Thin-layer chromatography was performed on Merck $60F_{254}$ (0.25 mm) sheets, which were visualized with molybdophosphoric acid in ethanol. Merck 70–230 silica gel 60 was employed for column chromatography. A Perkin-Elmer 397 spectrophotometer was used to record the IR spectra (as Nujol films). A Bruker AM 300 spectrometer was employed for the $^1H$ and $^{13}C$ NMR spectra ($CDCl_3$ solutions). Mass spectra were obtained on an AEI MS-30 or VG 30F mass spectrometer (90 eV, direct insert probe). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Melting points were obtained with a Büchi-Tottoli apparatus and are not corrected. Microanalyses were performed by the Central Service of the CNRS.

**(2*S*,3*R*)-(−)-Methyl 2,3-Dihydroxy-3-phenylpropionate (2a).** A mixture of 1.74 g (3.74 mmol) of dihydroquinidine 4-chlorobenzoate (Aldrich) and 2.64 g (22.5 mmol) of *N*-methylmorpholine *N*-oxide in 10 mL of acetone and 1.4 mL of water was stirred under argon for 5 min at 20 °C and then cooled to −7 °C (bath temperature) and treated first with a solution of 30.5 mg (0.12 mmol) of osmium tetroxide in 254 μL of toluene and then over 48 h with a solution of 2.37 g (14.6 mmol) of methyl cinnamate in 4.4 mL of acetone. After the addition, the reaction mixture was stirred for an additional hour and then treated with 4.5 g of solid sodium metabisulfite. After being stirred for 1–2 min at −7 °C and 30 min at 20 °C, the mixture was diluted with dichloromethane, treated with anhydrous sodium sulfate, and then stirred for 30 min. After separation of the solids, the reaction mixture was processed with dichloromethane in the usual manner, and the crude product was purified by silica gel chromatography with 40% ether in hexane to give 2.36 g (82%) of diol **2a**: $[\alpha]^{24}_D$ −8.8° (*c* 1.0, chloroform), which corresponds to an enantiomeric excess of 82%.[9] One recrystallization of this material from dichloromethane–cyclohexane gave 1.47 g (51%) of enantiomerically pure[9] **2a**: mp 85–85.5 °C; $[\alpha]^{24}_D$ −10.7° (*c* 1.1, chloroform); IR 3460, 3375, 3060, 3050, 2950, 1710, 1445, 1438, 1390, 1320, 1300, 1270, 1220, 1200, 1102, 1080, 1040, 1022, 980, 920, 880, 850, 800, 760, 720, 700 $cm^{-1}$; $^1H$ NMR δ 2.71 (d, *J* = 7.0 Hz, 1 H), 3.07 (d, *J* = 6.0 Hz, 1 H), 3.81 (s, 3 H), 4.38 (dd, *J* = 2.9, 6.0 Hz, 1 H), 5.01 (dd, *J* = 2.9, 7.0 Hz, 1 H), 7.32–7.42 (m, 5 H); $^{13}C$ NMR δ 52.59, 74.44, 74.84, 126.20, 127.93, 128.32, 139.91, 173.06; mass spectrum (CI, ammonia–isobutane), *m/e* 254, 236, 214, 197, 196, 179, 168, 159, 151, 119, 107.

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.18; H, 6.18.

**(2*S*,3*R*)-(−)-Methyl 3-Hydroxy-3-phenyl-2-((*p*-tolylsulfonyl)oxy)propionate (2b).** To a stirred solution of 2.90 g (14.8 mmol) of diol **2a** in 74 mL of dichloromethane at 0 °C under argon was added 3.09 mL (2.24 g, 22.2 mmol) of triethylamine followed by 2.89 g (15.2 mmol) of *p*-toluenesulfonyl chloride. After being stirred for 63 h at 0 °C, the reaction mixture was processed with ethyl acetate and the crude product was purified by silica gel chromatography with 40% ether in hexane to give 4.58 g (88%) of the tosylate **2b**: mp 111–112 °C (dichloromethane–cyclohexane); $[\alpha]^{24}_D$ −47.5° (*c* 1.4, chloroform); IR 3500, 3100, 3050, 2950, 2920, 2850, 1750, 1595, 1490, 1450, 1435, 1360, 1290, 1190, 1175, 1095, 1062, 1030, 1020, 940, 920, 865, 810, 760, 745, 700, 685 $cm^{-1}$; $^1H$ NMR δ 2.42 (s, 3 H), 2.59 (s, 1 H), 3.60 (s, 3 H), 4.93 (d, *J* = 4.6 Hz, 1 H), 5.10 (d, *J* = 4.6 Hz, 1 H), 7.20–7.28 (m, 7 H), 7.56–7.60 (m, 2 H).

Anal. Calcd for $C_{17}H_{18}O_6S$: C, 58.27; H, 5.18. Found: C, 58.48; H, 5.08.

**(2*R*,3*R*)-(+)-Methyl 3-Phenyloxiranecarboxylate (3).** A solution of 2.96 g (8.46 mmol) of tosylate **2b** and 761 μL (42.3 mmol) of water in 42 mL of *N*,*N*-dimethylformamide at 20 °C was treated with 3.50 g (25.4 mmol) of potassium carbonate. After being stirred for 24 h at 20 °C, the reaction mixture was processed with ether in the usual way, and the crude product was purified by silica gel chromatography with 10% ether in hexane to provide 1.37 g (91%) of epoxide **3**: $[\alpha]^{24}_D$ +14° (*c* 1.6, chloroform). The IR and NMR spectra were identical with those previously[4] obtained.

**(2*R*,3*S*)-(+)-Methyl 3-Azido-2-hydroxy-3-phenylpropionate (4).** A 1.35-g (7.58-mmol) sample of epoxide **3** in 40 mL of methanol–water (8:1) was treated with 6.3 mL of methyl formate and 2.46 g (37.8 mmol) of sodium azide and then stirred under argon at 50 °C for 46 h. The crude product was isolated with ether in the normal way and then purified by silica gel chromatography with 10% ethyl acetate in hexane to give 1.59 g (95%) of hydroxy azide **4**: mp 56–57 °C (pentane); $[\alpha]^{24}_D$ +142° (*c* 1.1, chloroform). The IR and NMR spectra were identical with those previously[4] obtained.

**(2*R*,3*S*)-(−)-*N*-Benzoyl-3-phenylisoserine Methyl Ester (5).** A mixture of 1.51 g (6.83 mmol) of hydroxy azide **4**, 1.59 mL (1.93 g, 13.7 mmol) of benzoyl chloride, 2.85 mL (2.07 g, 20.4 mmol) of triethylamine, and 30.2 mg (0.25 mmol) of 4-(dimethylamino)pyridine in 27 mL of ethyl acetate was stirred under argon at 20 °C for 4 h, whereupon 1.4 mL of methanol was added. After being stirred for an additional 3 h, the reaction mixture was treated with 152 mg of 10% palladium on carbon and then placed under a hydrogen atmosphere. The resulting mixture was stirred for 68 h and then processed with dichloromethane in the usual manner to afford the crude product, which was purified by silica gel chromatography with 5% ether in dichloromethane to give 1.88 g (92%) of hydroxy amide **5**: mp 184–185 °C (lit.[1,4] mp 183–185 °C, 184–185 °C); $[\alpha]^{24}_D$ −48° (*c* 1.0, methanol) [lit.[1,4] $[\alpha]^{23}_D$ −49.6° (methanol), $[\alpha]^{26}_D$ −48° (*c* 0.92, methanol)]. The IR and NMR spectra were identical with those previously[4] obtained.

**(2*R*,3*S*)-(−)-*N*-(*tert*-Butoxycarbonyl)-3-phenylisoserine Methyl Ester (6).** A suspension of 148 mg of 10% palladium on carbon in 3 mL of ethyl acetate was stirred at 20 °C under a hydrogen atmosphere for 10 min, whereupon a solution of 1.75 g (8.02 mmol) of di-*tert*-butyl dicarbonate and 1.48 g (6.70 mmol) of hydroxy azide **4** in 12 mL of ethyl acetate was added. The resulting mixture was stirred under a hydrogen atmosphere for 56 h and then processed with ethyl acetate in the normal manner to afford the crude product, which was purified by silica gel chromatography with 5% ether in dichloromethane to give 1.81 g (92%) of hydroxy carbamate **6**: mp 130.5–131.5 °C (dichloromethane–cyclohexane); $[\alpha]^{24}_D$ −7° (*c* 1.2, chloroform); IR 3500, 3380, 3110, 3060, 3000, 2975, 2930, 1735, 1690, 1518, 1500, 1442, 1390, 1360, 1300, 1250, 1170, 1100, 1050, 1030, 980, 940, 930, 900, 705 $cm^{-1}$; $^1H$ NMR δ 1.42 (br s, 9 H), 3.11 (br s, 1 H), 3.84 (s, 3 H), 4.47 (br s, 1 H), 5.21 (~d, *J* = 9.4 Hz, 1 H), 5.36 (~d, *J* = 8.5 Hz, 1 H), 7.26–7.37 (m, 5 H); mass spectrum (CI, ammonia–isobutane), *m/e* 313, 296, 257, 240, 206, 196.

Anal. Calcd for $C_{15}H_{21}O_5N$: C, 61.00; H, 7.17. Found: C, 60.85; H, 7.17.

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**Registry No.** **1**, 1754-62-7; **2a**, 124649-67-8; **2b**, 124605-43-2; **3**, 99528-65-1; **4**, 99458-15-8; **5**, 32981-85-4; **6**, 124605-42-1; RP 56976, 114977-28-5; taxol, 33069-62-4.

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## An Improved Method for the Synthesis of α-Diazo Ketones

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Recent work in our laboratory has led to the development of a new aromatic annulation strategy based on the photochemically induced reaction of acetylenes with α,β-unsaturated α′-diazo ketones.[2] During the course of this

(1) MIT Undergraduate Research Opportunities Program participant.
(2) Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. K.; Miller, R. F. *J. Am. Chem. Soc.*, in press.

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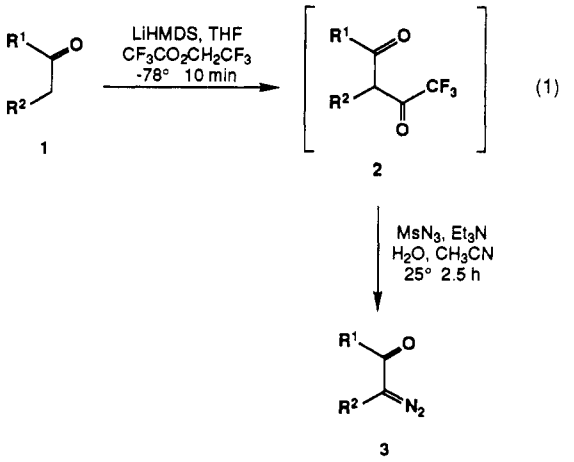
investigation it became apparent that many of the diazo ketones we required could not be prepared in satisfactory yield using existing methodology.[3] For example, one popular approach, the acylation of diazoalkanes with acid chlorides, is generally not applicable to the synthesis of $\alpha,\beta$-unsaturated derivatives, since dipolar cycloaddition to the conjugated double bond rapidly occurs, resulting in the formation of mixtures of isomeric pyrazolines.[4] Another widely used method, "diazo group transfer",[5] could be employed successfully for the synthesis of several of the requisite diazo ketones, but in other cases proceeded in disappointingly low yield (vide infra). We have consequently carried out a systematic investigation of conditions for effecting diazo group transfer to $\alpha,\beta$-unsaturated ketones, and we report herein an improved protocol for this transformation, which expands the scope of the reaction and provides more efficient access to a variety of $\alpha$-diazo ketones.

*Direct* diazo transfer to ketone enolates is usually not a feasible process,[6,7] although *highly stabilized* $\beta$-dicarbonyl enolates do react with sulfonyl azide reagents to afford $\alpha$-diazo ketones in good yield.[5] Diazo transfer to simple ketones can be achieved, however, by employing an indirect "deformylative diazo transfer" strategy in which the ketone is first formylated under Claisen condensation conditions and then treated with a sulfonyl azide reagent such as *p*-toluenesulfonyl azide.[8,9] The triazoline intermediate which forms under these conditions undergoes a facile fragmentation, eliminating tosylformamide and thereby generating the desired $\alpha$-diazo ketone. The application of this method to the preparation of a variety of diazocarbonyl compounds is now well documented, although we have found that in a number of crucial cases the desired $\alpha$-diazo ketones are produced in relatively low (0–50%) yield. Particularly problematic are reactions involving base-sensitive substrates such as $\alpha,\beta$-enones; these results are attributable in part to the harsh conditions typically required for the Claisen condensation step. The lack of regioselectivity associated with this thermodynamically controlled formylation also limits the utility of the method when applied to the synthesis of diazo derivatives of unsymmetrical ketones.

We have found that the efficiency of the diazo transfer reaction can be improved, in some cases quite dramatically, by substituting the trifluoroacetylation of kinetically generated lithium enolates for the usual Claisen formylation step. The new protocol is outlined in eq 1. Thus,



(1)

reaction of the ketone substrate with 1.1 equiv of lithium hexamethyldisilazide in THF at −78 °C for 30 min produces the corresponding lithium enolate, which is acylated by exposure to 1.2 equiv of trifluoroethyl trifluoroacetate (TFEA) at −78 °C for 5–10 min. The resulting $\alpha$-trifluoroacetyl ketone **2** is then treated at room temperature for 2.5 h with 1.5 equiv of methanesulfonyl azide in acetonitrile containing 1 equiv of water and 1.5 equiv of triethylamine. Column chromatography on silica gel furnishes the desired $\alpha$-diazo ketone, generally in excellent yield. Table I summarizes our results and compares the efficiency of the new procedure to the classical deformylative diazo transfer approach.

A key feature of the new procedure is the activation of the ketone starting material as the corresponding $\alpha$-trifluoroacetyl derivative. To our knowledge the use of TFEA to activate ketones in this fashion has not previously been reported, although Doyle has employed a similar strategy to achieve diazo transfer to a base sensitive *N*-acyloxazolidone derivative.[10] In our experience, TFEA has proved superior to other trifluoroacetylating agents (e.g. $CF_3CO_2Et$, $(CF_3CO)_2O$) for this transformation; the reaction of ketone enolates with this ester takes place essentially instantaneously at −78 °C. Note that the formylation of ketone enolates with ethyl formate is usually carried out using NaH or NaOEt as base and generally requires 12–48 h at room temperature for complete reaction.

In one case (propiophenone, entry 3), the initial acylation step was complicated by competing O-trifluoroacetylation of the lithium enolate, leading after hydrolysis to the recovery of a small amount of the ketone starting material. Crucial to the success of the trifluoroacetylation reaction in some cases is the selection of lithium hexamethyldisilazide (LiHMDS) as base for generation of the ketone enolate. As illustrated in Table II, under otherwise identical conditions diazo transfer to several aryl ketones proceeds in dramatically reduced yield when LDA is employed for the initial trifluoroacetylation step. Although the mechanistic basis for this remarkable effect is presently unclear, it should be noted that disilazide bases have previously been shown to be superior to LDA for several

(3) For reviews of methods for the synthesis of $\alpha$-diazo ketones, see: (a) Regitz, M.; Maas, G. *Diazo Compounds, Properties and Synthesis*; Academic Press: New York, 1986. (b) Regitz, M. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Chapter 17.

(4) For discussion and examples, see (a) pp 498–99 of ref 3a. (b) Fink, J.; Regitz, M. *Synthesis* **1985**, 569. (c) Itoh, M.; Sugihara, A. *Chem. Pharm. Bull.* **1969**, *17*, 2105. (d) Regitz, M.; Menz, F.; Liedhegener, A. *Justus Liebigs Ann. Chem.* **1970**, *739*, 174. (e) Harmon, R. E.; Sood, V. K.; Gupta, S. K. *Synthesis* **1974**, 577. (f) Rosenquist, N. R.; Chapman, O. L. *J. Org. Chem.* **1976**, *41*, 3326 and references cited therein.

(5) For reviews of diazo group transfer, see: (a) Regitz, M. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 733. (b) Regitz, M. *Synthesis* **1972**, 351. (c) Chapter 13 of ref 3a.

(6) Diazo transfer from 2,4,6-triisopropylphenylsulfonyl azide to the enolate derivatives of hindered cyclic ketones can be achieved by using phase-transfer conditions: Lombardo, L.; Mander, L. N. *Synthesis* **1980**, 368.

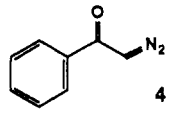
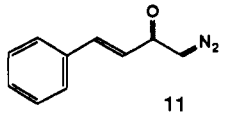
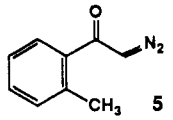
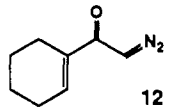
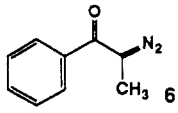
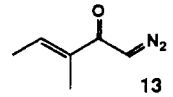
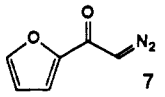
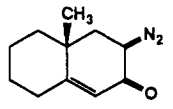
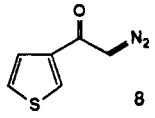
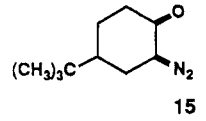
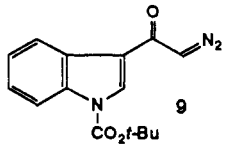
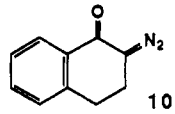
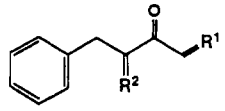
(7) Evans and Britton have reported successful diazo transfer from *p*-nitrobenzenesulfonyl azide (PNBSA) to the enolate derivatives of an *N*-acyloxazolidinone and a benzyl ester: (a) Evans, D. A.; Britton, T. C. *J. Am. Chem. Soc.* **1987**, *109*, 6881. (b) Britton, T. C. Ph.D. Dissertation, Harvard University, 1987. However, we have thus far been unable to achieve efficient diazo transfer to *ketone* enolates employing these conditions. For example, exposure of the lithium enolate of acetophenone to 1.2 equiv of PNBSA in THF at −78 °C for 15 min gave $\alpha$-diazoacetophenone in only 21% yield.

(8) See refs 5a, 5c, and (a) Regitz, M.; Menz, F. *Chem. Ber.* **1968**, *101*, 2622. (b) Hendrickson, J. B.; Wolf, W. A. *J. Org. Chem.* **1968**, *33*, 3610. (c) Rosenberger, M.; Yates, P.; Hendrickson, J. B.; Wolf, W. *Tetrahedron Lett.* **1964**, 2285.

(9) Other indirect diazo transfer routes to $\alpha$-diazo ketones have been reported involving initial activation of the ketone by benzoylation and acylation with diethyl oxalate: (a) Reference 4e. (b) Metcalf, B. W.; Jund, K.; Burkhart, J. P. *Tetrahedron Lett.* **1980**, *21*, 15.

(10) Doyle, M. P.; Dorrow, R. L.; Terpstra, J. W. Rodenhouse; R. A. *J. Org. Chem.* **1985**, *50*, 1663.

**Table I. Synthesis of α-Diazo Ketones**

| entry | α-diazo ketone[a] | diazo transfer procedure (yield, %)[b] via formylation | via trifluoroacetylation[c] | entry | α-diazo ketone[a] | diazo transfer procedure (yield, %)[b] via formylation | via trifluoroacetylation[c] |
|---|---|---|---|---|---|---|---|
| 1 |  4 | 73[d] | 95 | 8 |  11 | 17[e] | 85 |
| 2 |  5 | 74[e] | 81 | 9 |  12 | 45[i] | 87 |
| 3 |  6 | 71[f] | 63, 90[g] | 10 |  13 | 44[i] | 84 |
| 4 |  7 | 53[d] | 71 | 11 |  14 | 33[e] | 48 |
| 5 |  8 | 57[e] | 92 | 12 |  15 | 68[f] | 61 |
| 6 |  9 | 0[e] | 86-92 | | | | |
| 7 |  10 | 56[h] | 81 | 13 |  16 $R^1$=$N_2$ $R^2$=$H_2$ 17 $R^1$=$H_2$ $R^2$=$N_2$ | 53[e] 16:17 = 4:1 | 67 16:17 = 4:1 |

[a] IR, UV, $^1$H NMR, and $^{13}$C NMR spectral data were fully consistent with the assigned structures. Elemental analyses and/or high-resolution mass spectra were obtained for all new compounds. [b] Isolated yields of products purified by column chromatography on silica gel. [c] These diazo transfer reactions were conducted by using the LiHMDS–$CF_3CO_2CH_2CF_3$ method (see text). [d] Reference 8a. [e] This diazo transfer reaction was conducted employing the general method of Taber (ref 12a): an ethereal solution of the ketone (0.5 M) and methyl formate (3 equiv) was allowed to react with NaH for 3–4 h at 0 °C. After the mixture was stirred at 25 °C for 12–18 h, mesyl azide (3.0 equiv, 0.6 M in $Et_2O$) was added, and the resulting mixture was allowed to stir at 25 °C for 2–3 h. [f] Reference 12a. [g] Yield corrected for recovered propiophenone. [h] Reference 20. [i] This diazo transfer reaction was conducted using the following procedure: a solution of the ketone and methyl formate (1.1–1.2 equiv) in ether (0.5 M) was allowed to react with freshly cut sodium metal (1.0 equiv) at 0–25 °C for 12–18 h. The resulting formyl salt was then collected by filtration, suspended in EtOH (0.5 M), and allowed to react with 1 equiv of mesyl azide at 0 °C for 2–3 h.

other carbonyl metalation reactions.[11]

Although tosyl azide has traditionally been the reagent of choice for effecting diazo transfer reactions, we have found methanesulfonyl azide[12] to be a more convenient and generally superior reagent. As pointed out recently by Taber,[12a] the use of this reagent has the advantage that excess mesyl azide as well as certain formamide byproducts are easily separated from the desired diazo ketone product by extraction into dilute aqueous base during workup. The reagent mesyl azide is available in greater than 90% yield by the reaction of MsCl with sodium azide using a modification of the method of Boyer.[13] Specifically, we have found that by substituting acetone for methanol as solvent the formation of methyl mesylate can be avoided, and mesyl azide can then be isolated (by filtration) in a state of purity (>95%) sufficient for use in diazo transfer reactions without further purification. Although we therefore recommend mesyl azide as a particularly convenient reagent for diazo transfer, it should be noted that other azide reagents[14] are available which may in some applications have advantages with respect to safety, economy, and facility of product separation.

The examples listed in Table I document the superiority of the new diazo transfer procedure over the classical de-

(11) For example, see: (a) Williams, R. M.; Im, M.-N. *Tetrahedron Lett.* **1988**, *29*, 6075. (b) Ireland, R. E.; Thompson, W. J. *J. Org. Chem.* **1979**, *44*, 3041. (c) Schow, S. R.; Bloom, J. D.; Thompson, A. S.; Winzenberg, K. N.; Smith, A. B. *J. Am. Chem. Soc.* **1986**, *108*, 2662.

(12) (a) Taber, D. F.; Ruckle, R. E., Jr.; Hennessy, M. *J. Org. Chem.* **1986**, *51*, 4077. (b) Lowe, G.; Ramsay, M. V. *J. Chem. Soc., Perkin Trans. 1* **1973**, 479. (c) Stork, G.; Szajewski, R. P. *J. Am. Chem. Soc.* **1974**, *96*, 5787.

(13) Boyer, J. H.; Mack, C. H.; Goebel, N.; Morgan, L. R., Jr. *J. Org. Chem.* **1958**, *23*, 1051.

(14) For example (a) *p*-carboxybenzenesulfonyl azide: ref 8b. (b) Polymer-bound tosyl azide: Roush, W. R.; Feitler, D.; Rebek, J. *Tetrahedron Lett.* **1974**, 1391. (c) *p*-Dodecylbenzenesulfonyl azide: Hazen, G. G.; Weinstock, L. M.; Connell, R.; Bollinger, F. W. *Synth. Commun.* **1981**, *11*, 947. (d) *p*-Acetamidobenzenesulfonyl azide: Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709.

Table II. Effect of Amide Base on the Diazo Transfer Reaction

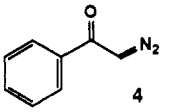
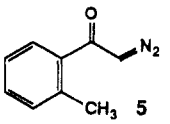
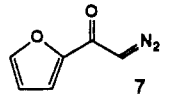
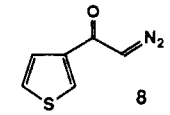
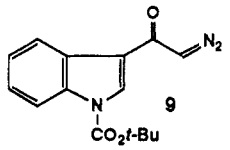
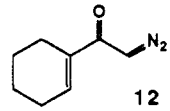
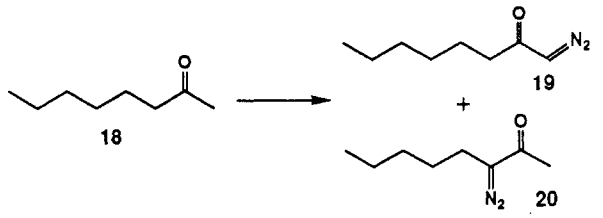
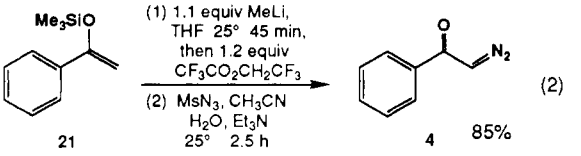
| entry | α-diazo ketone product | yield, % LDA | yield, % LiHMDS |
|---|---|---|---|
| 1 |  4 | 90 | 95 |
| 2 |  5 | 30 | 81 |
| 3 |  7 | 24 | 71 |
| 4 |  8 | 27 | 92 |
| 5 |  9 | 56-62 | 86-92 |
| 6 |  12 | 87 | 87 |

Table III. Regioselectivity of Diazo Transfer to 2-Octanone



| entry | base | yield, % | 19/20 |
|---|---|---|---|
| 1 | LiHMDS | 54 | 2.1/1 |
| 2 | LDA | 44 | 5/1 |
| 3 | LiTMP | 37 | 9/1 |

formylative strategy as a method for the synthesis of a wide range of vinyl and aryl α-diazo ketones. In the case of saturated ketones such as 4-*tert*-butylcyclohexanone (entry 12), both methods give comparable results, although the application of the new procedure should prove advantageous for reactions involving unsymmetrical ketones. Thus, as illustrated in Table III, diazo transfer to 2-octanone can be achieved with significant regiocontrol, especially when lithium tetramethylpiperidide[15] is employed for the generation of the requisite kinetic enolate. In this connection it should also be noted that variants of our diazo transfer strategy based on other methods of kinetic enolate generation are also possible. For example, as illustrated in eq 2, the cleavage of TMS enol ethers with methyllithium provides another useful route to specific enolates[16] which can be trifluoroacetylated and converted




to α-diazo derivatives in excellent yield as described above.

In summary, the method described in this report provides an efficient and convenient route to a variety of α-diazo ketones including unsaturated derivatives which were previously not available by diazo transfer. α-Diazo ketones serve as key intermediates in a number of important synthetic methods including the Arndt–Eistert homologation,[17] the photo-Wolff ring contraction strategy,[18] and the carbenoid-mediated cyclopropanation reaction.[19] We anticipate that improved access to α-diazo ketones will serve to enhance the utility of these valuable synthetic strategies.

## Experimental Section

**General Procedures.** All reactions were performed in flame-dried glassware under a positive pressure of argon or nitrogen. Reaction mixtures were stirred magnetically unless otherwise indicated. Air- and moisture-sensitive liquids and solutions were transferred via syringe or cannula into the reaction vessels through rubber septa. Reaction product solutions and chromatography fractions were concentrated using a Büchi rotary evaporator at ca. 20 mmHg. Column chromatography was performed using Baker silica gel (230–400 mesh).

**Materials.** Commercial grade solvents were used without further purification except as indicated below. Tetrahydrofuran was distilled from sodium benzophenone dianion. 1,1,1,3,3,3-Hexamethyldisilazane, 2,2,2-trifluoroethyl trifluoroacetate, and triethylamine were distilled from calcium hydride. Methanesulfonyl chloride was purified by distillation. All ketones were purified by distillation or column chromatography prior to use except for 3-acetylthiophene and 3-acetylindole, which were used as received from Aldrich Chemical Co. The petroleum ether used for column chromatography had a boiling range of 35–60 °C.

**Instrumentation.** Infrared spectra were obtained using a Perkin-Elmer 1320 grating spectrophotometer. Ultraviolet–visible spectra were measured on a Varian DMS 100 spectrophotometer. $^1$H NMR spectra were recorded with Bruker WM-250 (250 MHz) and Varian XL-300 (300 MHz), XL-400 (400 MHz), and VXR-500 (500 MHz) spectrophotometers. $^{13}$C NMR spectra were recorded on Bruker WM-270 (68 MHz) and Varian XL-300 (75 MHz) and XL-400 (100 MHz) spectrophotometers. Chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane. High-resolution mass spectra were obtained on a Finnegan Matt-8200 spectrometer. Elemental analyses were performed by Robertson Laboratory, Inc., of Madison, NJ. Melting points were determined with a Fischer-Johns melting point apparatus and are uncorrected.

**Methanesulfonyl Azide.** A 250-mL, three-necked, round-bottomed flask equipped with a rubber septum, argon inlet adapter, and a 50-mL powder addition funnel was charged with a solution of methanesulfonyl chloride (15.0 mL, 22.2 g, 194 mmol) in 100 mL of acetone. Sodium azide (18.9 g, 290 mmol) was then added over 30 min via the powder addition funnel, and the resulting mixture was stirred an additional 1.5 h at 25 °C. The reaction mixture was then filtered through a sintered-glass funnel, and the salts which were separated were washed with three 20-mL portions of acetone. Rotary evaporation of the filtrate removed most of the acetone, and the residual liquid was further concentrated with stirring at 25 °C (≤1 mmHg) for 1.5 h. Methanesulfonyl azide (22.7 g, 96%) was obtained as a clear, colorless oil which was used for diazo transfer reactions without further

(15) Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 582.
(16) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464.
(17) Bachmann, W. E.; Struve, W. S. *Org. React.* **1942**, *1*, 38.
(18) Meier, H.; Zeller, K.-P. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.
(19) Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75.

purification. The reagent could be stored at 0 °C (freezing point ca. 10 °C) for several months without detectable deterioration. ***Caution***: *Although we have never encountered any difficulty in handling $MsN_3$, like all sulfonyl azide derivatives this compound is potentially explosive.*

**General Procedure for Diazo Transfer. 2-Diazoacetophenone (4).** A 50-mL, three-necked, round-bottomed flask equipped with a rubber septum, argon inlet adapter, and a 25-mL pressure-equalizing addition funnel was charged with a solution of 1,1,1,3,3,3-hexamethyldisilazane (0.98 mL, 0.760 g, 4.71 mmol) in 12 mL of THF and then cooled at 0 °C in an ice–water bath while *n*-butyllithium solution (2.20 M in hexane, 2.14 mL, 4.71 mmol) was added rapidly dropwise. After 10 min, the resulting solution was cooled at −78 °C in a dry ice–acetone bath while a solution of acetophenone (0.50 mL, 0.515 g, 4.29 mmol) in 8 mL of THF was added dropwise over 15 min (the addition funnel was rinsed with 2 mL of additional THF). The reaction mixture was stirred at −78 °C for 30 min, and then 2,2,2-trifluoroethyl trifluoroacetate (0.69 mL, 1.00 g, 5.14 mmol) was added rapidly (1 s) by syringe in one portion. After 10 min, the reaction mixture was poured into a separatory funnel containing 25 mL of 5% aqueous HCl solution and 30 mL of $Et_2O$. The aqueous phase was extracted with two 20-mL portions of $Et_2O$, and the combined organic phases were then washed with 25 mL of saturated NaCl solution and concentrated at reduced pressure to give 0.95 g of a green oil which was immediately dissolved in 15 mL of $CH_3CN$ and transferred to a 50-mL, three-necked, round-bottomed flask equipped with a rubber septum, argon inlet adapter, and a 25-mL pressure-equalizing addition funnel. Water (0.8 mL, 0.077 g, 4.29 mmol) and $Et_3N$ (0.89 mL, 0.650 g, 6.44 mmol) were added, and a solution of methanesulfonyl azide (0.56 mL, 0.781 g, 6.44 mmol) in 15 mL of $CH_3CN$ was added dropwise over 20 min (the addition funnel was rinsed with another 2–3 mL of $CH_3CN$). The resulting solution was stirred at room temperature for 2.5 h and then concentrated to a volume of ca. 10 mL. The residue was diluted with 30 mL of $Et_2O$ and washed with three 20-mL portions of 10% aqueous NaOH solution and 25 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford 0.7 g of a yellow-orange oil. Column chromatography on silica gel (elution with 25% EtOAc–hexane) provided 0.596 g (95%) of the diazo ketone **4** as yellow crystals, mp 48–49 °C (lit.[8a] mp 48–49 °C), with spectral characteristics identical with those reported previously.[8a]

**2-Diazo-2′-methylacetophenone (5).** Reaction of 2′-methylacetophenone (0.251 g, 1.87 mmol) with LiHMDS (2.06 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.50 mL, 0.733 g, 3.74 mmol) in 8 mL of THF according to the general procedure provided a yellow solid which was then treated with $H_2O$ (0.034 mL, 0.034 g, 1.87 mmol), $Et_3N$ (0.392 mL, 0.285 g, 2.81 mmol), and methanesulfonyl azide (0.24 mL, 0.342 g, 2.81 mmol) in 13 mL of $CH_3CN$ at room temperature for 2.5 h to yield a brown oil. Column chromatography on silica gel (elution with 25% EtOAc–hexane) provided 0.222 g (81%) of the diazo ketone **5**[20] as a yellow oil: IR ($CCl_4$) 2940, 2920, 2860, 2100, 1630, 1460, 1380, 1350, 1285, 1210, 1150, 1120, 875, and 660 $cm^{-1}$; UV max ($CH_3CN$) 285 ($\epsilon$ = 10000), 251 (10700), and 206 (15000) nm; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.32–7.39 (m, 2 H), 7.10–7.25 (m, 2 H), 5.59 (s, 1 H), and 2.50 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 189.7, 137.1, 136.4, 131.2, 130.5, 126.9, 125.4, 56.0, and 19.9. Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.59; H, 5.09; N, 17.19.

**2-Diazopropiophenone (6).** Reaction of propiophenone (0.595 g, 4.43 mmol) with LiHMDS (4.88 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (1.19 mL, 1.74 g, 8.86 mmol) in 16 mL of THF according to the general procedure provided 1.2 g of a yellow oil, which was then treated with $H_2O$ (0.08 mL, 0.080 g, 4.43 mmol), $Et_3N$ (0.93 mL, 0.673 g, 6.65 mmol), and methanesulfonyl azide (0.57 mL, 0.805 g, 6.65 mmol) in 30 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.75 g of an orange-yellow oil. Column chromatography on silica gel (elution with 20% EtOAc–petroleum ether) provided 0.181 g of unreacted propiophenone and 0.447 g (63%) of the diazo ketone **6** as a yellow oil with spectral characteristics identical with those reported previously.[12a]

**2-Diazo-1-(2-furyl)-1-ethanone (7).** Reaction of 2-acetylfuran 0.197 g, 1.79 mmol) with LiHMDS (1.97 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.48 mL, 0.702 g, 3.58 mmol) in 8 mL of THF according to the general procedure provided 0.35 g of a yellow oil, which was then treated with $H_2O$ (0.03 mL, 0.032 g, 1.79 mmol), $Et_3N$ (0.38 mL, 0.272 g, 2.69 mmol), and methanesulfonyl azide (0.233 mL, 0.327 g, 2.69 mmol) in 12 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.6 g of a yellow oil. Column chromatography on silica gel (elution with 25% EtOAc–hexane) provided 0.173 g (71%) of the diazo ketone **7** as a yellow oil, exihibiting spectral characteristics identical with those reported peviously.[8a]

**2-Diazo-1-(3-thienyl)-1-ethanone (8).** Reaction of 3-acetylthiophene (0.548 g, 4.34 mmol) with LiHMDS (4.77 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (1.16 mL, 1.70 g, 8.67 mmol) in 16 mL of THF according to the general procedure provided 2.2 g of a yellow oil, which was then treated with $H_2O$ (0.08 mL, 0.078 g, 4.34 mmol), $Et_3N$ (0.91 mL, 0.659 g, 6.51 mmol), and methanesulfonyl azide (0.56 mL, 0.788 g, 6.51 mmol) in 30 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.7 g of a yellow oil. Column chromatography on silica gel (elution with 33% EtOAc–petroleum ether) provided 0.610 g (92%) of the diazo ketone **8** as yellow crystals: mp 55–57 °C; IR ($CCl_4$) 3140, 3110, 2170, 2110, 1630, 1620, 1520, 1415, 1380, 1350, 1230, 1190, 1160, 1080, 980, 930, 850, 730, and 700 $cm^{-1}$; UV max ($CH_3CN$) 292 ($\epsilon$ = 14000), 257 (13000), and 222 (14000) nm; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.89 (dd, $J$ = 1.9 and 2.8 Hz, 1 H), 7.41 (dd, $J$ = 1.9 and 5.3 Hz, 1 H), 7.33 (dd, $J$ = 2.8 and 5.3 Hz, 1 H), and 5.80 (s, 1 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 180.5, 140.7, 129.1, 126.6, 125.8, and 54.5. Anal. Calcd for $C_6H_4N_2OS$: C, 47.36; H, 2.65; N, 18.41; S, 21.07. Found: C, 47.61; H, 2.43; N, 18.15; S, 20.83.

**1-(3-(1-*tert*-Butoxycarbonyl)indolyl)-2-diazo-1-ethanone (9).** Reaction of 1-(3-(1-*tert*-butoxycarbonyl)indolyl)-2-diazo-1-ethanone (1.53 g, 5.91 mmol) with LiHMDS (7.09 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.95 mL, 1.39 g, 7.09 mmol) in 35 mL of THF according to the general procedure provided 2.22 g of a tan solid which was then treated with $H_2O$ (0.11 mL, 0.11 g, 5.91 mmol), $Et_3N$ (1.23 mL, 0.896 g, 8.86 mmol), and methanesulfonyl azide (0.77 mL, 0.107 g, 8.86 mmol) in 20 mL of $CH_3CN$ at room temperature for 2.5 h to yield 1.52 g of a bright yellow solid. Column chromatography on silica gel (elution with 20% EtOAc–hexane) provided 1.45 g (86%) of the diazo ketone **9** as a yellow solid: mp 119–122 °C; IR ($CCl_4$) 2970, 2930, 2860, 2100, 1740, 1625, 1450 1390, 1370, 1360, 1330, 1310, 1260, 1235, 1185, 1150, 1100, and 1045 $cm^{-1}$; UV max ($CH_3CN$) 308 ($\epsilon$ = 18000), 245 (19000), and 217 (28000) nm; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.28–8.30 (m, 1 H), 8.10–8.13 (m, 1 H), 8.02 (s, 1 H), 7.34–7.41 (m, 2 H), 5.79 (s, 1 H), and 1.70 (s, 9 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 181.7, 149.0, 135.5, 128.5, 127.3, 125.4, 124.2, 122.1, 119.3, 115.0, 85.3, 54.3, and 28.0. Anal. Calcd for $C_{15}H_{15}N_3O_3$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.37; H, 5.40; N, 14.79.

**2-Diazo-1-tetralone (10).** Reaction of tetralone (0.200 g, 1.37 mmol) with LiHMDS (1.51 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.22 mL, 0.322 g, 1.64 mmol) in 17 mL of THF according to the general procedure provided 0.413 g of a brown solid, which was then treated with $H_2O$ (0.025 mL, 0.025 g, 1.37 mmol), $Et_3N$ (0.287 mL, 0.208 g, 2.06 mmol), and methanesulfonyl azide (0.178 mL, 0.249 g, 2.06 mmol) in 10 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.348 g of a brown solid. Column chromatography on silica gel (elution with 10% EtOAc–hexane) provided 0.190 g (81%) of the diazo ketone **10** as a yellow solid, mp 47–49 °C (lit.[21a] mp 52–53 °C), with spectral characteristics identical with those previously reported.[21b]

**(*E*)-1-Diazo-4-phenyl-3-buten-2-one (11).** Reaction of (*E*)-4-phenyl-3-buten-2-one (0.200 g, 1.37 mmol) with LiHMDS (1.50 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.22 mL, 0.322 g, 1.64 mmol) in 15 mL of THF according to the general procedure provided 0.393 g of a yellow solid, which was then treated with $H_2O$ (0.025 mL, 0.025 g, 1.37 mmol), $Et_3N$ (0.286 mL, 0.207 g, 2.05 mmol), and methanesulfonyl azide (0.177 mL, 0.249 g, 2.05 mmol) in 10 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.276 g of a yellow solid. Column chromatography on

(20) Steinberg, G. M.; Lieske, C. N.; Ash, A. B.; Blumbergs, P. U.S. Patent 3729S558, 1973.

(21) (a) Horner, L.; Kirmse, W.; Muth, K. *Chem. Ber.* **1958**, *91*, 430. (b) Tamura, Y.; Ikeda, H.; Mukai, C.; Bayomi, S. M.; Ikeda, M. *Chem. Pharm. Bull.* **1980**, *28*, 3430.

silica gel (elution with 10% EtOAc–hexane) provided 0.201 g (85%) of the diazo ketone **11** as a yellow solid, mp 64.5–66 °C (lit.[4e] mp 66–68 °C), with spectral characteristics identical with those previously reported.[4e]

**1-(1-Cyclohexenyl)-2-diazo-1-ethanone (12).** Reaction of 1-acetyl-1-cyclohexene (0.20 mL, 0.193 g, 1.57 mmol) with LiHMDS (1.70 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.42 mL, 0.610 g, 3.11 mmol) in 8 mL of THF according to the general procedure provided 1.2 g of a forest green oil, which was then treated with $H_2O$ (0.03 mL, 0.028 g, 1.57 mmol), $Et_3N$ (0.33 mL, 0.236 g, 2.33 mmol), and methanesulfonyl azide (0.20 mL, 0.283 g, 2.33 mmol) in 11 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.6 g of an orange-brown oil. Column chromatography on silica gel (elution with 12% EtOAc–hexane) provided 0.204 g (87%) of the diazo ketone **12** as a yellow oil: IR ($CCl_4$) 3125, 2940, 2865, 2280, 2240, 2100, 1615, 1450, 1430, 1387, 1353, 1348, 1305, and 1190 $cm^{-1}$; UV max ($CH_3OH$) 290 ($\epsilon$ = 10 400) and 243 (10 300) nm; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 6.58 (m, 1 H), 5.53 (s, 1 H), 2.10–2.30 (m, 4 H), and 1.40–1.70 (m, 4 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 187.7, 137.7, 135.4, 52.3, 25.7, 23.8, 21.9, and 21.5; HRMS $m/e$ calcd for $C_8H_{10}N_2O$ 150.0793, found 150.0793.

**(*E*)-1-Diazo-3-methyl-3-penten-2-one (13).** Reaction of (*E*)-3-methyl-3-penten-2-one (0.212 g, 2.16 mmol) with LiHMDS (2.36 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.35 mL, 0.509 g, 2.06 mmol) in 20 mL of THF according to the general procedure provided 0.3 g of a yellow oil, which was then treated with $H_2O$ (0.04 mL, 0.039 g, 2.16 mmol), $Et_3N$ (0.46 mL, 0.331 g, 3.24 mmol), and methanesulfonyl azide (0.28 mL, 0.393 g, 3.24 mmol) in 30 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.3 g of a yellow oil. Column chromatography on silica gel (elution with 20% EtOAc–petroleum ether) provided 0.226 g (84%) of the diazo ketone **13** as a yellow oil: IR ($CCl_4$) 3130, 2990, 2930, 2220, 2105, 1650, 1615, 1440, 1395, 1380, 1355, 1335, and 1235 $cm^{-1}$; UV max ($CH_3OH$) 292 ($\epsilon$ = 9800) and 241 (9400) nm; $^1H$ NMR (250 MHz, $CDCl_3$) $\delta$ 6.39 (q, $J$ = 6.6 Hz, 1 H), 5.58 (s, 1 H), 1.83 and 1.80 (s and d overlapping, 6 H total); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 188.4, 136.4, 132.8, 52.6, 14.0, and 11.7; HRMS $m/e$ calcd for $C_6H_8N_2O$ 124.0637, found 124.0637.

**3-Diazo-4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone (14).** Reaction of 4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone (0.200 g, 1.22 mmol) with LiHMDS (1.34 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.196 mL, 0.286 g, 1.46 mmol) in 17 mL of THF according to the general procedure provided 0.294 g of a yellow oil, which was then treated with $H_2O$ (0.022 mL, 0.022 g, 1.22 mmol), $Et_3N$ (0.255 mL, 0.185 g, 1.83 mmol), and methanesulfonyl azide (0.158 mL, 0.222 g, 1.83 mmol) in 10 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.246 g of a yellow oil. Column chromatography on silica gel (elution with 10% EtOAc–hexane) provided 0.111 g (48%) of the diazo ketone **14** as a yellow oil: IR ($CCl_4$) 2900, 2860, 2070, 1625, 1600, 1450, 1355, 1300, 1220, 1190, 1170, 1135, 1110, 1060, 1010, 980, 970, 935, 900, and 860 $cm^{-1}$; UV max ($CH_3CN$) 319 ($\epsilon$ = 10 700), 242 (18 200), and 229 (17 500) nm; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.75 (s, 1 H), 2.89 (d, $J$ = 14.2 Hz, 1 H), 2.45 (d, $J$ = 14.2 Hz, 1 H), 2.29–2.40 (m, 2 H), 1.52–1.91 (m, 4 H), 1.32–1.46 (m, 2 H), and 1.27 (s, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 184.4, 164.6, 124.1, 58.2, 40.2, 36.1, 35.9, 31.8, 25.7, 23.8, and 21.5. Anal. Calcd for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.43; N, 14.72. Found: C, 69.36; H, 7.38; N, 14.56.

**4-*tert*-Butyl-2-diazocyclohexanone (15).** Reaction of 4-*tert*-butyl-2-diazocyclohexanone (0.200 g, 1.30 mmol) with LiHMDS (1.43 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.21 mL, 0.305 g, 1.56 mmol) in 17 mL of THF according to the general procedure provided 0.307 g of a yellow oil, which was then treated with $H_2O$ (0.023 mL, 0.023 g, 1.30 mmol), $Et_3N$ (0.272 mL, 0.197 g, 1.95 mmol) and methanesulfonyl azide (0.168 mL, 0.236 g, 1.95 mmol) in 10 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.392 g of a yellow liquid. Column chromatography on silica gel (elution with 20% EtOAc–hexane) provided 0.143 g (61%) of the diazo ketone **15** as a yellow oil with spectral characteristics identical with those previously reported.[12a]

**1-Diazo-4-phenyl-2-butanone (16) and 3-Diazo-4-phenyl-2-butanone (17).** Reaction of 4-phenylbut-2-one (0.245 g, 1.65 mmol) with LiHMDS (1.82 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.27 mL, 0.389 g, 1.98 mmol) in 10 mL of THF according to the general procedure provided a yellow oil, which was then treated with $H_2O$ (0.03 mL, 0.03 g, 1.65 mmol), $Et_3N$ (0.35 mL, 0.251 g, 2.48 mmol), and methanesulfonyl azide (0.21 mL, 0.300 g, 2.48 mmol) in 16 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.3 g of a yellow liquid. Column chromatography on silica gel (gradient elution with 5–20% EtOAc–hexane) provided 0.198 g (67%) of a 4:1 mixture of the diazo ketones **16**[22] and **17**[8b] as a yellow oil with spectral characteristics identical with those previously reported.

**1-Diazo-2-octanone (19) and 2-Diazo-2-octanone (20).** Reaction of 2-octanone (0.244 mL, 0.200 g, 1.56 mmol) with LiHMDS (1.72 mmol) and 2,2,2-trifluoroethyl trifluoroacetate (0.25 mL, 0.367 g, 1.87 mmol) in 17 mL of THF according to the general procedure provided 1.24 g of a yellow oil, which was then treated with $H_2O$ (0.028 mL, 0.028 g, 1.56 mmol), $Et_3N$ (0.326 mL, 0.237 g, 2.34 mmol), and methanesulfonyl azide (0.202 mL, 0.284 g, 2.34 mmol) in 10 mL of $CH_3CN$ at room temperature for 2.5 h to yield 0.130 g of a yellow oil. $^1H$ NMR analysis of the crude product indicated the presence of a 2.1:1 mixture of regioisomers **19**[23] and **20**. Column chromatography on silica gel (elution with 20% EtOAc–hexane) provided 0.130 g (54%) of a mixture of the diazo ketones **19** and **20**: IR (film) 2980, 2940, 2880, 2260, 2120, 1640, 1465, 1360, 1330, 1150, 1070, 1005, 920, and 730 $cm^{-1}$; UV max ($CH_3CN$) 246 nm ($\epsilon$ = 14 600); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.31 (s, 1 H, **19**), 2.32 (m, 2 H, **19**), 2.25 (s, 3 H, **20**), 2.00 (m, 2 H, **20**), 1.63 (m, 2 H, **19**), 1.30 (m, 6 H), 0.91 (m, 3 H); $^{13}C$ NMR (75 MHz, $CDCl_3$) for **19** $\delta$ 195.7, 53.9, 40.7, 31.2, 28.5, 24.8, 22.1, and 13.6.

**2-Diazoacetophenone (4). Preparation from $\alpha$-(Trimethylsiloxy)styrene (21).** A 25-mL, two-necked, round-bottomed flask equipped with a rubber septum and an argon inlet adapter was charged with a solution of $\alpha$-(trimethylsiloxy)styrene[24] (0.253 g, 1.31 mmol) in 5 mL of THF. Methyllithium solution (1.2 M in $Et_2O$, 1.20 mL, 1.44 mmol) was added dropwise over 5 min, and the resulting solution was stirred for 45 min at 25 °C. The reaction mixture was then cooled at −7 °C in a dry ice–acetone bath while 2,2,2-trifluoroethyl trifluoroacetate (0.21 mL, 0.309 g, 1.58 mmol) was added rapidly via syringe in one portion. After 10 min the resulting solution was worked up according to the general procedure to afford a yellow oil, which was then treated with $H_2O$ (0.024 mL, 0.024 g, 1.31 mmol), $Et_3N$ (0.28 mL, 0.201 g, 1.97 mmol), and methanesulfonyl azide (0.17 mL, 0.239 g, 1.97 mmol) in 16 mL of $CH_3CN$ at room temperature for 2.5 h to yield a yellow oil. Column chromatography on silica gel (elution with 25% ethyl acetate–hexane) provided 0.164 g (85%) of the 2-diazoacetophenone as yellow crystals.

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