A New Route To Hindered Tertiary Amines

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The $Rh_2(OAc)_4$-stabilized carbenoid derived from dimethyl diazomalonate has been found to insert into the N−H bond of sterically hindered secondary aliphatic amines to afford hindered tertiary aliphatic amines in quite satisfactory yields. For example dimethyl 2-(dicyclohexylamino)-propanedioate was formed in 85% yield from dicyclohexylamine, and the severely hindered dimethyl 2-(2,2,6,6-tetramethyl-1-piperidinyl)propanedioate was formed in 38% yield from 2,2,6,6-tetramethylpiperidine. The $Rh_2(OAc)_4$ - dimethyl diazomalonate reaction was found to work also for arylalkylamines and diarylamines. In these cases, small amounts of products resulting from formal insertion of the carbenoid into an aromatic C−H bond were detected. Substitution at ortho positions caused the yield of C−H insertion products to increase. Other diazo compounds, viz. ethyl diazoacetoacetate, 2-diazocyclohexane-1,3-dione, and 2-diazo-5,5-dimethylcyclohexane-1,3-dione, performed satisfactorily in $Rh_2(OAc)_4$-catalyzed reactions with arylalkylamines and diarylamines, but led to complicated reaction mixtures with dialkylamines.

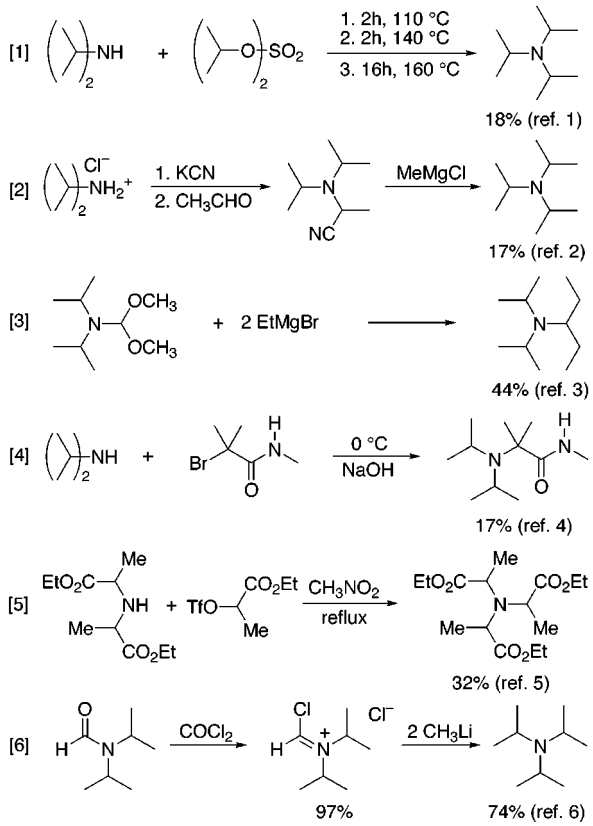
Introduction

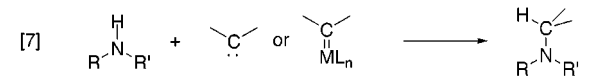
In the course of studies in our laboratory, the need arose for hindered tertiary amines similar to triisopropylamine. The desired amines were tertiary aliphatic amines in which all α-positions were branched, and which carried other functionality in addition. A search of the literature for possible synthetic methods was disheartening. Collected in Scheme 1 are all reported routes to such compounds, to the best of our knowledge.

Most of these methods give the hindered amine product in low or, at best, modest yields. The method of eq 6 is an exception, but the necessity of using phosgene makes this route less attractive. The use of Grignard reagents, organolithiums, or high temperatures limits the generality of these methods since the presence of a large variety of functional groups is thereby precluded.

The insertion of a carbene or carbenoid into an N−H bond is a known process which leads to C−N bond formation (eq 7).[7,8] The case in which the substrate is an amide and the carbenoid is generated from a diazo compound and $Rh_2(OAc)_4$ has been used widely with great success. For example, this approach has been particularly fruitful in the synthesis of penicillins and related β-lactams.[7a] On the other hand, $Rh_2(OAc)_4$-catalyzed carbenoid insertion into an *amine* N−H bond

Scheme 1





(1) (a) Kuffner, F.; Koechlin, W. *Monatsh. Chem.* **1962**, *93*, 476. For other processes that may have led to triisopropylamine, see: (b) Whitehead, W.; Imperial Chemical Industries, Ltd. Brit. Pat. 659,980; *Chem. Abstr.* **1951**, *45*, 8547. (c) Popov, M. A.; Shuikin, N. I. *Chem. Abstr.* **1956**, *50*, 4769.

(2) Bock, H.; Göbel, I.; Havlas, Z.; Liedle, S.; Oberhammer, H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 187−190.

(3) Eisele, G.; Simchen, G. *Synthesis* **1978**, 757−758.

(4) Guziec, F. S., Jr.; Torres, F. F. *J. Org. Chem.* **1993**, *58*, 1604−1606.

(5) Stachel, S. J.; Ziller, J. W.; Van Vranken, D. L. *Tetrahedron Lett.* **1999**, *40*, 5811−5812.

(6) Wieland, G.; Simchen, G. *Liebigs Ann. Chem.* **1985**, 2178−2193.

(7) For reviews of this area, see: (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998; Chapter 8. (b) Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75−253 (c) Davies, H. M. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 4, Chapter 4.8. (d) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385−5453 (e) Kirmse, G. *Carbene Chemistry*, 2nd ed.; Academic: New York, 1971; pp 409−412. (f) Aller, E.; Buck, R. T.; Drysdale, M. J.; Ferris, L.; Haigh, D.; Moody, C. J.; Pearson, N. D.; Sanghera, J. B. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2879−2884.

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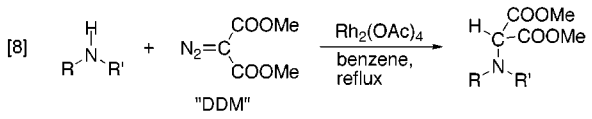
has been reported much less.[9] Dirhodium tetraacetate and related compounds are known to form strong complexes with Lewis bases.[10] Therefore it is reasonable to suggest that attempted $Rh_2(OAc)_4$-catalyzed amine N−H insertion reactions may have failed, and have gone unreported, because the rhodium catalyst was rendered inactive by complexation with the amine substrate. Nevertheless, we reasoned that amine N−H insertion (eq 7) might succeed for the particular class of amines which was of interest to us, namely those amines in which R and R′ are bulky groups, because complexation with the catalyst would be sterically inhibited. We have indeed found that secondary amines bearing bulky groups perform successfully in the reaction of eq 7 and we report our results herein.

Results and Discussion

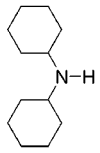
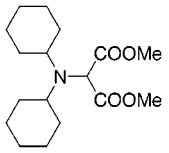
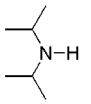
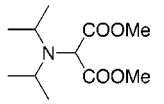
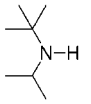
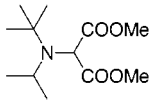
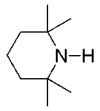
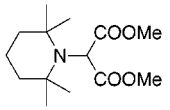
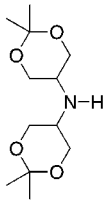
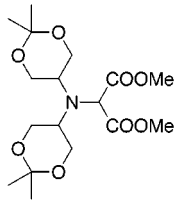
In refluxing benzene, dimethyl diazomalonate ("DDM"), catalyzed by $Rh_2(OAc)_4$, reacts with a variety of hindered secondary amines to afford hindered tertiary amine diesters in good yield (eq 8). Results are organized,



mainly, according to the secondary amine used: Table 1 pertains to dialkylamines, Table 2 to arylalkylamines, and Table 3 to diarylamines. Table 4 reports results obtained with diazo compounds other than DDM.

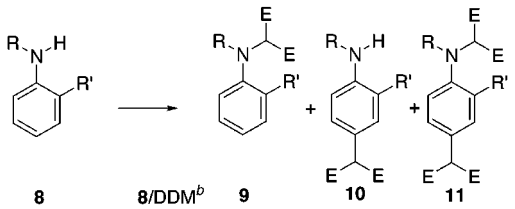
Dialkylamines. Table 1 shows generally good yields (isolated) of hindered tertiary trialkylamines by the present method. However, in the cases of diallylamine and 2,6-dimethylpiperidine no reaction took place under our standard conditions (refluxing benzene, 3 h). We presume that these amines bound to the catalyst to the exclusion of DDM and thereby prevented catalysis of diazo decomposition. In studies of binding of Lewis bases by dirhodium tetracarboxylates, piperidine was found to be among the most strongly bound amines examined.[10c]

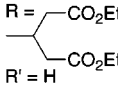
Table 1. $Rh_2(OAc)_4$-Catalyzed Reactions of Dimethyl Diazomalonate (DDM) with Dialkylamines

Entry	Reactant	Solvent, duration of reflux	Product	Yield[a]
<1>		PhH, 3h	 **1**	85%
<2>		PhH, 3h	 **2**	73%
<3>		PhH, 3h	 **3**	49%
<4>	 **4**	PhH, 8h	 **5**	10%
<5>	**4**	excess **4**, 5 h	**5**	38%
<6>	 **6**	PhH, 3h	 **7**	71%

[a] All yields are isolated yields.

Table 2. $Rh_2(OAc)_4$-Catalyzed Reactions of Dimethyl Diazomalonate (DDM) with Arylalkylamines, 8[a]



Entry	8	8/DDM[b]	9	10	11
<1>	**8a**, R = cyclohexyl; R′ = H	1:1	71%	8%	11%
		1:2	24%	7%	66%
<2>	**8b**, R = isopropyl; R′ = H	1:1	73%	8%	7%
		1:2	32%	2%	62%
<3>	**8c**, R = isopropyl; R′ = OCH_3	1:1	29%	53%	4%
		1:2	20%	15%	60%
<4>	**8d**, R =  R′ = H	1:1	70%	8%	12%
		1:2	39%	3%	50%

[a] All yields are isolated yields.

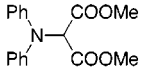
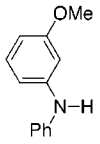
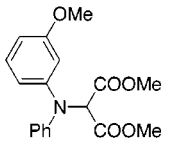
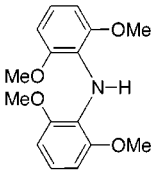
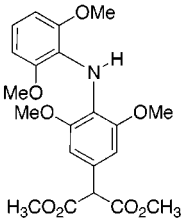
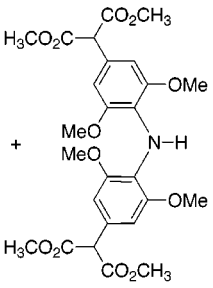
Di-*tert*-butylamine was tried as a substrate under a variety of conditions. In all cases, a very complex product mixture was obtained. The ^1H NMR "marker" for a successful reaction, a singlet at ca. 4.4 ppm corresponding

(8) Recent work: (a) Ferris, L.; Haigh, D.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2885−2888. (b) Bolm, C.; Kasyan, A.; Drauz, K.; Günther, K.; Raabe, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 2288−2290. (c) Galardon, E.; LeMaux, P.; Simonneaux, G. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2455−2456. (d) Moody, C. J.; Bagley, M. C. *J. Chem. Soc., Perkin Trans. 1* **1998**, 601−607. (e) Bagley, M. C.; Buck, R. T.; Hind, S. L.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 591−600. (f) Wang, J.; Hou, Y.; Wu, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2277−2280. (g) DelZotto, A.; Baratta, W.; Rigo, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3079−3081. (h) Simonneaux, G.; Galardon, E.; Paul-Roth, C.; Gulea, M.; Masson, S. *J. Organomet. Chem.* **2001**, *617*−*618*, 360−363. (i) Fehn, S.; Burger, K. *Tetrahedron: Asymmetry* **1997**, *8*, 2001−2005. (j) Moody, C. J.; Ferris, L.; Haigh, D.; Swann, E. *Chem. Commun.* **1997**, 2391−2392. (k) Moody, C. J.; Swann, E. *Synlett* **1998**, 135−136.

(9) (a) Paulissen, R.; Hayez, E.; Hubert, A. J.; Teyssie, P. *Tetrahedron Lett.* **1974**, 607−608. (b) Liu, J.-M.; Young, J.-J.; Li, Y.-J.; Sha, C.-K. *J. Org. Chem.* **1986**, *51*, 1120−1123. (c) Lawton, G.; Moody, C. J.; Pearson, C. J. *J. Chem. Soc., Perkin Trans. 1* **1987**, 899−902. (d) Chorvat, R. J.; Rorig, K. J. *J. Org. Chem.* **1988**, *53*, 5779−5781. (e) Haigh, D. *Tetrahedron* **1994**, *50*, 3177−3194. (f) Osipov, S. N.; Sewald, N.; Kolomiets, A. F.; Fokin, A. V.; Burger, K. *Tetrahedron Lett.* **1996**, *37*, 615−618. (g) Moody, C. J.; Swann, E. *Synlett* **1998**, 135−136

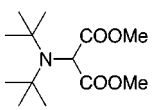
(10) (a) Doyle, M. P.; Colsman, M. R.; Chinn, M. S. *Inorg. Chem.* **1984**, *23*, 3684−3685. (b) Cotton, F. A.; Dikarev, E. V.; Petrukhina, M. A.; Stiriba, S.-E. *Polyhedron* **2000**, *19*, 1829−1835. (c) Drago, R. S.; Tanner, S. P.; Richman, R. M.; Long, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 2897−2903. (d) Pruchnik, F. P.; Starosta, R.; Kowalska, M. W.; Galdecka, E.; Galdecki, Z.; Kowalski, A. *J. Organomet. Chem.* **2000**, *597*, 20−28.

Table 3. $Rh_2(OAc)_4$-Catalyzed Reactions of Dimethyl Diazomalonate (DDM) with Diarylamines

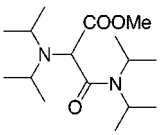
Entry	Reactant	Solvent, time at T = 50 °C	Product	Yield[a]
<1>		PhH, 1 h	 **12**	84%
<2>	 **13**	PhH, 3 h	 **14**	78%
<3>	 **15**	PhH, 4 h	 **16**	30%
+			 **17**	32%

[a] All yields are isolated yields.

to the methine proton neighboring nitrogen and two carbomethoxy groups, was absent from the spectra of the di-*tert*-butylamine product mixtures. Therefore, we conclude that the desired N−H insertion, leading to **18**, did not occur. However, **5**, an amine bearing two tertiary carbons and a secondary carbon, like **18**, *was* formed in 10% yield under standard conditions and in 38% yield when 2,2,6,6-tetramethylpiperidine was used in excess as solvent.



18

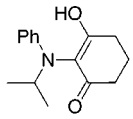
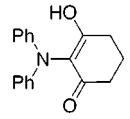
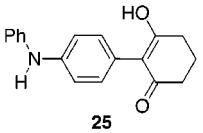
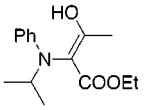
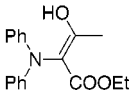


19

With diisopropylamine (Table 1, entry 2), a 12% yield of amide **19** was obtained in addition to **2**. The analogous amide was not observed in any other case.

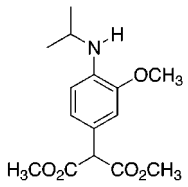
Arylalkylamines. The carbenoid derived from DDM reacted more rapidly with arylalkylamines than with dialkylamines. Thus, 1.5 h reflux in CH_2Cl_2, versus 3 h reflux in benzene for the dialkylamines, was sufficient to complete the reaction. The occurrence of aromatic C−H insertion in competition with N−H insertion led to slightly more complex reaction mixtures (see Table 2). (We use the phrase "C−H insertion" to describe the net change in the reaction. We do not intend the phrase to imply a particular mechanism). In all cases, the product

Table 4. $Rh_2(OAc)_4$-Catalyzed Reactions of Various Diazo Compounds with Arylalkylamines and Diarylamines[a]

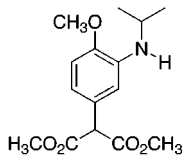
Entry	Amine	Diazo Compound	Product	Yield[b]
<1>	 **8b**	**22**	 **23**	65%
<2>	 **8b**	**22**	 **24**	75%
+			 **25**	17%
<3>	**8b**	**26**	 **27**	59%
<4>	 **8b**	**26**	 **28**	70%

[a] Solvent = CH_2Cl_2, reflux 1.5 h. [b] All yields are isolated yields.

of N−H insertion, **9**, the product of C−H insertion, **10**, and the product of both types of insertion, **11**, were observed. When the ratio of arylalkylamine **8** to DDM was close to 1.0, the N−H insertion product was formed in ≥70% yield, except in the case of *N*-isopropyl-*o*-anisidine, **8c**. Increasing the **8**/DDM ratio to 2.0 caused the N−H plus C−H insertion product, **11**, to become the major product. Proof of structure of **10c** was not trivial, since two chemically reasonable isomers, **10c** and **10c′**, could be drawn. A $^{13}C-^{13}C$ INADEQUATE experiment finally confirmed **10c** as the correct structure.



10c



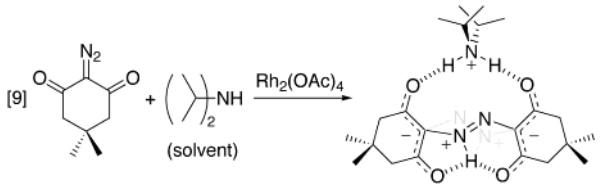
10c'

Diarylamines. Only a few examples of this type were examined (Table 3), since the tertiary amine produced was not judged to be particularly hindered per se. The carbenoid derived from DDM inserted into the N−H bond of diphenylamine in good yield and gave no sign of aromatic C−H insertion.

The relatively high yield of **10c** vs **9c** as compared to **10** vs **9** for other arylalkylamines in Table 2 (when **8**/DDM was 1:1) caused us to wonder whether the 2-methoxy group of **8c** was exerting a steric or an electronic effect. The presence of the 3-methoxy group of **13** gave rise to no detectable C−H insertion product.

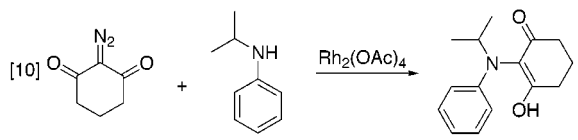
Therefore a steric explanation of the anomalous behavior of **8c** is probably correct. The steric effect of an *ortho* methoxy is carried to the limit in **15**, which gives only C−H insertion products **16** and **17**, and no N−H insertion product.

Other Diazo Compounds. The $Rh_2(OAc)_4$-catalyzed reaction of 2-diazo-5,5-dimethylcyclohexane-1,3-dione, **20**, with diisopropylamine (as solvent) gave only orange crystalline **21**, the structure of which was established by X-ray crystallography (eq 9). N−H insertion was not observed. The structural features of **21** are interesting and are only adumbrated in eq 9. A crystallographic C_2 axis passes through the N of the diisopropylammonium cation and the H bonded to the −N═N− linkage. All four C−O bond lengths are equal. The −N═N− linkage is disordered between two orientations, one of which is shown in lighter lines for clarity. The ^{1}H NMR chemical shift of the proton bonded to −N═N− and H-bonded to two oxygens was 17.1 ppm ($CDCl_3$ solvent).



20 **21**

By contrast, the carbenoid derived from **22** inserted into the N−H bond of *N*-isopropylaniline (eq 10), affording **23** in 35% yield. The solvent here was fluorobenzene. Other experience in our laboratory with a similar carbenoid in this solvent led us to believe that fluorobenzene had suffered attack by the **22**-derived carbenoid. Accordingly, we dispensed with fluorobenzene and used excess *N*-isopropylaniline as solvent, which afforded **23** in 65% yield. Similarly, the low mp of diphenylamine allowed it to function as solvent, giving **24** in 75% yield. In this case C−H insertion product **25** was obtained in 17% yield. In contrast to the results of $Rh_2(OAc)_4$-catalyzed reactions presented here, the *photochemical* reaction of **20** or **22** with primary and secondary amines has been reported to proceed by a Wolff rearrangement to give ring-contracted N-substituted or N,N-disubstituted 2-oxocyclopentane-1-carboxamides.[11,12]



22 **8b** **23**

Ethyl diazoacetoacetate, $CH_3C(=O)C(=N_2)COOEt$, **26**, reacts smoothly with **8b** and diphenylamine in CH_2Cl_2 solvent to afford, respectively, **27** (59% yield) and **28** (70% yield).

In contrast to the satisfactory results obtained with arylalkylamines and diarylamines, the $Rh_2(OAc)_4$-catalyzed reactions of diazo compounds **20**, **22**, and **26** with hindered dialkylamines generally produced complex mixtures of little value to the synthetic chemist.

Further transformations of some of the amines reported in Table 1 have resulted in amines that are even more planar about nitrogen than triisopropylamine, which had been thought to be the most nearly planar trialkylamine known.[13] These results will be reported in due course.

Experimental Section

Diazo compounds DDM, **20**, **22**, and **26** were prepared by a literature method.[14]

General Procedures for the Reaction of Dimethyl Diazomalonate ("DDM") with Hindered Secondary Amines. Procedure A. A mixture of DDM, hindered secondary dialkylamine, rhodium acetate, and dry benzene (10−20 mL) was heated at reflux under nitrogen for 3 h. Procedure B for arylalkylamine and diarylamine substrates: the solvent was CH_2Cl_2, and the time of reflux was 1.5 h. In both procedures, following removal of solvent at reduced pressure, the residue was purified by column chromatography on silica gel (60−200 mesh). Elution systems are described in each case below. Yields are given in Tables 1−4. Characterization data are given in the Supporting Information.

Dimethyl 2-(Dicyclohexylamino)propanedioate, 1. Procedure A. Dicyclohexylamine (226 mg, 1.25 mmol), DDM (161 mg, 1.02 mmol), rhodium acetate (5 mg, 0.01 mmol). Column eluted with benzene. Obtained 269 mg of **1** as a colorless solid, mp 51−52 °C.

Dimethyl 2-(Diisopropylamino)propanedioate, 2. Procedure A. Diisopropylamine (253 mg, 2.50 mmol), DDM (316 mg, 2.00 mmol), rhodium acetate (8 mg, 0.02 mmol). Elution with EtOAc/hexanes 1:4 (v/v). Obtained 337 mg **2** as a colorless oil, and 73 mg **19** as a colorless crystalline solid, mp 96−7 °C.

Dimethyl 2-(*N*-*tert*-Butyl-*N*-isopropylamino)propanedioate, 3. Procedure A. *tert*-Butylisopropylamine (131 mg, 1.14 mmol), DDM (165 mg, 1.04 mmol), rhodium acetate (4 mg, 0.009 mmol). Eluted with benzene. Obtained 137 mg of **3** as a colorless oil.

Dimethyl 2-(2,2,6,6-Tetramethyl-1-piperidinyl)propanedioate, 5. When procedure A was followed, **5** was obtained in only 10% yield. Therefore, we used excess amine as solvent: 2,2,6,6-tetramethylpiperidine (2.201 g, 15.61 mmol), DDM (501 mg, 3.17 mmol), rhodium acetate (13 mg, 0.030 mmol). Eluted with EtOAc/hexanes 1:6 (v/v). Afforded 332 mg **5** as a colorless oil.

Dimethyl 2-(Di(4,4-dimethyl-3,5-dioxanyl)amino)propanedioate, 7. Procedure A. Compound **6** (220 mg, 0.898 mmol),[15] DDM (169 mg, 1.07 mmol), rhodium acetate (16 mg, 0.036 mmol). Eluted with EtOAc/hexanes 1:3 (v/v). Afforded 240 mg **7** as a white solid, mp 63−64.5 °C

Arylalkylamines, 8a−d. These were prepared by reductive amination of aniline or *o*-anisidine according to literature procedure,[16] in yields of 99% (**8a**), 81% (**8b**), 95% (**8c**), and 81% (**8d**). Amine **8a** was isolated chromatographically (silica gel, EtOAc/hexanes 1:6 (v/v)) instead of by vacuum distillation. Spectroscopic characteristics agreed with those previously reported for **8a**,[16] **8b**,[16] **8c**,[17] and **8d**.[18]

Dimethyl 2-(*N*-Cyclohexyl-*N*-phenylamino)propanedioate, 9a. Procedure B. Aniline **8a** (0.210 g, 1.20 mmol), DDM

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(18) For **8d**, ref 16 reports the dimethyl ester rather than the diethyl ester.

(0.182 g, 1.15 mmol), rhodium acetate (5 mg, 0.01 mmol). Elution solvent EtOAc/hexanes 1:5 (v/v). Three products were isolated: **9a**, **10a**, and **11a**, in order of elution. Compound **9a** 260 mg (71%), colorless oil. Compound **10a** 30 mg (8%), colorless oil. Compound **11a** 60 mg (11%), colorless oil.

Dimethyl 2-(*N*-Isopropyl-*N*-phenylamino)propanedioate, 9b. Procedure B. Aniline **8b** (0.221 g, 1.66 mmol), DDM (0.215 g, 1.36 mmol), rhodium acetate (7 mg, 0.02 mmol). Elution solvent EtOAc/hexanes 1:5 (v/v). Three products were isolated; **9b**, **10b**, and **11b**, in order of elution. Compound **9b** 288 mg (73%), colorless oil. Compound **10b** 35 mg (8%), colorless oil. Compound **11b** 46 mg (7%), colorless oil.

Dimethyl 2-(*N*-Isopropyl-*N*-(2-methoxyphenyl)amino)-propanedioate, 9c. Procedure B. *N*-Isopropyl-*o*-anisidine **8c** (0.350 g, 2.12 mmol), DDM (0.310 g, 1.96 mmol), rhodium acetate (8 mg, 0.02 mmol). Elution solvent EtOAc/hexanes 1:5 (v/v). Three products were isolated: **9c**, **10c**, and **11c**, in order of elution. Compound **9c** 171 mg (29%), colorless solid mp 67−68 °C. Compound **10c** 305 mg (53%), colorless solid mp 69−69.5 °C. Compound **11c** 17 mg (4%), colorless oil.

Diethyl 3-(*N*-Phenyl-*N*-(bis(carbomethoxy)methyl)-amino)pentanedioate, 9d. Procedure B. Diester **8d** (0.501 g, 1.81 mmol), DDM (0.289 g, 1.83 mmol), rhodium acetate (7 mg, 0.02 mmol). Elution solvent EtOAc/hexanes 1:4 (v/v). Three products were isolated: **9d**, **10d**, and **11d**, in order of elution. Compound **9d** 513 mg (70%), colorless solid, mp 53−54 °C. Compound **10d** 59 mg (8%), colorless oil. Compound **11d** 102 mg (12%), colorless oil.

Dimethyl 2-(Diphenylamino)propandioate, 12. Procedure B. Diphenylamine (341 mg, 2.01 mmol), DDM (312 mg, 1.97 mmol), rhodium acetate (9 mg, 0.02 mmol). Eluted with EtOAc/hexanes 1:1 (v/v). Compound **12** (498 mg) was obtained as a colorless oil.

Dimethyl 2-(*N*-(3-Methoxyphenyl)-*N*-phenylamino)-propandioate, 14. Procedure B. 3-Methoxyphenylphenylamine (401 mg, 2.01 mmol), DDM (312 mg, 1.97 mmol), rhodium acetate (6 mg, 0.01 mmol). Eluted with EtOAc/hexanes 1:4 (v/v). Compound **14** (510 mg) was obtained as a colorless oil.

Reaction of DDM with Bis(2,6-dimethoxyphenyl)-amine, 15. Procedure B followed, except heating for 4 h: **15**[19] (398 mg, 1.38 mmol), DDM (426 mg, 2.70 mmol), rhodium acetate (9 mg, 0.02 mmol). Eluted with EtOAc/hexanes 1:2 (v/v). Obtained 169 mg of **16** as a colorless solid, mp 158−9 °C, and 235 mg of **17** as a colorless solid that darkens in air, mp 131−2 °C.

Azo Salt 21. A solution of 226 mg (1.36 mmol) of 2-diazo-5,5-dimethylcyclohexane-1,3-dione and 7 mg (0.02 mmol) of rhodium acetate in 3.150 g (30.88 mmol) of diisopropylamine was brought to reflux in a nitrogen atmosphere. Within 5 min, an orange precipitate was observed to form. The reaction was refluxed for 5 h. Even though TLC showed diazo compound remaining, the reaction was halted and the orange solid **21** collected by filtration, affording 213 mg after recrystallization from EtOAc: mp 155−6 °C dec; ^{1}H NMR (250 MHz, $CDCl_3$) 17.09 (br s, ca. 1H), 10.14 (br s, ca. 2H), 3.33 (br septet, 2H), 2.43 (br m, 8H), 1.26 (d, J = 6.4 Hz, 12H), 1.07 (s, 12H) ^{13}C NMR (63 MHz, $CDCl_3$): 194.7, 193.0, 186.4 (br), 127.0, 117.5, 52.2 (br), 51.3 (br), 46.3, 31.4, 28.7, 19.4. A prism 0.20 × 0.20 × 0.20 mm suitable for X-ray crystallography was chosen, orthorhombic, *Pbcn*, $Z = 4$, $a = 18.631(2)$ Å, $b = 10.067(5)$ Å, $c = 12.5880(8)$ Å. The diffractometer used was a Rigaku AFC8 with a CCD detector, Mo Kα radiation, ambient temperature, 20 723 reflections (6353 unique) collected to a maximum 2θ of 61.6°. The structure was solved by direct methods with refinement by full-matrix least-squares on F^2, resulting in final R indices of R1 = 0.0731, wR2 = 0.2039 ($I > 2\sigma(I)$), R1 = 0.2211, wR2 = 0.2663 (all data) and a goodness of fit on F^2 of 1.079.

2-(*N*-Isopropyl-*N*-phenylamino)cyclohexane-1,3-dione, 23. Under a nitrogen atmosphere, a mixture of 138 mg (0.999 mmol) of 2-diazocyclohexane-1,3-dione and 1.35 g (9.98 mmol) of *N*-isopropylaniline, **8b**, was stirred until homogeneous. To this was added 2.2 mg (0.0050 mmol) rhodium acetate and the stirring continued at room temperature for 4 h. Silica gel chromatography using EtOAc/hexanes 1:30 (v/v) removed excess **8b**. Subsequent elution with EtOAc/hexanes 1:4 (v/v) afforded 0.16 g **23** as a colorless solid: 65%, mp 166−8 °C; ^{1}H NMR (250 MHz, $CDCl_3$) 7.90 (br s, 1H), 7.18 (t, J = 7.8 Hz, 2H), 6.75−6.81 (m, 3H), 4.07 (septet, J = 6.4 Hz, 1H), 2.48 (br s, 4H), 1.98 (s, 2H), 1.10 (d, J = 6.3 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) 194.9, 175.1, 147.3, 129.3, 119.1, 115.9, 49.1, 37.7, 27.8, 21.9, 21.1, 20.5. Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.34; H, 7.84; N, 5.69.

2-(Diphenylamino)cyclohexane-1,3-dione, 24. Diphenylamine, 0.85 g (5.0 mmol), was heated to approximately 57 °C to melt it. 2-Diazocyclohexane-1,3-dione, 138 mg (0.999 mmol), was added with stirring. After dissolution of the diazo compound, 2.2 mg of rhodium acetate (0.0050 mmol) was added and the reaction stirred 3 h at 57 °C under nitrogen. Chloroform, 1.0 mL, was added, and silica gel chromatography with the same step gradient as for **23** was performed, affording 0.21 g **24** (75%) as a colorless solid, mp 202−4 °C. When the reaction was run on a larger scale, C−H insertion product **25**, mp 194−6 °C, could be isolated in addition to **24**. For **24**: ^{1}H NMR (250 MHz, $CDCl_3$) 7.23 (t, J = 8.0 Hz, 2H), 6.95−7.05 (m, 3H), 2.68 (t, J = 6.2 Hz, 2H), 2.48 (t, J = 6.5 Hz, 2H), 2.07 (quintet, J = 6.4 Hz, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) 194.7, 173.0, 146.4, 129.5, 122.9, 122.0, 120.9, 37.8, 27.8, 20.4. Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.18; H, 6.26; N, 4.92. For **25**: ^{1}H NMR (250 MHz, DMSO-d_6) 10.46 (br s, approximately 1H), 8.08 (s, 1H), 7.18−7.24 (m, 2H), 7.00−7.08 (m, 6H), 6.80−6.75 (m, 1H), 2.45 (br m, 4H), 1.91 (br m, 2H); ^{13}C NMR (63 MHz, DMSO-d_6) ca. 185 (very br), 143.8, 141.0, 131.5, 129.0, 125.5, 119.1, 116.2, 115.9, 33.1 (br), 20.3. EIMS (*m*/*z* (rel int)) 280 (15, M + 1), 279 (65, M), 196 (23), 195 (23), 167 (19), 149 (29), 129 (46), 112 (23), 97 (16), 89 (28), 87 (28), 83 (30), 81 (18), 77 (27), 73 (59), 58 (100).

Ethyl 3-Oxo-2-(*N*-isopropyl-*N*-phenylamino)butanoate, 27. Procedure B. N-isopropylaniline (0.28 g, 2.1 mmol), ethyl diazoacetoacetate (0.48 g, 3.1 mmol), rhodium acetate (4 mg, 0.009 mmol). Eluted with 1:9 (v/v) EtOAc/hexanes, affording 0.32 g (59%) **27** as a colorless oil.

Ethyl 3-Oxo-2-(diphenylamino)butanoate, 28. Procedure B. Diphenylamine (0.24 g, 1.4 mmol), ethyl diazoacetoacetate (0.32 g, 2.0 mmol), rhodium acetate (5 mg, 0.01 mmol). Eluted with 1:8 (v/v) EtOAc/hexanes, affording 0.30 g (70%) **28** as a colorless oil.

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Supporting Information Available: Crystallographic data for **21**, characterization data for **1**−**3**, **5**, **7**, **9a**−**11a**, **9b**−**11b**, **9c**−**11c**, **9d**−**11d**, **12**, **14**, **16**, **17**, **19**, **27**, **28**. This material is available free of charge via the Internet at http://pubs.acs.org. This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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