3, 62.2, 113.4, 160.5, and 180.2; Anal. Calcd for $C_7H_7N_3O_3$: C, 46.41; H, 3.89; N, 23.20; Found: C, 46.51; H, 3.87; N, 23.29.

In addition, 114 mg (8%) of ethyl methyl 2-diazo-malonate (**29**) was obtained as a yellow oil; IR (neat) 2140 and 1720 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.5 Hz), 3.81 (s, 3H), and 4.29 (q, 2H, *J* = 7.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 52.4, 61.6, 160.8, and 161.5; HRMS Calcd for $C_6H_8N_2O_4$: 172.0484. Found: 172.0481.

Ethyl 2-Diazo-4-(3-diazo-3-ethoxycarbonyl-2-oxo-propylsulfanyl)-3-oxo-butanoate (25). To a solution containing 2.17 g (38.7 mmol) of NaSH in 90 mL of a 2:1 mixture of MeOH/H_2O at 0° C was added 3.42 g (14.5 mmol) of bromo diazobutanoate **10** in 40 mL of MeOH. After stirring at 0° C for 20 min, the

solution was warmed to rt, diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was filtered through a silica gel plug with ether as the eluent and the filtrate was concentrated under reduced pressure to give 2.01 g (81%) of **25** as a yellow solid after recrystallization from ethyl ether-isopropyl ether; mp 76-78° C; IR (neat) 3398, 2139, 1713, and 1652 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.0 Hz), 3.81 (s, 2H), and 4.29 (q, 2H, *J* = 7.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 38.3, 61.7, 161.0, and 187.1; HRMS Calcd for $C_{12}H_{15}N_4O_6S$ ($M+H^+$): 343.0712. Found: 343.0696.

Ethyl 2-Diazo-3-oxo-4-(N-phthalimido)-butanoate (26)[40]. To a solution containing 4.5 g (24.3 mmol) of potassium phthalimide in 50 mL of anhydrous DMF under argon at 0° C was added 3.08 g (13.1 mmol) of bromo diazobutanoate **10** in 50 mL of anhydrous DMF. After stirring for 2.5 h at 0° C, the reaction was filtered and the filtrate was cooled in an ice bath and treated with cold H_2O. The yellow solid that precipitated was collected by filtration and washed with cold H_2O to furnish 3.62 g (92%) of **26**. Recrystallization from CH_2Cl_2-ethyl ether gave pale yellow crystals; mp 149-150° C; IR (KBr) 2160, 1770, 1715, and 1660 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.36 (t, 3H, *J* = 7.0 Hz), 4.35 (q, 2H, *J* = 7.0 Hz), 4.93 (s, 2H), 7.72 (dd, 2H, *J* = 5.5 and 3.0 Hz), and 7.86 (dd, 2H, *J* = 5.5 and 3.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 45.3, 61.9, 123.5, 132.1, 134.1, 161.0, 167.8, and 184.6; Anal. Calcd for $C_{14}H_{11}N_3O_5$: C, 55.82; H, 3.68; N, 13.95; Found: C, 55.82; H, 3.71; N, 13.95.

Rhodium(II) Catalyzed Reaction of Ethyl 2-Diazo-3-oxo-4-(N-phthalimido)-butyrate (27) with N-Phenylmaleimide. A solution containing 113 mg of N-phenylmaleimide and 5 mg of rhodium (II) acetate in 0.5 mL of CH_2Cl_2 was treated dropwise with a solution containing 37 mg of diazo phthalimido ester **27** in 0.2 mL of CH_2Cl_2. A deep dark red color and gas evolution ensued with each addition followed by rapid color dissipation. Removal of the solvent afforded cycloadduct **31** (87%) which was isolated as a white solid, mp 249-250° C, IR ($CHCl_3$) 1750, 1725, 1390, 1300, 1210, and 1075 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.41 (t, 3H, *J* = 7.1 Hz), 3.98 (d, 1H, *J* = 7.6 Hz), 4.16 (d, 1H, *J* = 7.6 Hz), 4.30 (d, 1H, *J* = 18 Hz), 4.30 (q, 2H, *J* = 7.1 Hz), 4.85 (d, 1H, *J* = 18 Hz), and 7.31-7.86 (m, 9H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.9, 47.5, 50.4, 51.8, 61.8, 88.3, 94.6, 123.3, 125.1, 127.1, 129.1, 129.3, 131.5, 131.8, 132.2, 132.3, 136.8, 162.3, 163.2, 171.8, 172.2, and 191.5; Anal. Calcd for $C_{24}H_{18}N_2O_7$: C, 64.57; H, 4.06; N, 6.28. Found: C, 64.29; H, 4.08; N, 6.18.

Diethyl 5-Cyano-2-diazo-3-oxo-hexanedioate (27). To a mixture containing 0.09 g (2.3 mmol) of NaH (60% dispersion in mineral oil, previously washed with anhydrous benzene) in 7 mL of dry THF under argon at 0° C was added dropwise 0.23 mL (2.1 mmol) of ethyl cyanoacetate in 6 mL of dry THF. After stirring at 0° C for 5 min, 0.50 g (2.1 mmol) of bromo diazobutanoate **10** in 5 mL of dry THF was added. The mixture was stirred for an additional 5 min and was quenched with 95% EtOH followed by a saturated ammonium chloride solution. The mixture was warmed to rt, diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, and filtered. Concentration under reduced pressure gave 0.42 g (74%) of **27** as a yellow oil; IR (neat) 2252, 2142, 1750, 1710, and 1652 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.28 (t, 3H, *J* = 7.0 Hz), 1.29 (t, 3H, *J* = 7.0 Hz), 3.39 (dd, 1H, *J* = 17.0 and 5.5 Hz), 3.58 (dd, 1H, *J* = 17.0 and 6.0 Hz), 3.98 (dd, 1H, *J* = 6.0 and 5.5 Hz), 4.24 (q, 2H, *J* = 7.0 Hz), and 4.29 (q, 2H, *J* = 7.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 14.3, 31.8, 39.4, 61.9, 63.2, 116.1, 160.8, 165.2, and 187.2; HRMS Calcd for $C_{11}H_{14}N_3O_5$ ($M+H^+$): 268.0933. Found: 268.0935.

Ethyl 2-Diazo-3-oxo-4-phenoxy-butanoate (28). To a solution containing 1.98 g (11.6 mmol) of sodium phenolate trihydrate in 25 mL of H_2O at rt was added 1.80 g (7.7 mmol) of bromo diazobutanoate **10** in 30 mL of acetone. After stirring for 4 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, 10% NaOH, brine, H_2O, dried over $MgSO_4$, and filtered. Concentration of the mixture under reduced pressure afforded 0.59 g (31%) of **28** as a yellow solid. Recrystallization from ethyl ether-petroleum ether furnished pale yellow needles; mp 52-53° C; IR (neat) 2140, 1710, 1670, and 1600 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, 3H, *J* = 7.0 Hz), 4.32 (q, 2H, *J* = 7.0 Hz), 5.14 (s, 2H), 6.95 (m, 3H), and 7.28 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 61.9, 71.0, 114.8, 121.5, 129.4, 158.0, 161.1, and 186.9; Anal. Calcd for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.28; Found: C, 58.25; H, 4.93; N, 11.36.

Ethyl [4-(2-Aminothiazolyl)-diazoacetate (32). To a solution containing 4.0 g (17 mmol) of bromo diazobutanoate **10** in 37 mL of dry THF under argon at rt was added 2.09 g (27.5 mmol) of thiourea and the reaction was stirred at rt for 2.5 h. The resulting mixture was filtered and the solid was washed with THF. The filtrate was washed with H_2O and the aqueous phase was extracted several times with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give 1.29 g (36%) of **32** as an orange solid; mp 126-127° C; IR (KBr) 3390, 3305, 3170, 2085, 1680, 1640, and 1530 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 300 MHz) δ 1.20 (t, 3H, *J* = 7.0 Hz), 4.19 (q, 2H, *J* = 7.0 Hz), 6.50 (s, 1H), and 7.13 (s, 2H); ^{13}C-NMR (DMSO-d_6, 75 MHz) δ 14.7, 61.2, 98.7, 132.9, 164.8, and 168.7; HRMS Calcd for $C_7H_9N_4O_2S$ (M+H$^+$): 213.0446. Found: 213.0444.

General Procedure for the Aldol Reaction. To a solution containing 8.0 mmol of the appropriate diazo compound in 10 mL of acetaldehyde at 0° C was added 8.0 mmol of DABCO and the solution was stirred at 0°C for 3 h. The mixture was allowed to warm to rt and was stirred for an additional 25-40 h. The solution was concentrated under reduced pressure, the resulting residue was taken up in CH_2Cl_2, washed with H_2O, dried over $MgSO_4$ and filtered. Concentration under reduced pressure furnished an oil that was subjected to flash silica gel chromatography to afford the diazo-aldol product.

Ethyl 4-Azido-2-diazo-5-hydroxy-3-oxo-hexanoate (33) was obtained as a yellow oil (71%) and consisted of a 2.5:1-diastereoisomeric mixture (*syn/anti*); IR (neat) 3480, 2145, 2110, 1715, and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (m, 6H), *syn*-2.23 (d, 1H, *J* = 5.5 Hz), *anti*-2.28 (d, 1H, *J* = 7.0 Hz), 4.15-4.40 (m, 3H), *anti*-4.73 (d, 1H, *J* = 7.0 Hz), and *syn*-4.77 (d, 1H, *J* = 3.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) *syn*-isomer: δ 14.2, 20.1, 62.0, 67.9, 68.3, 160.8, and 188.2; *anti*-isomer: δ 14.2, 19.7, 62.1, 67.2, 68.1, 161.0, and 188.5; HRMS Calcd for $C_8H_{12}N_5O_4$ (M+H$^+$): 242.0889. Found: 242.0897.

Ethyl 4-Azido-2-diazo-5-hydroxy-3-oxo-5-phenyl-pentanoate (34) was obtained as a yellow oil (83%) and consisted of a 3:1-diastereoisomeric mixture; *anti*-isomer: IR (neat) 3480, 2145, 2112, 1710, and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, 3H, *J* = 7.0 Hz), 2.82 (d, 1H, *J* = 6.0 Hz), 4.30 (q, 2H, *J* = 7.0 Hz), 5.01 (dd, 1H *J* = 8.0 and 6.0 Hz), 5.09 (d, 1H *J* = 8.0 Hz), and 7.30-7.55 (m, 5H). *syn*-isomer: IR (neat) 3480, 2146, 2112, 1710, and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.33 (t, 3H, *J* = 7.0 Hz), 2.66 (d, 1H, *J* = 5.5 Hz), 4.32 (q, 2H, *J* = 7.0 Hz), 5.12 (d, 1H, *J* = 4.0 Hz), 5.28 (m, 1H), and 7.30-7.55 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 62.1, 68.5, 73.7, 126.2, 128.2, 128.5, 139.5, 160.7, and 187.6; HRMS Calcd for $C_{13}H_{14}N_5O_4$ (M+H$^+$): 304.1046. Found: 304.1031.

Ethyl 5-Acetoxy-4-azido-2-diazo-3-oxo-hexanoate (35). To a solution containing 2.0 mmol of **33** in 5 mL of benzene at rt was added 6.0 mmol of acetic anhydride followed by 2.5 mmol of pyridine. After

stirring for 18 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel to give **35** as a pale yellow oil (98%); IR (neat) 2145, 2110, 1745, 1712, and 1662 cm^{-1}. The major diastereomer showed the following spectral properties: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3H, *J* = 7.0 Hz), 1.42 (d, 3H, *J* = 6.5 Hz), 2.04 (s, 3H), 4.29 (m, 2H), 4.58 (d, 1H, *J* = 2.5 Hz), and 5.46 (dq, 1H, *J* = 6.5 and 2.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 17.8, 20.6, 61.9, 65.7, 70.0, 160.9, 170.0, and 187.6. The minor diastereomer exhibited the following spectral properties: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (d, 3H, *J* = 6.5 Hz), 1.33 (t, 3H, *J* = 7.0 Hz), 2.04 (s, 3H), 4.29 (m, 2H), 5.09 (d, 1H, *J* = 5.5 Hz) and 5.29 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 15.8, 20.9, 62.1, 65.6, 69.5, 160.4, 169.4, and 185.8; HRMS Calcd for $C_{10}H_{14}N_5O_5$ ($M+H^+$): 284.0995. Found: 284.0994.

Ethyl 5-Acetoxy-4-azido-2-diazo-3-oxo-5-phenyl-pentanoate (36). To a solution containing 2.0 mmol of **34** in 5 mL of benzene at rt was added 6.0 mmol of acetic anhydride followed by 2.5 mmol of pyridine. After stirring for 18 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel to give **36** as a yellow oil (94%); IR (neat) 2145, 2110, 1750, 1710, and 1662 cm^{-1}. The major diastereomer showed the following spectral properties: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.31 (t, 3H, *J* = 7.0 Hz), 2.12 (s, 3H), 4.31 (m, 2H), 4.96 (d, 1H, *J* = 4.0 Hz), 6.40 (d, 1H, *J* = 4.0 Hz), and 7.25-7.55 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 20.7, 62.1, 66.5, 74.4, 126.5, 128.6, 128.7, 136.4, 160.8, 169.7, and 187.1. The minor diastereomer exhibited the following spectral properties: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.29 (t, 3H, *J* = 7.0 Hz), 2.00 (s, 3H), 4.31 (m, 2H), 5.30 (d, 1H, *J* = 9.0 Hz), 6.06 (d, 1H, *J* = 9.0 Hz), and 7.30-7.55 (m 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 20.9, 61.9, 64.4, 74.0, 126.5, 127.5, 128.6, 136.3, 160.7, 169.4, and 186.1; HRMS Calcd for $C_{15}H_{16}N_5O_5$ ($M+H^+$): 346.1151. Found: 346.1135.

Ethyl 2-Diazo-5-hydroxy-3-oxo-4-phenyl-hexanoate (37) was obtained as a yellow oil (91%) and consisted of a 1:1 mixture of diastereoisomers. The first isomer eluted from the column was identified as the *syn*-diastereomer (**37**) which exhibited the following spectral properties: IR (neat) 3500, 2138, 1717, and 1648 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.13 (d, 3H, *J* = 6.5 Hz), 1.26 (t, 3H, *J* = 7.0 Hz), 2.68 (d, 1H, *J* = 2.0 Hz), 4.22 (m, 2H), 4.43 (m, 1H), 4.72 (d, 1H, *J* = 5.7 Hz), and 7.25-7.40 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 20.7, 59.5, 61.5, 68.7, 127.6, 128.4, 130.0, 134.5, 160.5, and 193.2. The *anti*-diastereomer **37** exhibited the following spectral properties: IR (neat) 3500, 2140, 1715, and 1650 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.04 (d, 3H, *J* = 6.5 Hz), 1.26 (t, 3H, *J* = 7.0 Hz), 2.53 (d, 1H, *J* = 5.0 Hz), 4.22 (m, 2H), 4.43 (m, 1H), 4.70 (d, 1H, *J* = 9.5 Hz), and 7.25-7.40 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 20.6, 61.4, 61.6, 69.7, 127.5, 128.6, 129.2, 135.8, 160.6, and 192.9; HRMS Calcd for $C_{14}H_{17}N_2O_4$ ($M+H^+$): 277.1188. Found: 277.1188.

A minor by-product that was also isolated (4%) was identified as 1-diazo-3-phenyl-pent-3-en-2-one (**38**); IR (neat) 2105, 1645, and 1602 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.67 (d, 3H, *J* = 7.0 Hz), 4.96 (s, 1H), 7.01 (q, 3H, *J* = 7.0 Hz), and 7.10-7.40 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 15.2, 55.6, 127.9, 128.6, 129.8, 135.5, 135.7, 140.8, and 186.3; HRMS Calcd for $C_{11}H_{11}N_2O$ ($M+H^+$): 187.0871. Found: 187.0865.

Still another minor by-product (3%) that could be obtained from the silica gel column was identified as 2,6-dimethyl-5-phenyl-[1,3]dioxan-4-one (**39**); mp 63-64°C (lit[48]); IR (neat) 1745 cm^{-1}; ^{1}H-NMR ($CDCl_3$,

300 MHz) δ 1.22 (d, 3H, *J* = 6.0 Hz), 1.55 (d, 3H, *J* = 5.5 Hz), 3.48 (d, 1H, *J* = 10.5 Hz), 4.04 (dq, 1H, *J* = 10.5 and 6.0 Hz), 5.69 (q, 1H, *J* = 5.5 Hz), and 7.10-7.40 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 19.5, 21.3, 55.7, 77.3, 101.0, 127.9, 129.0, 129.2, 135.2, and 169.5; HRMS Calcd for $C_{12}H_{15}O_3$ ($M+H^+$): 207.1021. Found: 207.1027.

Ethyl 5-Acetoxy-2-diazo-3-oxo-4-phenyl-hexanoate (40). To a solution containing 2.0 mmol of **37** in 5 mL of benzene at rt was added 6.0 mmol of acetic anhydride followed by 2.5 mmol of pyridine. After stirring for 18 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel to give **40** as a yellow oil (99%); IR (neat) 2140, 1742, 1715, and 1652 cm^{-1}. The major diastereomer exhibited the following spectral properties: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.00 (d, 3H, *J* = 6.5 Hz), 1.27 (t, 3H, *J* = 7.0 Hz), 1.99 (s, 3H), 4.23 (m, 2H), 4.99 (d, 1H, *J* = 10.5 Hz), 5.62 (m, 1H), and 7.25-7.50 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 17.7, 21.2, 57.9, 61.4, 71.5, 128.0, 128.7, 129.4, 134.4, 160.7, 169.9, and 190.2. The minor diasteromer showed the following spectral properties: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.26 (d, 3H, *J* = 6.5 Hz), 1.27 (t, 3H, *J* = 7.0 Hz), 1.74 (s, 3H), 4.23 (m, 2H), 4.98 (d, 1H, *J* = 9.5 Hz), 5.62 (m, 1H) and 7.25-7.50 (m, 5H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.1, 20.7, 58.0, 61.5, 71.0, 127.6, 128.2, 129.5, 135.0, 160.6, 169.8, and 190.4; HRMS Calcd for $C_{16}H_{19}N_2O_5$ ($M+H^+$): 319.1294. Found: 319.1282.

Ethyl 2-Diazo-4,5-diphenyl-5-hydroxy-3-oxo-pentanoate (41) was obtained as a 2:1-*anti/syn*-mixture of diastereomers in 74% yield. The *syn*-isomer was obtained as a pale yellow oil; IR (neat) 3500, 2142, 1715, and 1650 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, 3H, *J* = 7.0 Hz), 2.80 (d, 1H, *J* = 2.5 Hz), 4.18 (m, 2H), 5.18 (d, 1H, *J* = 7.0 Hz), 5.38 (dd, 1H, *J* = 7.0 and 2.5 Hz), and 7.20-7.40 (m, 10H). The *anti*-isomer was isolated as a pale yellow solid; mp 103-104° C; IR (neat) 3500, 2140, 1715, and 1650 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, 3H, *J* = 7.0 Hz), 2.89 (d, 1H, *J* = 4.5 Hz), 4.21 (m, 2H), 5.14 (d, 1H, *J* = 9.0 Hz), 5.30 (dd, 1H, *J* = 9.0 and 4.5 Hz), and 7.20-7.40 (m, 10H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 61.0, 61.5, 76.7, 126.8, 127.4, 127.6, 128.0, 128.3, 129.5, 134.7, 141.3, 160.7, and 192.8; Anal. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.45; H, 5.36; N, 8.28. Found: C, 67.51; H, 5.41; N, 8.35.

Two minor by-products were also isolated. One of them (11%) was identified as 1-diazo-3,4-diphenyl-2-but-3-en-2-one (**42**) as a pale yellow solid; mp 106-107° C; IR (KBr) 2105, 1638, and 1582 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.02 (s, 1H), 7.00-7.45 (m, 10H) and 7.72 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 56.3, 128.2, 128.4, 129.0, 129.3, 129.8, 130.9, 134.6, 135.9, 136.6, 138.0, and 186.6; Anal. Calcd for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.41; H, 4.91; N, 11.34.

The second minor by-product (8%) was assigned as 4-diazo-5-hydroxy-1,2,5-triphenyl-pent-1-en-3-one (**43**) and was obtained as a yellow solid; mp 109-111° C; IR (neat) 3395, 2095, 1620, and 1580 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 3.0-3.5 (d, 1H, *J* = 4.0 Hz), 6.05 (d, 1H, *J* = 4.0 Hz), and 7.05-7.55 (m, 16H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 69.7, 125.8, 128.2, 128.3, 128.7, 128.8, 128.9, 129.4, 129.7, 130.4, 134.6, 135.7, 136.4, 138.6, 139.1, and 188.2; Anal. Calcd for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90. Found: C, 78.20; H, 5.19; N, 7.74.

Ethyl 5-Acetoxy-2-diazo-4,5-diphenyl-3-oxo-pentanoate (44). To a solution containing 2.0 mmol of **41** in 5 mL of benzene at rt was added 6.0 mmol of acetic anhydride followed by 2.5 mmol of pyridine. After stirring for 18 h, the mixture was diluted with CH_2Cl_2, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel to give the

anti diastereomer (65%) as a white solid, mp 105-106° C; IR (neat) 2140, 1745, 1715, and 1655 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.29 (t, 3H, *J* = 7.0 Hz), 2.01 (s, 3H), 4.26 (m, 2H), 5.37 (d, 1H, *J* = 11.0 Hz), 6.36 (d, 1H, *J* = 11.0 Hz) and 7.10-7.40 (m, 10H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.3, 21.2, 58.1, 61.5, 76.9, 127.4, 127.7, 127.9, 127.95, 128.4, 129.7, 133.4, 137.9, 160.8, 169.4, and 190.1; Anal. Calcd for $C_{21}H_{20}N_2O_5$: C, 66.31; H, 5.30; N, 7.36; Found: C, 66.15; H, 5.29; N, 7.36.

The *syn* diastereomer (32%) was obtained as a white solid, mp 89-90° C: IR (neat) 2138, 1745, 1715, and 1652 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, 3H, *J* = 7.0 Hz), 1.72 (s, 3H), 4.26 (m, 2H), 5.56 (d, 1H, *J* = 11.0 Hz), 6.51 (d, 1H, *J* = 11.0 Hz), and 7.20-7.50 (m, 10H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 20.6, 57.9, 61.4, 76.0, 77.8, 127.8, 127.9, 128.35, 128.4, 128.45, 129.6, 135.1, 138.8, 160.5, 169.3, and 189.6; HRMS Calcd for $C_{21}H_{21}N_2O_5$(M+H$^+$): 381.1450. Found: 381.1463.

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