lution mass spectrum 373.1527, calculated for $C_{20}H_{23}NO_6$ 373.1525. Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.13; H, 6.33; N, 3.56. The NMR spectrum of **4a** taken in $CDCl_3$ was in agreement with the above interpreted spectrum except for the presence of an extra proton exchangeable with D_2O: NMR ($CDCl_3$) δ 1.57 (s, 1 H, exchangeable with D_2O), 2.0–2.6 (m, 4 H, CH_2CH_2), 2.66 (d, J = 15 Hz, 1 H, H-8), 3.16 (d, J = 15 Hz, 1 H, H-8), 3.59 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 3.92 (s, 3 H, OMe), 4.59 (s, 1 H, H-9), 5.71 (s, 1 H, H-11), 5.87 (s, 1 H, aromatic), 6.65 (s, 1 H, aromatic), 6.90 (s, 1 H, H-5).

Further elution produced 20 mg of starting material (**2a**) together with a minor unidentified product, followed by 200 mg (38%) of **3a** as a yellow syrup crystallized from acetonitrile as tan plates: mp 193–95 °C; NMR ($CDCl_3$) δ 1.8–2.6 (m, 5 H, one exchangeable with D_2O), 2.50 (s, 3 H, NCH_3), 3.62 (unresolved d, $J < 1$ Hz, 1 H, H-9), 3.71 (s, 3 H, OMe), 3.87 (s, 6 H, 2 × OMe), 4.90 (unresolved d, $J < 1$ Hz, 1 H, H-10) 6.28 (s, 1 H, H-4), 6.37 (s, 1 H, H-8), 6.76 (s, 1 H, H-1 or H-5), 6.90 (s, 1 H, H-5 or H-1); IR (KBr) 3550 (OH), 1682, 1660, 1638 cm^{-1}; mass spectrum, m/e (relative intensity) 357 (M^+, 83), 342 (40), 326 (37), 192 (100). Anal. Calcd for $C_{20}H_{23}NO_5$: C, 67.27; H, 6.47; N, 3.92. Found: C, 67.25; H, 6.37; N, 3.92.

Anodic Products from *O*-Benzylpallidine (2b). Oxidation of 0.4 g (0.92 mmol) of **2b** at 1.18 V produced, after passage of 2.1 F/mol, 0.38 g of brown oil. Chromatography on Al_2O_3 (III–IV) gave 140 mg (32%) of **4b** as a colorless oil, which crystallized on standing: NMR ($CDCl_3$) δ 1.54 (s, 1 H, exchangeable with D_2O), 2.43 (s, 3 H, NCH_3), 2.0–2.5 (m, 4 H), 2.66 (d, J = 16 Hz, 1 H), 3.16 (d, J = 16 Hz, 1 H), 3.59 (s, 3 H, OMe), 3.91 (s, 3 H, OMe), 4.56 (s, 1 H), 5.12 (s, 2 H), 5.66 (s, 1 H), 5.82 (s, 1 H), 6.68 (s, 1 H), 6.90 (s, 1 H), 7.3–7.4 (m, 5 H); IR (KBr) 1700 cm^{-1}; mass spectrum, m/e (relative intensity) 449 (M^+, 7), 434 (3) 363 (100), 358 (10), 340 (8), 272 (12), 108 (23), 91 (60), 79 (20), 58 (19); high-resolution mass spectrum 449.1839, calculated for $C_{26}H_{27}NO_6$ 449.1836.

Further elution gave 30 mg of starting material **2b** (TLC, NMR), followed by 170 mg (41%) of **3b** as a yellow oil: NMR ($CDCl_3$) δ 1.7–2.5 (m, 5 H, one exchangeable with D_2O), 2.47 (s, 3 H, NCH_3), 3.54 (d, $J < 1$ Hz, 1 H, H-9), 3.77 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 4.81 (d, $J < 1$ Hz, 1 H, H-10), 5.09 (s, 2 H), 6.30 (s, 1 H), 6.34 (s, 1 H), 6.80 (s, 1 H), 6.98 (s, 1 H), 7.3–7.6 (m, 5 H); IR (film) 3430 (OH), 1665, 1640, 1620 cm^{-1}; mass spectrum, m/e (relative intensity) 433 (M^+, 33), 418 (9), 402 (12), 390 (5), 342 (36), 192 (33), 91 (100), 57 (53), 42 (23); high-resolution mass spectrum 433.1902, calculated for $C_{26}H_{27}NO_5$ 433.1887.

Electrochemical Oxidation of *O*-Methylflavinine (2c). The compound (0.5 g, 1.5 mmol) was oxidized at 1.18 V. After passage of 2.6 F/mol the current had dropped from 150 to 40 mA and the electrolysis was discontinued. During the reaction the anolyte remained almost colorless. However, upon neutralization it turned completely black and extractive workup produced only 0.3 g of black semisolid. TLC indicated two major products besides starting material, but chromatography on Al_2O_3 (III–IV) only resulted in a few milligrams of an unidentified oil, followed by 70 mg (13%) of **3c** as a dark viscous oil, which crystallized upon standing: NMR ($CDCl_3$) δ 1.7–2.7 (m, 6 H, 2 exchangeable with D_2O), 3.77 (s, 3 H, OMe) 3.87 (s, 6 H, 2 × OMe), 4.75 (s, 1 H, H-10) 6.30 (s, 1 H), 6.32 (s, 1 H), 6.76 (s, 1 H), 6.92 (s, 1 H); IR (KBr) 3450 (OH, NH), 1665, 1645, 1620 cm^{-1}; mass spectrum, m/e (relative intensity) 343 (M^+, 44), 328 (24), 326 (18), 325 (25), 312 (36), 310 (22), 301 (18), 282 (26), 178 (46), 152 (14), 84 (21), 59 (27), 43 (100); high-resolution mass spectrum 343.1426, calculated for $C_{19}H_{21}NO_5$ 343.1420.

Acknowledgment. This work was supported by the National Institutes of Health.

Registry No. 1a, 1699-51-0; **1b**, 41183-02-2; **1c**, 26642-09-1; **2a**, 22169-18-2; **2b**, 27841-87-8; **2c**, 53403-81-9; **3a**, 79255-32-6; **3b**, 79255-33-7; **3c**, 79255-34-8; **4a**, 79313-46-5; **4b**, 79313-47-6.

Preparation of 3-Hydroxycyclohexaneacetonitriles

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Preparation of *cis*-4-*tert*-butyl-*cis*-3-hydroxycyclohexaneacetonitrile (**2**) and the parent *cis*-3-hydroxycyclohexaneacetonitrile (**1**) is described. In intermediates leading to **2** severe crowding at axially substituted C(3) leads to unusual reactions, including rapid intramolecular oxonium ion formation at 0–5 °C, abnormally easy hydride reduction of a nitrile, and formation of an open-chain hemiacetal that is relatively stable to aqueous acid.

In connection with another investigation we required *cis*-3-hydroxycyclohexaneacetonitrile (**1**, Chart I) and the related *cis*-4-*tert*-butyl derivative **2**, in which the *tert*-butyl group holds the other two substituents effectively locked in axial positions on the ring. We describe here routes to these two nitriles along with related transformations. As might be expected, reactions leading to **2** are dominated by interactions between the two axial substituents, and several examples of unusual chemical behavior resulting from these interactions are noted below. These effects, of course, are absent in **1** and its precursors.

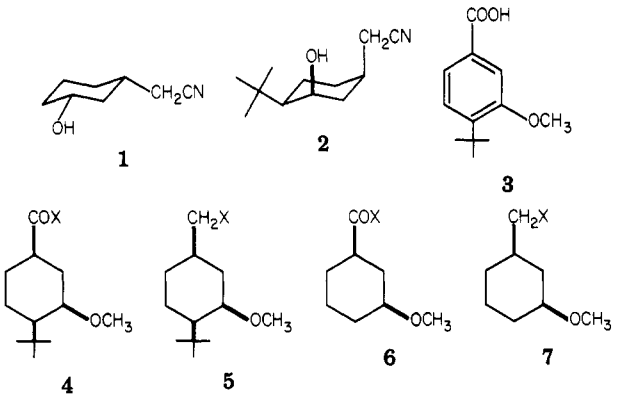
Our first approach to **2** was through the readily available aromatic acid **3**,[1] which absorbed 3 equiv of hydrogen over rhodium-on-alumina to furnish stereoselectively a cyclohexanecarboxylic acid. This was tentatively assumed to be the cis,cis isomer **4a**, since hydrogenation of the phenol corresponding to **3** gives largely the cis,cis product.[1] Furthermore, NMR evidence indicated the methoxy group in the hydrogenated acid to be axial, as the carbinyl proton at C(3) appears at δ 3.5. Our general observation with various compounds in this work has been that this carbinyl proton resonates at ~3.5 ppm when equatorial and at ~3.1 ppm when axial. Such stereochemical effects on chemical shifts are well-known in cyclohexanes.[2] Hydride reduction of **4a** gave the alcohol **5a**, which could be converted to its tosylate **5b** under controlled conditions. If the tosylation reaction was prolonged, the yield of **5b** was reduced with accumulation of a second product, assumed

(1) Noyce, D. S.; Dolby, L. J. *J. Org. Chem.* **1961**, *26*, 1732.

(2) Jackson, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed; Pergamon Press: Oxford, 1968; p 238.

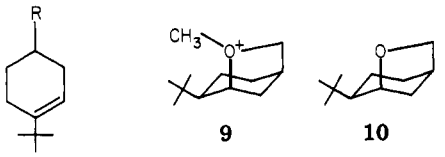
0022-3263/81/1946-4880$01.25/0

Chart I[a]



[a] a, X = OH; b, X = OTs; c, X = Cl; d, X = CN; e, X = CO_2CH_3; f, X = CH_2OH; g, X = CHO; h, X = COOH.

from its NMR spectrum to be the related chloride **5c**. Attempts to purify **5c** by vapor-phase chromatography (VPC) led to isolation of the stable (methoxymethyl)-cyclohexene **8**. Similarly, handling of crude **5b** produced

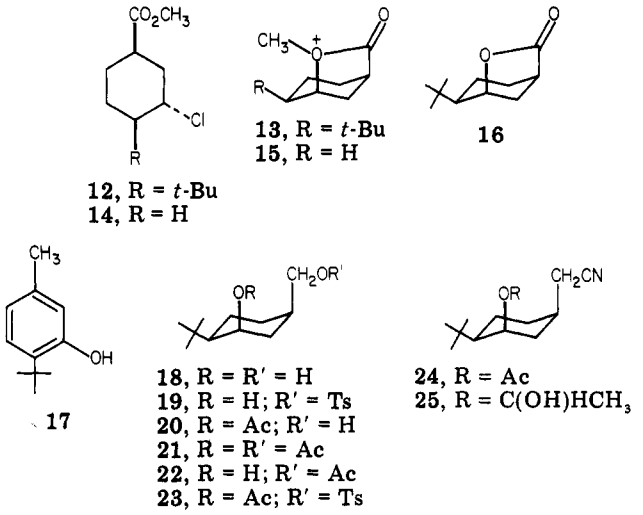


8, R = CH_2OCH_3
11, R = CO_2CH_3

variable amounts of **8**. We interpret this behavior as evidence of easy internal displacement of the tosylate group in **5b** by methoxyl, yielding the methoxonium ion **9**.[3] This intermediate could undergo reversible attack by chloride ion to form **5c** or lose a proton to furnish the methyl ether **8**. An additional reaction of **9** is apparent in the subsequent treatment of the isolated tosylate **5b** with sodium cyanide in dimethyl sulfoxide. This led not only to the desired nitrile **5d** but also to a considerable amount of cyclic ether **10**, as well as some **8**. These transformations requiring such ready cyclization to **9** provide chemical proof of the stereochemistry of this series. The two groups involved must be axial, and this is reasonable only in the cis,cis isomers shown.

We encountered another easily formed oxonium ion in attempting to prepare the acyl chloride from methoxy acid **4a**. Treatment of **4a** with oxalyl chloride yielded largely the unsaturated methyl ester **11**,[4] along with ~15% of the chloro ester **12** (Chart II), even at 0–5 °C. Thus, cyclization to **13** appears to occur very readily. This behavior contrasts with that of the parent acyl halide **6c**, where the ring substituents are preferentially diequatorial. Compound **6c** is stable at room temperature but rearranges at 75 °C by way of oxonium ion **15**, mainly to ester **14** plus some of the related cyclohexene.[5] We ascribe the difference in behavior of **13** and **15** largely to steric hindrance to displacement by chloride ion due to the adjacent *tert*-butyl group in **13**.[6]

Chart II



The same effect presumably influences the behavior of **9**, where nucleophilic displacement at the ring position is absent. Cleavage of the methyl ether in **5d** should lead to the desired hydroxy nitrile **2**, but, unlike results in the parent series discussed below, we were not able to define conditions to achieve this. On exposure of **5d** to boron trihalides or trimethylsilyl iodide[7] a relatively stable complex formed, which under forcing conditions suffered elimination of methanol or apparent displacement of methoxy by halogen but no cleavage of the methyl ether. We attribute this behavior to the considerable hindrance about the axial ether grouping, which thus frustrated this route to **2**.

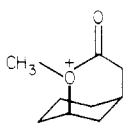
This problem was avoidable by starting with bicyclic lactone **16**, obtained as previously reported from 2-*tert*-butyl-5-methylphenol (**17**).[1] Reduction of **16** with lithium aluminum hydride yielded diol **18**. Attempts to convert **18** preferentially to the primary monotosylate **19** were unrewarding and gave only ether **10**. This was prevented through blocking the secondary hydroxy group as the monoacetate **20**. Acetylation of the diol **18** with excess acetyl chloride and pyridine in methylene chloride at room temperature led to the diacetate **21**, which underwent slow (7–10 h) hydrolysis in aqueous methanol containing potassium carbonate to yield preferentially **20**. Interestingly, hydrolysis of **21** using the same base in *dry* methanol furnished diol **18** in about 1 h. Since cyanoacetate **24** described below is stable to these latter conditions, this behavior of **21** suggests that in dry solvent rapid formation of **20** is followed by rearrangement to the isomeric primary monoacetate **22** and then hydrolysis to **18**. Ester **22** was itself available directly on esterification of diol **18** under milder conditions with 1 equiv of acetyl chloride. Conversion of **20** to the tosylate **23** and then acetoxy nitrile **24** as described above for methyl ether **5a** was straightforward. Removal of the acetyl blocking group of **24**, however, required special attention. Direct hydrolysis of the hindered ester took place only under conditions leading to concomitant reaction of the cyano group. Also, reductive removal of the ester with hydride reagents resulted in attack on the nitrile under conditions that nitriles ordinarily withstand. In some cases the nitrile was completely destroyed before the acetate was totally reduced. We attribute this behavior to a combination of hindrance to external attack on the acetate and very favorable intra-

(3) Perst, H. "Oxonium Ions in Organic Chemistry"; Verlag Chemie: Weinheim/Bergstr., Germany, 1971; Chapter 6 and references cited therein.
(4) Nazarov, I. N.; Titov, Y. A.; Kuznetsova, A. I. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1959**, 1536. Aycard, J.-P.; Bodot, H. *Org. Magn. Reson.* **1975**, *7*, 226.
(5) Noyce, D. S.; Weingarten, H. I. *J. Am. Chem. Soc.* **1957**, *79*, 3093.
(6) For a discussion of factors suggested to be significant in the regiochemistry of the displacement on **15**, see ref 5.
(7) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 612.

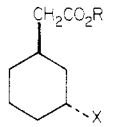
molecular delivery of hydride to the nitrile function from an intermediate derived from the ester group. Successful conditions were finally established through use of sodium bis(2-methoxyethoxy)aluminum hydride[8] at −78 to −40 °C in ether–benzene as solvent. Under these conditions the nitrile was not attacked, and the acetate was reduced to the unusually stable hemiacetal **25**, which could be recognized by its NMR spectrum and also by that of the acetaldehyde released when the mixture was allowed to stand and warm. Even after mild acid workup of the reduction reaction mixture, **25** constituted 80% of the product, and it was hydrolyzed only slowly on shaking with 5% hydrochloric acid. Heating at 50–60 °C permitted complete conversion to the desired hydroxy nitrile **2**. This unusual kinetic stability must reflect the severe hindrance to protonation of the ether oxygen of hemiacetal **25**.

The parent nitrile **1** was available from known *cis*-3-methoxycyclohexanecarboxylic acid (**6a**).[5] This acid was reduced to the alcohol **7a** and converted sequentially to tosylate **7b** and nitrile **7d** without incident. Cleavage of the ether in **7d** with boron tribromide[9] in the desired manner was unsuccessful, and we obtained a mixture of bromocyclohexanes. Trimethylsilyl iodide[7] was more useful, however, and furnished the desired alcohol **1** in good yield.

In related work we have carried out some reactions of the homologous cyclohexaneacetate **7e**, which is available from **6a** by Arndt–Eistert synthesis.[10] Reduction of **7e** with lithium aluminum hydride gave alcohol **7f**, and this was oxidized by chromium trioxide in pyridine[11] to the aldehyde **7g**. Saponification of **7e** gave **7h**. With an interest in determining whether formation of the six-membered cyclic oxonium ion **26**, which is homologous with **15**,



26



27, R = CH_3; X = Cl
28, R = CH_3; X = Br
29, R = H; X = Cl
30, R = H; X = Br

was possible, we treated **7h** with thionyl chloride and also phosphorus tribromide at 110 °C. These reactions gave methyl *trans*-3-chlorocyclohexaneacetate (**27**) and the corresponding bromo ester **28** without difficulty. In the chloro series a considerable amount of alkene was also formed. Ester cleavage with boron tribromide[12] then gave the related carboxylic acids **29** and **30**. These transformations provide convenient access to the 3-trans-substituted series and demonstrate that formation of oxonium ion **26** is indeed favored, although at temperatures much below 90 °C the rearrangement is quite slow. The two homologues **6a**[5] and **7h** then behave similarly.

Experimental Section

General Methods. All VPC was carried out on a Varian Aerograph Model 920 gas chromatograph using a column prepared from aluminum tubing (0.25 in. × 8 ft) packed with 25% QF-1 on 40/60 Chromosorb W and operating at a helium flow rate of 95–120 mL/min. Unless otherwise specified, IR and NMR spectra were obtained for CCl_4 solutions, the former on a Perkin-Elmer Model 237B spectrophotometer and the latter on a Varian T-60A (60 MHz) spectrometer. All NMR signals are reported relative to tetramethylsilane (~1% internal reference; 0 ppm). Melting points were obtained on a Thomas-Hoover apparatus in sealed capillaries and are corrected. Unless otherwise noted, solutions were dried over $MgSO_4$, K_2CO_3, or Na_2SO_4, and solvents were removed in vacuo with a rotary evaporator.

***cis*-3-Methoxycyclohexanemethanol (7a).** A solution of pure cis acid **6a** (2.41 g, 15.3 mmol) in anhydrous ether (70 mL) was added to a cold slurry of $LiAlH_4$ (1.07 g, 28 mmol) in ether (90 mL). The mixture was stirred for 10 min at 0 °C and 2 h at room temperature. A standard workup (see **18**) gave a colorless oil (2.2 g, 100%). A sample was purified by VPC (130 °C, t_r = 11 min) and characterized as **7a**: IR 3633 (w), 3600–3200 (m), 2925 (s), 2856 (m), 2820 (w), 1462 (w), 1444 (m), 1366 (w), 1350 (w), 1094 (s), 1019 (m), 914 (w) cm^{-1}; NMR δ 3.80 (br s, 1 H, variable), overlapping signals 3.33, 3.30, and 3.07 (m, s, and m; 2, 3, and 1 H, respectively), 2.30–0.40 (m, 9 H).

Anal. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.77; H, 11.23.

***cis*-3-Methoxycyclohexaneacetonitrile (7d).** Treatment of **7a** (1.62 g, 11.25 mmol) with *p*-toluenesulfonyl chloride (4.30 g, 22.56 mmol) in pyridine (29 mL) for 24 h at 4 °C afforded (see preparation of **23**) a nearly colorless oil, 3.18 g. The crude product was purified by oiling out from warm pentane, as before, to give **7b**: 3.04 g (10.20 mmol, 91%); IR 2956 (s), 2878 (w), 2839 (w), 1597 (w), 1464 (w), 1450 (w), 1369 (s), 1186 (s), 1174 (s), 1094 (s), 978 (m), 950 (m), 823 (m), 658 (m) cm^{-1}; NMR δ 7.69 (d, J = 8 Hz, 2 H), 7.28 (br d, J = 8 Hz, 2 H), 3.78 (br d, J = 6 Hz, 2 H), 3.23 (s, 3 H), 3.00 (br m, 1 H), 2.45 (br s, 3 H), ~2.2–1.3 (m, 5 H), ~1.3–0.5 (m, 4 H).

A solution of tosylate **7b** (1.23 g, 4.13 mmol) in dimethyl sulfoxide (13.5 mL) was treated with NaCN (386 mg, 7.88 mmol) for 1.75 h at 85–90 °C. Workup as before (see **24**) gave a colorless oil, 568 mg (90%). An analytically pure sample was obtained by VPC (155 °C, t_r = 10 min) and identified as **7d**: IR 2930 (s), 2850 (m), 2820 (w), 2245 (w), 1463 (w), 1447 (m), 1419 (m), 1372 (m), 1355 (w), 1194 (w), 1172 (w), 1128 (br, m), 1094 (s), 978 (w), 944 (w), 914 (w) cm^{-1}; NMR δ 3.30 (s, 3 H), 3.07 (br m, 1 H), 2.28 (br d, J = 6, 2 H), ~2.2–1.4 (m, 5 H), ~1.4–0.6 (m, 4 H).

Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.47; H, 9.95; N, 9.03.

***cis*-3-Hydroxycyclohexaneacetonitrile (1).** Hexamethyldisilane (PCR; 2.029 mL, 10.13 mmol) was added to a solution of iodine (2.565 g, 10.09 mmol) in CH_2Cl_2 (26 mL) under an argon atmosphere.[7] After 15 min at room temperature a solution of nitrile **7d** (1.322 g, 8.64 mmol) in CH_2Cl_2 (3 mL) was added to the reagent dropwise through a septum. The resulting brown mixture was stirred for 2 days at room temperature and poured over ice. The aqueous phase was saturated with sodium chloride and extracted with ether. The combined organic solution was washed with saturated aqueous $NaHSO_3$ and brine and dried. Removal of solvent gave a yellow oil, 1.081 g (90%). A sample, purified by VPC (160 °C, t_r = 12 min), was characterized as **1**: IR ($CHCl_3$) 3639 (w), 3600–3200 (m), 2950 (s), 2875 (m), 2255 (w), 1458 (w), 1444 (m), 1417 (m), 1364 (w), 1320 (vw), 1213 (m, br), 1067 (m), 1031 (s), 1003 (s), 947 (w) cm^{-1}; NMR ($CDCl_3$) δ 3.33 (br m, 1 H), 2.73 (s, 3 H, variable), 2.32 (br d, $J \approx 5.5$ Hz, 2 H), ~2.3–1.4 (m, 5 H), ~1.4–0.7 (m, 4 H); mass spectrum, m/z 139.0985 (M^+ calcd for $C_8H_{13}NO$, 139.0997).

Attempted demethylation of **7d** with BBr_3[9,12] gave a mixture of three products (1:6:12 by NMR and VPC) which were separated by VPC (150 °C, 85% recovered yield). The minor component (t_r = 4 min) appeared to be cyclohexeneacetonitrile from spectral data. The major products were *trans*- and *cis*-3-bromocyclohexylacetonitrile (1:2 ratio) as evidenced by the following spectral properties. For the trans compound (t_r = 18 min): IR 2933 (s), 2883 (w), 2850 (w), 2250 (w), 1442 (m), 1433 (w), 1422 (w, split), 1347 (w, split), 1328 (w), 1247 (m, split), 1230 (m), 1208 (w), 958 (w), 931 (w), 850 (w), 833 (w) cm^{-1}; NMR δ 4.63 (br s, 1 H), 2.40–2.13 (m, 3 H) 2.13–0.08 (m, 8 H). For the cis compound (t_r = 23 min): IR 2933 (s), 2853 (m), 1458 (w), 1442 (m), 1417 (w), 1325 (w), 1231 (w), 1203 (w, split), 1019 (w), 953 (w), 928 (w) cm^{-1};

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(11) Ratcliffe, R.; Rodehorst, R. *J. Org. Chem.* **1970**, *35*, 4000. Collins, J. C.; Hess, W. W.; Frank, F. J. *Tetrahedron Lett.* **1968**, 3363.
(12) Felix, A. M. *J. Org. Chem.* **1974**, *39*, 1427.
(13) Klein, J. *Isr. J. Chem.* **1963**, 387.

NMR δ 4.20–3.60 (m, 1 H, axial CHBr), 2.60–2.13 and 2.13–0.80 (2 m, 11 H).

***cis*-3-Methoxycyclohexaneacetaldehyde (7f).** A solution of ester **7e**[10] (>90% cis isomer; 1.275 g, 6.85 mmol) in anhydrous ether (25 mL) was added to a cold slurry of $LiAlH_4$ (513 mg, 13.5 mmol) in ether (55 mL). The mixture was stirred for 10 min at 0 °C and 1 h at room temperature. The workup (see **18**) gave alcohol **7f**: 1.057 g (97%); IR 3630 (w), 3600–3150 (m), 1462 (w), 1447 (m), 1369 (w, with shoulder), 1089 (s), 1044 (m), 922 (w) cm^{-1}; NMR δ 3.58 (m, 2 H), 3.30 (s, 3 H), 3.25–2.30 (m, 2 H), 2.30–0.50 (m, 11 H).

The above alcohol (1.057 g, 6.69 mmol) in CH_2Cl_2 (4 mL) was oxidized with $CrO_3 \cdot pyr_2$ complex [freshly prepared from 3.96 g (39.6 mmol) of CrO_3 and 6.4 mL (79.2 mmol) of pyridine in 100 mL of CH_2Cl_2][11] in ca. 90% yield (containing traces of trans isomer). The cis aldehyde **7g** was separated by VPC (145 °C, t_r = 7.5 min): IR 2950 (s), 2876 (m), 2840 (m), 2733 (w), 1728 (s), 1461 (w), 1447 (m), 1372 (w), 1178 (w), 1139 (w, split), 1100 (s, with shoulder), 922 (w) cm^{-1}; NMR δ 9.78 (t, $J \approx 1.5$ Hz, 1 H), 3.28 (s, 3 H), ~3.3–2.8 (m, 1 H), 2.48–2.23 (m, 2 H), 2.23–1.35 (m, 5 H), 1.35–0.55 (m, 4 H); mass spectrum, *m/z* 156.1152 (M^+ calcd for $C_9H_{16}O_2$, 156.1150).

The minor trans isomer had the following spectral properties: IR 2927 (s), 2822 (w), 2710 (w), 1726 (s), 1456 (w), 1439 (w), 1358 (w), 1264 (w), 1136 (w), 1117 (w), 1083 (s), 925 (w) cm^{-1}; NMR δ 9.77 (m, 1 H), 3.45 (m, 1 H), 3.28 (s, 3 H), 2.30–0.70 (m, 11 H).

***cis*-3-Methoxycyclohexaneacetic Acid (7h).** The methyl ester **7e** (1.054 g, 5.67 mmol; ≥90% cis isomer) was treated with 20% aqueous NaOH (5.5 mL) for 2.5 h at 100 °C. The resulting solution was washed with a small portion of ether, neutralized with 10% aqueous HCl and extracted with ether. The organic phase was washed with brine and dried. Removal of solvent yielded a viscous, nearly colorless oil (0.942 g, 97%) which was identified as **7h**: IR 3600–2400 (s), with overlapping 2950, 2880, and 2833 (m, w, and w, respectively), 1708 (s), 1447 (w), 1408 (w), 1372 (w), 1353 (w), 1283 (m), 1200 (w, split), 1169 (w), 1131 (w), 1092 (m), 917 (w) cm^{-1}; NMR δ 10.60 (br s, 1 H, variable), 3.30 (s, 3 H), 3.30–2.80 (m, 1 H), 2.40–1.47 (m, 7 H), 1.47–0.50 (m, 4 H); mass spectrum, *m/z* 172.1115 (M^+ calcd for $C_9H_{16}O_3$, 172.1100).

Methyl *trans*-3-Chlorocyclohexaneacetate (27). Acid **7h** (296 mg, 1.72 mmol; ~95% cis isomer) was treated with oxalyl chloride (450 μL, 5.16 mmol; Aldrich) at room temperature under an argon atmosphere. After 1.5 h the mixture was heated in an oil bath (110 °C) for 3.25 h and poured over ice and saturated aqueous $NaHCO_3$. (Aliquots analyzed by IR during a separate run revealed that the rearrangement of the intermediate acid chloride was very slow below 70 °C and not even complete after 2.5 h at 100 °C.) Pentane workup afforded a pale yellow oil consisting of two esters [2:3 cyclohexenyl and chlorocyclohexyl ester, respectively, by NMR; 200 mg, 70% yield (based on *cis*-**7h**)] which were separated by VPC (155 °C, t_r = 3 and 10 min). The minor product was assumed to be methyl cyclohex-3-eneacetate[13] on the basis of the analogous product reported[5] in the rearrangement of acid **6a** and of spectral data: IR 3050 (w), 2944 (m), 2861 (w), 1742 (s), 1647 (vw), 1431 (m), 1342 (w, split), 1275 (w), 1203 (w), 1147 (m), 1003 (w) cm^{-1}; NMR δ 5.63 (m, 2 H), 3.67 (s, 3 H), 2.35–0.80 (m, 9 H). The major product (t_r = 10 min) was characterized as the *trans*-chloride **27**: IR 2956 (s), 2888 (w), 2856 (w), 1739 (s), 1442 (w), 1431 (m), 1322 (w, split), 1314 (w, split), 1264 (m, split), 1242 (w), 1150 (m), 1133 (w), 1011 (w), 994 (w), 853 (m), 678 (w) cm^{-1}; NMR δ 4.38 (m, 1 H), 3.63 (s, 3 H), 2.37–2.00 (m, 4 H), 2.00–0.70 (m, 7 H); mass spectrum, *m/z* 190.0805 (M^+ calcd for $C_9H_{15}{}^{35}ClO_2$, 190.0761).

Similar results were obtained with $SOCl_2$ and **7b** (alkene/chloride ratio ca. 1:1).

Methyl *trans*-3-Bromocyclohexaneacetate (28). Acid **7h** (300 mg, 1.74 mmol; ~95% cis) was treated with PBr_3 (150 μL, 1.60 mmol; Aldrich) under an argon atmosphere, and the mixture was heated in an oil bath (75–90 °C) for 2 h. The workup (see preparation of **27**) gave a colorless oil (280 mg, 72% based on *cis*-**7h**) which appeared to be mainly one product (no alkene by NMR or VPC). A sample purified by VPC (175 °C, t_r = 7 min) was characterized as **28**: IR 2974 (s), 2883 (vw), 1739 (s), 1433 (m), 1356 (w), 1189 (w), 1144 (w), 1006 (w, split), 851 (w, with shoulder) cm^{-1}; NMR δ 4.55 (br s, 1 H), 3.63 (s, 3 H), 2.50–0.80 (m, 11 H); mass spectrum, *m/z* 234.0247 (M^+ calcd for $C_9H_{15}{}^{79}BrO_2$, 234.0255).

***trans*-3-Chlorocyclohexaneacetic Acid (29).** A solution of ester **27** (80 mg, 0.42 mmol) in CH_2Cl_2 (11 mL) was cooled in a −10 °C bath and treated with BBr_3 (2.25 mL, 1 M solution in CH_2Cl_2).[12] The resulting solution was stirred for 1 h at −10 °C and 2 h at room temperature under an argon atmosphere. Toluene (~3 mL) was added, and excess reagent and solvent were removed under a stream of nitrogen followed by evaporation under vacuum (aspirator). The residue was diluted with toluene and treated with ice–water (~15 mL). The layers were separated, and the aqueous phase was saturated with NaCl and extracted with pentane. The combined organic solution was washed with brine and dried. Removal of solvent gave a yellowish oil which solidified upon standing (75 mg, 100%). A sample was purified further by extraction (base/acid), recrystallized from *n*-hexane, and identified as **29**: mp 87.0–88.0 °C; IR 3600–2500 (s), with overlapping 2960 (m), 1711 (s), 1444 (w), 1405 (w), 1280 (w), 1244 (w), 858 (m) cm^{-1}; NMR δ 11.70 (br s, 1 H, variable), 4.40 (m, 1 H), 2.60–2.10 (m, 3 H), 2.10–0.70 (m, 8 H); mass spectrum, *m/z* 176.0602 (M^+ calcd for $C_8H_{13}{}^{35}ClO_2$, 176.0613).

***trans*-3-Bromocyclohexaneacetic Acid (30).** Ester **28** (311 mg, 1.32 mmol) was demethylated by following the procedure for **27**. Workup gave a greenish oil (299 mg, 100%) which solidified. Repurification by extraction gave a nearly white solid, 270 mg (93%). A sample recrystallized from *n*-hexane was characterized as **30**: mp 91.5–94.0 °C; IR 3500–2400 (s), with overlapping 2960 (m), 1708 (s), 1442 (w), 1408 (w), 1289 (w), 1247 (w), 1200 (w), 928 (w), 853 (w) cm^{-1}; NMR δ 11.10 (s, 1 H, variable), 4.59 (br s, 1 H), 2.80–0.70 (m, 11 H); mass spectrum, *m/z* 222.0055 (M^+ calcd for $C_8H_{13}{}^{81}BrO_2$, 222.0031).

***cis*-4-*tert*-Butyl-*cis*-3-Hydroxycyclohexanemethanol (18).** The procedure of Noyce and Dolby[1] was used to prepare *cis*-4-*tert*-butyl-*cis*-3-hydroxycyclohexanecarboxylic acid lactone (**16**) from 6-*tert*-butyl-3-methylphenol (**17**; ICN or Fluka). A solution of the recrystallized lactone (1.72 g, 9.4 mmol) in anhydrous ether (55 mL) was added to a cold (0–5 °C) slurry of $LiAlH_4$ (0.79 g, 21 mmol) in ether (90 mL) over 10 min. The mixture was stirred for 10 min at 5 °C and 2.5 h at room temperature under nitrogen. The resulting slurry was cooled in an ice bath and hydrolyzed with saturated aqueous Na_2SO_4 (8 mL). The solids were filtered and washed with warm ether. The combined solution was washed with brine and dried. Removal of solvent followed by recrystallization from ether gave a white solid (1.60 g, 91%) which was characterized as diol **18**: mp 134–135 °C; IR ($CHCl_3$) 3610 (m), 3550–3125 (m), 3000 (w), 2950 (s, with shoulders), 1465 (w, split), 1431 (w), 1387 (w), 1358 (w), 1213 (m, br), 1019 (m), 990 (w), 949 (w), 925 (w) cm^{-1}; NMR ($CDCl_3$) δ 4.18 (br s, 1 H), 3.72 (m, 2 H), 2.83 (br s, 2 H, variable), 2.20–1.20 (m, 8 H), 0.95 (s, 9 H). An analytical sample was prepared by recrystallization from CH_2Cl_2–ether; mp 134.5–135.0 °C (shiny white needles).

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.92; H, 11.90. Found: C, 71.11; H, 11.94.

***cis*-4-*tert*-Butyl-*cis*-3-hydroxycyclohexanemethyl Acetate (22).** Acetyl chloride (120 μL, 1.68 mmol; MCB) was added over a period of 60 min to a cold (0 °C) solution of diol **18** (313 mg, 1.68 mmol) in CH_2Cl_2 (34 mL) containing pyridine (140 μL, 1.73 mmol). The mixture was stirred for an additional 20 min at 0 °C and 30 min at room temperature and treated with ice. Ether was added and the aqueous phase separated. Workup with ether gave a yellowish oil which solidified (100%). VPC and NMR analysis revealed the presence of ~75% of desired acetate **22** and minor quantities of **18**, **20**, and **21**. A portion of the product was purified by VPC (180 °C, t_r = 8 min; sticky white solid) and characterized as **22**: IR 3610 (w), 3600–3300 (m), 2930 (s, split), 2850 (w), 1737 (s, with shoulder), 1475 (w), 1463 (w), 1445 (w), 1386 (w), 1358 (m), 1242 (s, br), 1169 (w), 1022 (m) cm^{-1}; NMR δ 4.23 (m, $J \approx$ 0–4 Hz, concentration dependent, and $J \approx 7$ Hz, 3 H), 2.20 (br s, 1 H, variable), 2.00 (s, 3 H), 2.00–1.20 (m, 8 H), 0.95 (s, 9 H); mass spectrum, *m/z* 228.1724 (M^+ calcd for $C_{13}H_{24}O_3$, 228.1726.

***cis*-4-*tert*-Butyl-*cis*-3-acetoxycyclohexanemethanol (20).** A solution of diol **18** (605 mg, 3.25 mmol) in dichloromethane (70 mL) containing pyridine (980 μL; 12.11 mmol) was treated with acetyl chloride (860 μL, 12.11 mmol) at 5 °C. The mixture was stirred for 20 h at room temperature. Workup (see **22**) gave a

yellow oil (880 mg, 100% yield; essentially pure **21** as evidenced by NMR and VPC) which was used without further purification. A colorless sample obtained by VPC (180 °C, t_r = 13 min) had the following spectral properties: IR 2950 (s), 2855 (w), 1738 (s), 1469 (w, split), 1448 (w), 1433 (w), 1392 (w), 1362 (s), 1236 (s), 1192 (w), 1175 (w), 1028 (m), 1011 (m), 950 (w), 908 (w) cm^{-1}; NMR δ 5.17 (br s, 1 H), 4.00 (m, 2 H), 2.33–1.03 (m, with overlapping s at 1.98, 8 + 6 H), 0.90 (s, 9 H). Diacetate **21** was also prepared by acetylation of **22** with excess acetyl chloride and pyridine as above.

A solution of **21** (831 mg, 3.08 mmol) in methanol (14.6 mL) was treated with aqueous K_2CO_3 (428 mg, 3.10 mmol, in 8.4 mL of H_2O) at room temperature. The progress of the hydrolysis was followed by VPC. After 11 h, ether workup afforded a quantitative yield of yellow oil (90% desired acetate by NMR) which solidified. The product was used as is. A recrystallized sample (fine white needles from hexane or from cyclohexane/pentane) was identified as **20**: mp 73.5–74.5 °C; IR 3625 (w), 3625–3100 (m), 2950 (s), 2911 (w), 2874 (w), 1737 (s), 1475 (w), 1445 (w), 1430 (w), 1392 (w), 1372 (w), 1361 (m), 1242 (s), 1189 (w), 1092 (w), 1022 (m), 909 (w), 853 (w) cm^{-1}; NMR 5.15 (s with fine structure, 1 H), 3.52 (m, 2 H), 2.20 (s, 1 H, variable), 2.20–1.10 (m, with overlapping s at 1.97, 11 H), 0.90 (s, 9 H); mass spectrum m/z 185.1553 ($M^+ - CH_3CO$ calcd for $C_{11}H_{21}O_2$, 185.1541).

Anal. Calcd for $C_{13}H_{24}O_3$: C, 68.38; H, 10.59. Found: C, 68.40; H, 10.66.

***cis*-4-*tert*-Butyl-*cis*-3-acetoxycyclohexaneacetonitrile (24).** A solution of alcohol **20** (0.72 g, 3.1 mmol of crude) in pyridine (4.5 mL) was cooled in an ice bath and treated with *p*-toluenesulfonyl chloride (1.25 g, 6.6 mmol). The mixture was stored at 4 °C for 29 h, poured over ice, and extracted with ether. The combined ether solution was washed several times with saturated aqueous $CuSO_4$ (until no more Cu–pyr complex could be detected) and brine and dried. Removal of solvent gave a yellow oil which was partially purified by shaking with warm pentane (1–2 mL) and separating the tosylate that oiled out: 1.14 g (97% yield; 98% pure **23** by NMR); IR 2960 (m), 2865 (w), 1742 (s), 1597 (w), 1447 (w), 1361 (s), 1181 (m), 1170 (s), 964 (m), 653 (w) cm^{-1}; NMR δ 7.69 (d, J = 8 Hz, 2 H), 7.28 (d, J = 8 Hz, 2 H), 5.20 (br s, 1 H), 4.03 (m, 2 H), 2.45 (br s, 3 H), 2.20–1.00 (m, with overlapping s at 1.97, 8 + 3 H), 0.87 (s, 9 H).

Tosylate **23** (1.14 g, 2.98 mmol) in anhydrous dimethyl sulfoxide (14 mL) was treated with NaCN (312 mg, 6.37 mmol) under a nitrogen atmosphere. The solution was stirred for 3.5 h at 85–95 °C and for 1 h at room temperature and poured over a mixture of saturated aqueous NH_4Cl and ice. The aqueous phase was extracted with pentane, and the combined organic solution was washed with water and brine and dried. Removal of the solvent afforded a yellow oil, 668 mg (95% yield consisting of 95% **23** and 5% starting material by NMR; the latter was avoided by prolonging reaction times). Bulb-to-bulb distillation [140–180 °C (0.15 torr)] afforded a colorless oil, 592 mg (2.50 mmol, 84%). A sample purified by VPC (178 °C, t_r = 29 min) was characterized as **24**: IR 2980 (m, with shoulders), 2880 (w), 2250 (w), 1740 (s), 1446 (w), 1431 (w), 1419 (w), 1392 (w), 1367 (m, split), 1222 (s, with shoulders), 1197 (w), 1177 (w), 1086 (m), 1008 (m) cm^{-1}; NMR δ 5.27 (s with fine structure, 1 H), 2.63–2.40 (m, 2 H), 2.40–2.07 (br s, 1 H), 2.07–1.07 (m, with overlapping s at 2.00, 7 + 3 H), 0.89 (s, 9 H).

Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found: C, 71.07; H, 9.76; N, 5.86.

***cis*-4-*tert*-Butyl-*cis*-3-hydroxycyclohexaneacetonitrile (2).** A solution of acetate **24** (346 mg, 1.46 mmol) in anhydrous ether (6.2 mL) was cooled (−70 °C, nitrogen atmosphere), and sodium bis(2-methoxyethoxy)aluminum hydride[8] (1.2 mL of 70% Vitride solution in benzene, ~6.1 mmol; Realco Co.) was added dropwise over a period of 40 min. The solution was gradually (ca. 30 min) warmed up to −40 °C, stirred for 2 h at −40 °C, and treated with ice. More ether was added and the mixture stirred for 10 min in an ice bath and 10 min at room temperature. The two layers were separated, and the aqueous layer was extracted with ether. The combined organic phase was washed with 5% aqueous HCl, water, and brine and dried. Removal of solvent gave a yellow oil which upon being heated at 50 °C in vacuo yielded a crude solid, 271 mg (1.39 mmol, 96% yield from crude **24**, 85% pure by NMR). Recrystallization from pentane afforded a pure sample for characterization of **2**: mp 83.5–84.5 °C; IR 3600 (w), 3600–3250 (m), 2950 and 2910 (s, merged), 2860 (w), 2249 (w), 1476 (w), 1464 (w), 1447 (w), 1416 (w), 1383 (w), 1358 (s), 1297 (w), 1225 (w), 1172 (w), 1097 (m), 1024 (vw), 1010 (vw), 970 (m), 947 (w), 855 (w) cm^{-1}; NMR δ 4.22 (br s with fine structure, 1 H), ~3.2–2.4 (sharp m, pattern variable with concentration, 2 H), ~2.4–1.1 (m, 9 H), 0.95 (s, 9 H).

Anal. Calcd for $C_{12}H_{21}NO$: C, 73.79; H, 10.84; N, 7.17. Found: C, 73.96; H, 10.96; N, 7.08.

Spectroscopic analysis of the initial oil obtained in several runs, after acid workup, indicated the presence of hemiacetal **25** (up to 80% of mixture) as the initial product of the hydride reduction. In comparison to **2**: IR, more intense bands in the 1125–1025-cm^{-1} region; NMR, additional signals at δ 4.91 (br q, $J \simeq$ 5 Hz, 1 H, $OC(OH)HCH_3$) and 1.30 (sharp d, $J \simeq$ 5 Hz, overlapping with other signals, $OC(OH)HCH_3$). Further treatment with 5% aqueous HCl hydrolyzed only a portion of the hemiacetal. Heating in vacuo as above or over molecular sieves (4A) in solution resulted in complete conversion to **2**. When a saturated pentane solution of the oil (**25** plus **2**) was seeded with **2**, the hydroxy nitrile gradually crystallized out (1 week, 4 °C). The supernatant contained acetaldehyde, as evidenced by its characteristic odor and NMR signals: δ 9.68 (q, $J \approx$ 3 Hz), 2.15 (d, $J \approx$ 3 Hz).

***cis*-3-Methoxy-*cis*-4-*tert*-butylcyclohexanecarboxylic Acid (4a).** A mixture of 3-methoxy-4-*tert*-butylbenzoic acid[1] (2.27 g, 10.9 mmol) and 5% rhodium-on-alumina catalyst (0.69 g) in glacial acetic acid (35 mL) was hydrogenated in a Parr apparatus at an initial pressure of 49 psi. After 25 h, filtration and removal of solvent gave a quantitative yield of a white solid (2.33 g) which appeared to be ≥90% pure by NMR and VPC (180 °C, t_r = 6.5 min). The product was used in subsequent reactions without further purification. However, traces of trans isomers and/or hydrogenolysis products were removed by recrystallization from *n*-hexane, followed by pentane, to afford an analytically pure sample of **4a**: mp 123.0–124.0 °C; IR 3625–2300 (s), with overlapping 2980 and 2840 (s and w), 1702 (s), 1476 (w), 1455 (w), 1412 (w), 1361 (w), 1330 (w), 1295 (w), 1238 (m), 1202 (w), 1094 (m), 1080 (w), 1063 (w), 1038 (w), 935 (w) cm^{-1}; NMR δ 11.97 (br s, 1 H, variable) 3.53 (br s, 1 H), 3.20 (s, 3 H), ~2.9–1.0 (m, 8 H), 0.90 (s, 9 H).

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35. Found: C, 67.43; H, 10.25.

***cis*-4-*tert*-Butyl-*cis*-3-methoxycyclohexanemethanol (5a).** A solution of acid **4a** (2.33 g, 10.8 mmol) in anhydrous ether (80 mL) was added to a slurry of $LiAlH_4$ (0.74 g, 19.5 mmol) in ether (65 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C and 2 h at room temperature and hydrolyzed (see **18**). The usual workup gave a viscous oil, 2.15 g (98% yield, 90% pure). A sample, purified by VPC (150 °C, t_r = 9 min), was identified as **5a**: IR 3635 (w), 3600–3100 (s), 2950 (s), 2910 and 2875 (shoulders), 1474 (w), 1450 (w), 1387 (w), 1358 (m, with shoulder), 1330 (w), 1225 (w), 1179 (w), 1100 (m), 1079 (m), 1065 (m), 1022 (m), 922 (m) cm^{-1}; NMR δ 3.60 (m, 3 H), 3.28 (s, 3 H), 3.00 (br s, 1 H, variable), 2.33–1.10 (m, 8 H), 0.91 (s, 9 H); mass spectrum, m/z 200.1777 (M^+ calcd for $C_{12}H_{24}O_2$, 200.1776).

***cis*-4-*tert*-Butyl-*cis*-3-methoxycyclohexaneacetonitrile (5d).** A cold (0–5 °C) solution of **5a** (748 mg, 3.74 mmol) in pyridine (10 mL) was treated with *p*-toluenesulfonyl chloride (1.64 g, 8.60 mmol). After 44 h at 4 °C the workup (see **23**) gave a crude oil (1.1 g) consisting of ~70% desired tosylate **5b** and 25% chloride **5c** (by NMR). Aliquots taken during various preparations of **5b** revealed that no starting material remained after 24 h (**5b**/**5c** ratio of ca. 4:1), and the ratio of **5b** to **5c** decreased with prolonged reaction times (after 65 h, **5b**/**5c** ratio was ca. 3:2). Recrystallization of the above crude oil from petroleum ether (crude **5b** difficult to handle due to decomposition) gave nearly pure **5b** as a white solid: 644 mg (49% from crude **5a**); IR 2950 (s), 1597 (w), 1447 (w), 1367 (s), 1185 (m), 1172 (s), 1077 (w), 964 (m), 655 (w) cm^{-1}; NMR δ 7.69 (d, J = 8 Hz, 2 H), 7.24 (d, J = 8 Hz, 2 H), 4.08 (m, pattern variable with concentration, 2 H), 3.47 (br s, 1 H), 3.18 (s, 3 H), 2.43 (br s, 3 H). 2.30–1.10 (m, 8 H), 0.86 (s, 9 H).

The supernatant from the above crystallization contained a mixture (440 mg) of **5b** and **5c** (4:5 ratio). The characteristic NMR signals of **5c** [δ 3.67 (m, CH_2Cl), 3.27 (s, OCH_3), 0.88 (s, *t*-Bu)] were deduced by comparison of the spectrum of pure **5b** with that of the mixture. The attempted isolation (VPC) of **5c** (from a

mixture with **5d**) resulted in rearrangement to **8** (see preparation of **5d**, below). Ether **8** was also obtained as the only identifiable product from the decomposition of **5b**.

A mixture of pure tosylate **5b** (560 mg, 1.58 mmol) and NaCN (147 mg, 3.00 mmol) in anhydrous dimethyl sulfoxide (5 mL) was heated in an oil bath for 2.5 h at 85–90 °C. The workup (see nitrile **24**) gave a colorless oil (239 mg) which appeared to be a mixture of **5d**, **10**, and **8** (ca. 5:3:2, respectively, by NMR). Bulb-to-bulb distillation at aspirator pressure (90–120 °C) gave a fraction (120 mg) containing mainly the ethers (**10**/**8**/**5d**, ca. 10:7:3). Further distillation at 1 torr (80–180 °C) gave a second fraction (119 mg, 35% recovered yield) containing mainly the desired nitrile **5d** (ethers ≤10%). A sample obtained by VPC (170 °C, t_r = 10 min) was used for identification: IR 2950 (s), 2820 (w), 2248 (w), 1472 (w), 1456 (w, split), 1422 (w, split), 1387 (w), 1356 (m), 1224 (w), 1200 (w), 1174 (w), 1092 (s), 1067 (m, split), 1038 (w), 939 (w), 928 (w), 849 (w) cm^{-1}; NMR δ 3.57 (s, with fine structure, 1 H), 3.33 (s, 3 H), 3.00–2.00 (m, 4 H), 2.00–1.20 (m, 6 H), 0.92 (s, 9 H); mass spectrum, m/z 209.1777 (M^+ calcd for $C_{13}H_{23}NO$, 209.1779). Varying reaction conditions did not improve the yield of **5d** appreciably (maximum 60% in crude mixture).

A mixture of **5b** and **5c** (ca. 56% **5c**) was treated with NaCN as above. Inspection of the crude mixture by NMR (ca. 50% **5c**, plus products from **5b**) revealed that **5c** was recovered unchanged. Attempted isolation of **5c** from the above mixture by VPC gave ether **8** as the major volatile product (ca. 55% of isolated material), characterized from the following data: IR 3075 (w), 2984, 2939, and 2888 (s, merged), 1473 (w), 1456 (m), 1386 (w), 1356 (w), 1240 (w), 1161 (w), 1127 (m), 1109 (m), 1089 (m), 947 (w) cm^{-1}; NMR δ 5.37 (br s, 1 H), 3.25 and 3.15 (s and m, 3 + 2 H), 2.40–1.20 (m, 8 H), 1.03 (s, 9 H); mass spectrum, m/z 182.1681 (M^+ calcd for $C_{12}H_{22}O$, 182.1670).

***endo*-4-*tert*-Butyl-6-oxabicyclo[3.2.1]octane (10).** Treatment of alcohol **18** with 1 equiv of *p*-toluenesulfonyl chloride in pyridine or with 1 equiv of $SOCl_2$ in CH_2Cl_2 (containing 1 equiv of pyridine) gave ether **10** as the major product. The colorless volatile liquid was isolated by VPC (120 °C, 7 min) and characterized as follows: IR 2950 (s), 2869 (s), 1475 (w), 1464 (w), 1448 (w), 1385 (w), 1363 (m, split), 1281 (w), 1255 (w), 1180 (w), 1163 (w), 1083 (m, split), 999 (w), 975 (w), 960 (w), 908 (w), 897 (w), 886 (w), 863 (m) cm^{-1}; NMR δ 4.28 (d, J = 6.0–6.5 Hz, 1 H), 3.65 (d, J = 2.0–2.5 Hz, 2 H), 2.27 (br s, 1 H), ~2.3–1.1 (m, 7 H), 0.87 (s, 9 H).

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.38; H, 11.85.

Methyl 4-*tert*-Butyl-3-cyclohexenecarboxylate (11) and Methyl *cis*-4-*tert*-Butyl-*trans*-3-chlorocyclohexanecarboxylate (12). Oxalyl chloride (160 μL, 1.83 mmol) was added to a cold (ca. 5 °C) solution of acid **4a** (70 mg, 0.33 mmol) in benzene (0.5 mL). After 1 h at 0–5 °C, the IR spectrum of an aliquot revealed only an ester carbonyl and no acid chloride or starting material. Excess reagent and solvent were removed in vacuo. VPC (155 °C) of the residue gave two products, identified as **11** (54.4 mg, 84%; t_r 7 min)[4] and **12** (11.3 mg, 15%; t_r = 16 min). For **11**: IR 3080 (w), 2985 (s, split), 2890 (w), 2820 (w), 1738 (s), 1473 (w), 1455 (w), 1430 (m), 1355 (m), 1244 (w), 1220 (w), 1187 (w), 1156 (m), 1078 (w), 1062 (w), 1025 (m), 917 (w), 892 (w), 853 (m) cm^{-1}; NMR δ 5.43 (s, with fine structure, 1 H), 3.63 (s, 3 H), 2.65–1.37 (m, 7 H), 1.03 (s, 9 H). For **12**: IR 2978 (s), 2891 (w), 1737 (s), 1430 (w), 1389 (w), 1362 (w), 1240 (w), 1186 (m), 1162 (m), 1022 (w), 851 (m) cm^{-1}; NMR δ 4.33 (m, 1 H), 3.63 (s, 3 H), 3.10–2.50 (m, 1 H), 2.50–1.30 (m, 7 H), 1.00 (s, 9 H); mass spectrum (CI), m/z 233.1297 [$(M + H)^+$ calcd for $C_{12}H_{21}{}^{35}ClO_2$, 233.1347].

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Palladium(0)-Catalyzed Arylation of Olefins by Arylamines and an Alkyl Nitrite

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Various olefins were arylated by the combination of arylamines and *tert*-butyl nitrite under palladium catalysis in the presence of acid such as monochloroacetic or acetic. The reaction proceeded in good yields without serious effects from substituents on either the olefinic substrates or the arylamines, including 3-aminopyridine.

Recently we reported that palladium(0) effectively catalyzed the arylation of olefins by arenediazonium salts.[1] The arylation was applicable to olefins bearing either electron-releasing or -withdrawing group(s) but was limited to the diazonium salts which we were able to manipulate at room temperature. Preliminary study[2] suggested that the limitation could be overcome by the use of the combination of an arylamine and *tert*-butyl nitrite for the arylation. The present paper deals with the effects of reaction conditions and of substituents of both the olefins and the arylamines on the reaction.

Results and Discussion

Effects of Reaction Conditions and Substituents of Arylamines on Arylation of Styrene. Dropwise addition of *tert*-butyl nitrite in acetic acid to a stirred mixture of an arylamine, styrene, bis(dibenzylideneacetone)palla-

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