286.4 (3.96), 469 (sh) (3.99), 480 (4.00), 494.4 (4.01), 512 (inf) (3.85), 529.6 (3.77).

1,4-Dihydroxy-8-methoxy-2-methylanthraquinone (16b). The procedure described above for the preparation of **14a** was used to acetylate reductively 0.252 g of **6b** to **14b**, which crystallized in long needles when the extraction solvent, methylene chloride, was evaporated. The entire product **14b** was oxidized and hydrolyzed by the procedure described for the preparation of **16a**, giving 141 mg of **16b** (50% yield based on **6b**): mp 208–210.5 °C (chloroform–hexane) (lit.[5a] mp 209–211 °C); IR (KBr) 1610 cm^{-1}; MS *m/e* 284 (M^+), 266, 254, 238; NMR ($CDCl_3$) 2.30 (s, 3 H), 4.01 (s, 3 H), 7.03 (s, 1 H), 7.60 (m, 3 H), 12.85 (s, 1 H), 13.60 (s, 1 H); UV (log ε) 231 (4.56), 247.5 (4.31), 285.5 (3.95), 470 (sh) (4.00), 479.5 (4.01), 493 (4.01), 512 (inf) (3.87), 528 (3.77) nm.

Anal. Calcd for $C_{16}H_{12}O_5$: C, 67.60; H, 4.26. Found: C, 67.58; H, 4.30.

Islandicin (1a). A 50-mL flask was charged with 17.0 mg of methylislandicin (**16a**) and dissolved in 7 mL of glacial acetic acid and 7 mL of 48% hydrobromic acid. This solution was heated under reflux for 5 h under a nitrogen atmosphere. The hot solution was filtered and upon cooling to room temperature islandicin crystallized as dark red lustrous plates (14.1 mg, 87%). Recrystallization from chloroform–ligroin gave pure islandicin, mp 220–221 °C (lit.[1] mp 218 °C).

Digitopurpone (1b). Digitopurpone was prepared as described above for islandicin, starting with 7.0 mg of digitopurpone methyl ether and yielding 3.4 mg (51%) of bright red needles, mp 210.5–212 °C (lit.[2] mp 209–211 °C) from chloroform–ligroin.

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Registry No. 1a, 476-56-2; **1b**, 34425-57-5; **6a**, 71785-94-9; **6b**, 71785-95-0; **8**, 2944-49-2; **9**, 71785-96-1; **10**, 71785-97-2; **11**, 4792-33-0; **12**, 6293-55-6; **13**, 13070-25-2; **14a**, 71785-98-3; **14b**, 71785-99-4; **16a**, 71786-00-0; **16b**, 68047-75-6.

Pyridinium Halides as Reagents: Ring Fission Modes in α-Cyclopropyl Ketones and Oximes

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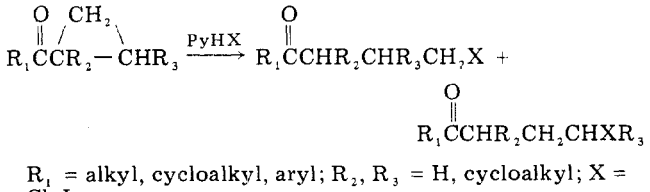
Cyclopropyl ring fission reactions by both nucleophilic and electrophilic reagents are the subject of current interest.[1]

We recently proposed pyridinium chloride in acetonitrile as a mild reagent for cyclopropyl ring fission of α-cyclopropyl ketones.[2,3] The products were γ-chloro ketones.



R_1 = alkyl, cycloalkyl, aryl; R_2, R_3 = H, cycloalkyl; X = Cl, I

Table I. Reaction of α-Cyclopropyl Ketones with Pyridinium Halides[a]

substrate	PyHCl	PyHI
1	2	3
4	5	6
7	8	9
10	11	12
13	14	15
16	17	18
19	20	21
22	23	24
25	26	27

[a] The residue percentage was the starting ketone.

Among the substrates we tested (**1**, **6**, **9**, **19**, and **22**), bicyclo[4.1.0]heptan-2-one (**6**) and 1-acetylbicyclo[4.1.0]-heptane (**19**) gave a selective ring fission reaction, while other substrates (**1** and **9**) gave products coming from the two possible modes of cyclopropyl ring fission (Table I).

Clearly this point is a limiting factor for the synthetic scope of this reaction, although, in most cases, a satisfactory chromatographic separation of the two chloro ketones is possible. In order to gain more information on the factors directing the reaction and to improve the synthetic potential, we enlarged the study to other substrates and conditions. First, we considered the possibility of changing the nucleophilic part of the reagent, and then we tested pyridinium iodide in the hope of gaining a more selective ring opening.

Most of the substrates (**1**, **6**, and **9**) were bicyclic compounds having a five-, six-, or seven-membered ring fused to the cyclopropyl ring. Here the carbonyl group is in a relatively fixed geometry with respect to the three-membered ring. Other substrates (**13** and **19**) contained similar bicyclic systems, but the carbonyl group was held by a free rotating side chain. Cyclopropyl methyl ketone (**22**) and cyclopropyl phenyl ketone (**25**) were also considered as peculiar terms.

The results obtained from the reactions on ketones in the presence of pyridinium chloride or iodide in acetonitrile are reported in Table I.

The following discussion is organized according to cyclopropyl ketone type.

Reaction between α-Cyclopropyl Ketones and Pyridinium Halides. Bicyclo[*n*.1.0]alkan-2-ones. On reaction with pyridinium chloride, bicyclo[3.1.0]hexan-2-one (**1**) gave the two possible products of ring fission, namely, 3-(chloromethyl)cyclopentanone (**2**) and 4-chlorocyclohexanone (**3**) after 28 h of reflux. Bicyclo-[4.1.0]heptan-2-one (**6**) regioselectively afforded a 76% yield of 3-(chloromethyl)cyclohexanone (**7**) in 11 h.[3] Bicyclo[5.1.0]octan-2-one (**9**) gave 3-(chloromethyl)cycloheptanone (**10**) and 4-chlorocyclooctanone (**11**) in 41 and 35% yield, respectively, in 42 h.[4] The product ratio (1.08) is quite close to that obtained from ketone **1** (1.17).

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In the reaction with pyridinium iodide, the above mentioned substrates satisfied in part the expectation of a higher selectivity. Actually, **1** gave both possible products, **4** and **5**, but compared to the reaction run with pyridinium chloride, a higher ratio of (halomethyl)cyclopentanone to 4-halocyclohexanone was produced. Iodo ketones **4** and **5**, as well as other iodo ketones reported below, were recognized by spectral data and, in most cases, by conversion to the previously reported[3,4] chloro ketones upon reflux with potassium chloride in acetonitrile or by the opposite reaction (see Experimental Section). Treatment of **6** with pyridinium iodide for 11 h gave 3-(iodomethyl)cyclohexanone (**8**) in 69% yield. Ketone **9**, after 39 h of reflux, afforded 3-(iodomethyl)cycloheptanone (**12**) as a single product in 67% yield.

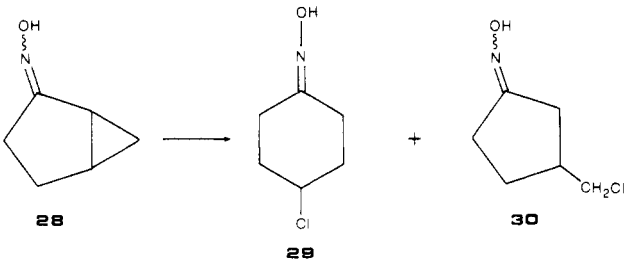
1-Acetylbicyclo[*n*.1.0]alkanes. On reaction with pyridinium chloride, 1-acetylbicyclo[3.1.0]hexane (**13**) gave only a very small amount (6%) of 1-acetyl-2-(chloromethyl)cyclopentane (**14**), the main product being a mixture of 62% *cis*-1-acetyl-3-chlorocyclohexane (**15**) and 24% *trans*-1-acetyl-3-chlorocyclohexane (**16**). In this case we noted a high regioselectivity (86:6) in ring fission, but here the ring enlargement was the main reaction. On the other hand, 1-acetylbicyclo[4.1.0]heptane (**19**) produced regio- and stereoselectively a 70% yield of *trans*-1-acetyl-2-(chloromethyl)cyclohexane (**20**).

A regioselective reaction resulted also from the treatment of **13** with pyridinium iodide. Only ring enlargement products, *cis*-1-acetyl-3-iodocyclohexane (**17**, 53%) and *trans*-1-acetyl-3-iodocyclohexane (**18**, 22%), were found. On the other hand, all attempts to cleave the cyclopropyl ring of 1-acetylbicyclo[4.1.0]heptane (**19**) by pyridinium iodide failed. However, when the reaction was run in the presence of a small amount of tetra-*n*-butylammonium iodide, a 46% yield of 1-acetyl-2-(iodomethyl)cyclohexane (**21**) was obtained.

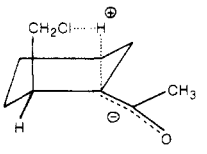
Cyclopropyl Methyl Ketone and Cyclopropyl Phenyl Ketone. Both substrates afforded the expected ring fission products **23** and **26** in 82 and 50% yield after 26 and 48 h, respectively. Even for these two ketones the ring opening by pyridinium iodide occurred only on addition of tetra-*n*-butylammonium iodide. Under these conditions **22** was transformed to **24**[5] in 5% yield after 5 h,[6] and **25** gave iodo ketone **27** in 30% yield after 48 h.

Reactions between α-Cyclopropyl Ketones Oximes and Pyridinium Halides. The reaction of the oximes derived from the above mentioned cyclopropyl ketones and pyridinium chloride showed some practical difficulties. In general, oximes were qualitatively less reactive than the corresponding ketones, and we often found products of hydrolysis with products of ring opening. Moreover, in addition to the previously reported results[2] concerning the oximes of **6**, we obtained a clean result only in the reaction of pyridinium chloride and the oxime **28**. Here the main product (65%) was 4-chlorocyclohexanone oxime (**29**), while 3-(chloromethyl)cyclopentanone oxime (**30**) was the minor one (35%), a significant difference compared with the results of the parent ketone ring-opening reaction.

The above results may be summarized as follows: (a) Ketones **6** and **19**, containing the bicyclo[4.1.0]heptane system, underwent the more selective reaction (with PyHCl only β-chloromethyl ketones) regardless of the endo- or



28 29 30



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exocyclic nature of the carbonyl group. (b) Compounds **1** and **13**, containing the more strained[7] bicyclo[3.1.0]-hexane system, and ketone **9**, containing the bicyclo-[5.1.0]octane moiety, gave a mixture of products. (c) The product distribution from **1** and **9** (both having an endocyclic carbonyl group) was very similar (in the reaction with PyHCl). (d) Ketone **13**, bearing an exocyclic carbonyl group, afforded mainly ring enlargement products, whereas **1**, containing the same bicyclic system, did not.

A comparison of the substrates **1**, **6**, and **9** with **13** and **19** allows some comments about the importance of the factors that may be invoked to rationalize the results. The following considerations are based on the assumption that a reasonable mechanism for the present ring-opening reaction is the one reported for other acid-catalyzed, nucleophilic, ring-opening reactions.[8] On this basis, the product composition could reflect both kinetic and thermodynamic controls. One of the factors often considered in opening reactions of cyclopropyl ketones (particularly in reductive ones) is the degree of overlap of a carbonyl p orbital with a cyclopropane σ bond. Another relevant point concerns ring strain, and a third noteworthy factor is assumed to be related to product stability.[9]

Considering the first group of compounds, we see that the bond either mainly or exclusively undergoing fission in reaction with pyridinium chloride is actually the one which best overlaps with the carbonyl orbital. The same is true in the reaction with pyridinium iodide. In this case the use of a less nucleophilic agent[10] allows a better selectivity according to a principle often verified in organic chemistry.[11] The lower reactivity of pyridinium iodide is qualitatively confirmed by the necessity of adding a small amount of tetra-*n*-butylammonium iodide to succeed in ring opening for substrates **19**, **22**, and **25**. On the other hand, we believe the difference in stability between **4** and **5** may account for the presence of a residue of 18% 4-iodocyclohexanone (**5**). The stability of **3** and **5** is greater than that of **2** and **4**, whereas the difference in stability between **10** and **11** is smaller.[12]

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Table II. Analytical Data by Mass Spectral Analysis

compd	formula	mol wt calcd	mol wt found
4, 5	C_6H_9IO	223.9700	223.9701
8	$C_7H_{11}IO$	237.9856	237.9854
12	$C_8H_{13}IO$	252.0013	251.9989
13	$C_8H_{12}O$	124.0888	124.0876
14-16	$C_8H_{13}ClO$	160.0655	160.0637
17, 18	$C_8H_{13}IO$	252.0013	251.9980
21	$C_9H_{15}IO$	266.0169	266.0160
29, 30	$C_6H_{10}ClNO$	147.0451	147.0441

If we compare the results from reactions on **13**, **19**, and the oxime **28**, we might assume that the factor connected to product stability plays a major role here owing to the possibility of free rotation for the acetyl group in **13** and **19** and owing to the lower electronegativity of the atom implied in the double bond for compound **28** (nitrogen in place of oxygen).

Stereochemical results (only trans-1,2-disubstituted cyclohexanes **20** and **21** from **19** and the main formation of cis-1,3-disubstituted cyclohexanes **15** and **17** from **13**) also agree with regioselectivity data, and both point to product stability as the relevant factor in these cases.

The trans stereochemistry of products **14**, **20**, and **21** (corresponding to a formal syn addition) might be rationalized by considering the proton transfer to be assisted through coordination by the chlorine atom of the chloromethyl group as in **31**.

Experimental Section

GC analyses were performed on a Perkin-Elmer F11 gas chromatograph with a column of 2% OV 17 (2 m × 2 mm) and on a Carlo Erba Fractovap GI gas chromatograph with a capillary column of 5% Apiezon L. GC–MS were obtained on a AEI-MS 12 spectrometer at an ionization potential of 70 eV, coupled to a Varian 1400 gas chromatograph equipped with a column of 2% OV 17 (2 m × 2 mm). High-resolution mass spectra (Table II) have been obtained with a VG Micromass 7070 F spectrometer. ^1H nuclear magnetic resonance spectra were recorded on a Perkin-Elmer R32 90-MHz spectrometer, using Me_4Si as an internal standard. Infrared spectra were obtained on a Perkin-Elmer 257 Infracord. Pyridinium chloride[13] and pyridinium iodide[14] were prepared using a reported procedure. Cyclopropyl phenyl ketone was a commercial product (Fluka).

1-Acetylbicyclo[3.1.0]hexane (13). The procedure of Corey and Chaykovsky was followed.[15] To a stirred suspension of 0.048 mol of sodium hydride, 10.56 g (0.048 mol) of trimethyloxosulfonium iodide, and 45 mL of dimethyl sulfoxide in an atmosphere of nitrogen, 4.95 g (0.045 mol) of 1-acetylcyclopentene[16] was added with cooling. After stirring at room temperature overnight, the mixture was worked up and distilled to afford 4.11 g (73.6%) of a colorless liquid, bp 80–82 °C (30 mm). The product showed one peak on GC analysis and was recognized as 1-acetylbicyclo[3.1.0]hexane (**13**) on the basis of spectral data: IR (CCl_4) 3070, 3030, 3000, 1680 cm^{-1}; NMR (CCl_4) δ 2.6–2.1 (m, 1 H), 2.0 (s, 3 H), 1.9–1.0 (m, 7 H), 0.95–0.7 (m, 1 H); mass spectrum m/e 124 (parent), 81 (base peak).

Bicyclo[3.1.0]hexan-2-one Oxime (28). To a solution of 1 g of hydroxylamine hydrochloride and 1.5 g of $CH_3COONa{\cdot}3H_2O$ in 4 mL of water heated at 40 °C, 1 g of **1** was added. After vigorous stirring for a few minutes, a dense oil separated. The mixture was refluxed for 3 h and then extracted with ether, dried, and evaporated to afford 1.1 g (96%) of an oil: bp 145–8 °C (25 mm) [lit.[17] bp 78 °C (0.8 mm)]; IR (CCl_4) 3590, 3280 cm^{-1}; NMR ($CDCl_3$) δ 6.85 (broad, 1 H), 2.9–1.5 (m, 6 H), 1.5–0.2 (m, 2 H); mass spectrum, m/e 111 (parent), 67 (base peak).

Reactions of α-Cyclopropyl Ketones with Pyridinium Chloride. The general procedure starting from ketones **1**, **6**, **9**, **19**, and **22** has been previously described.[3,4] The same procedure was also used for substrates **13** and **25**.

13 after 26 h gave **14** (6%), **16** (24%), and **15** (62%).

14: IR (CCl_4) 1710 cm^{-1}; NMR (CCl_4) δ 3.5 (m, 2 H), 2.1 (s, 3 H), 2.7–1.1 (m, 8 H); mass spectrum m/e 162 (isotopic), 160 (parent), 43 (base peak).

16: IR (CCl_4) 1710 cm^{-1}; NMR (CCl_4) δ 4.45 (m, 1 H), 2.1 (s, 3 H), 2.8–1.1 (m, 9 H); mass spectrum m/e 162 (isotopic), 160 (parent), 81 (base peak).

15: IR (CCl_4) 1710 cm^{-1}; NMR (CCl_4) δ 3.9–3.6 (m, 1 H), 2.1 (s, 3 H) 2.6–1.0 (m, 9 H); mass spectrum m/e 162 (isotopic), 160 (parent), 43 (base peak).

25 after 46 h gave **26** (50%), successively purified by preparative TLC, bp 115–120 °C (3 mm) (external bath) [lit.[18] bp 110–111 °C (2.5 mm)]; IR (CCl_4) 1685 cm^{-1}; NMR (CCl_4) δ 7.9 (m, 2 H), 7.4 (m, 3 H), 3.6 (t, 2 H), 3.1 (t, 2 H), 2.2 (quintuplet, 2 H); mass spectrum m/e 184 (isotopic), 182 (parent), 105 (base peak).

Reaction of α-Cyclopropyl Ketones with Pyridinium Iodide. α-Cyclopropyl ketone (8 mmol) and pyridinium iodide (16 mmol) were refluxed in 20 mL of acetonitrile (distilled from calcium hydride) for 11–43 h. The reaction mixture was poured into 20 mL of cold water and extracted several times with ether. The ethereal layer was dried and evaporated.

3-(Iodomethyl)cyclopentanone (4) and 4-Iodocyclohexanone (5). **1**, after 21 h, gave a mixture of **4** (50%) and **5** (18%): IR (CCl_4) 1745, 1715 cm^{-1}; NMR (CCl_4) δ 4.7 (m, CHI), 3.3 (m, CH_2I), 2.7–1.1 (m); GC–MS, m/e (relative intensity) (**4**) 224 (14, parent peak), 127 (2), 97 (72), 69 (45), 55 (28), 41 (100), 39 (34); (**5**) 224 (8, parent peak), 127 (3), 97 (69), 69 (39), 55 (26), 41 (100), 39 (46).

3-(Iodomethyl)cyclohexanone (8). **6**, after 11 h, gave **8** (69%): IR ($CHCl_3$) 1710 cm^{-1}; NMR ($CDCl_3$) δ 3.2 (m, 2 H), 2.7–1.2 (m, 9 H); mass spectrum m/e 238 (parent), 55 (base peak).

3-(Iodomethyl)cycloheptanone (12). **9**, after 39 h, gave **12** (67%): IR (CCl_4) 1700 cm^{-1}; NMR (CCl_4) δ 3.15 (m, 2 H), 2.5–1.2 (m, 11 H); mass spectrum m/e 252 (parent), 55 (base peak).

***cis*- and *trans*-3-Iodoacetylcyclohexane (17 and 18).** **13**, after 43 h, gave a mixture of **17** (53%) and **18** (22%): IR (CCl_4) 1710 cm^{-1}; NMR ($CDCl_3$) δ 4.1 (m, CHI of **18**), 4.0–3.4 (m, CHI of **17**), 2.1 (2s), 2.9–1.0 (m). GC–MS, m/e (relative intensity) (**17**) 252 (4, parent peak), 125 (46), 124 (7), 81 (21), 80 (6), 79 (9), 67 (6), 43 (100); (**18**) 252 (1, parent peak), 125 (47), 124 (14), 81 (32), 80 (7), 79 (15), 67 (10), 43 (100).

Reaction of α-Cyclopropyl Ketones with Pyridinium Iodide and Tetra-*n*-butylammonium Iodide. The procedure described above was modified by adding a 10% (weight) of tetra-*n*-butylammonium iodide.

***trans*-2-(Iodomethyl)acetylcyclohexane (21).** **19**, after 48 h, gave **21** (46%): IR (CCl_4) 1710 cm^{-1}; NMR (CCl_4) δ 3.1 (m, 2 H), 2.1 (s, 3 H), 2.6–0.9 (m, 10 H); mass spectrum m/e 266 (parent), 43 (base peak).

5-Iodopentan-2-one (24). **22**, after 4 h, gave **24** (5%), whose IR and NMR spectra were in good agreement with the reported data.[5] The crude product was distilled in microtube to afford a specimen: bp 68–70 °C (4 mm) (external bath) [lit.[5] bp 94 °C (14 mm)]; mass spectrum m/e (relative intensity) 212 (M^+, undetected), 127 (2), 85 (59), 84 (10), 43 (100).

γ-Iodobutyrophenone (27). **25**, after 48 h, gave **27** (ca. 30%, estimated by NMR). A pure specimen was obtained by preparative TLC on silica gel, using benzene as eluent: IR (CCl_4) 1685 cm^{-1}; NMR (CCl_4) δ 8.1–7.85 (m, 2 H), 7.5–7.2 (m, 3 H), 3.65 (t, 2 H), 3.0 (t, 2 H), 1.9 (quintuplet, 2 H); mass spectrum m/e (relative intensity) 274 (M^+, undetected), 147 (13), 120 (53), 105 (100), 77 (47), 51 (12).

General Procedure for Conversion of Chlorides into Iodides. A mixture of 0.74 g of anhydrous sodium iodide and 5.2 mL of ethyl methyl ketone was refluxed for 1 h; 0.5 g of the

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appropriate chloride (or mixture of chlorides) was added, and reflux was maintained for an additional 23 h. The cooled mixture was filtered, and the filtrate was concentrated. The residue was poured into cold water. The organic layer was washed with a 10% sodium bisulfite solution and a 5% sodium bicarbonate solution and dried over magnesium sulfate. The conversion was good (>80%) for primary halides and partial for secondary ones. With the above procedure, a mixture of **2** and **3** (1:1) was transformed into a mixture of **4** and **5** (5:1). Product **20** was converted into **21**.

The identity of these iodides with those obtained in the reactions with pyridinium iodide was confirmed by comparison of retention times and spectral data (IR, NMR, and mass).

General Procedure for Conversion of Iodides into Chlorides. A mixture of 2 mmol of the appropriate iodide and 4 mmol of dry potassium chloride in 5 mL of acetonitrile (distilled on calcium hydride) was placed in a sealed glass tube and heated at 105 °C for 38 h. The cooled mixture was diluted with water and extracted with ether. The ethereal layer was dried over anhydrous sodium sulfate, and the solvent was removed. The amount of conversion ranged between 32 and 50%.

Product **8** was transformed into **7**, **12** into **10**, **17** + **18** into **15** + **16**, **27** into **26**. All chlorides showed retention times as well as spectral data (IR, NMR, and mass) in excellent agreement with those obtained in the reactions with pyridinium chloride.

4-Chlorocyclohexanone Oxime (29) and 3-(Chloromethyl)cyclopentanone Oxime (30). **28** (2 mmol) and pyridinium chloride (4 mmol) were refluxed for 27 h in 5 mL of acetonitrile (distilled from calcium hydride). The usual workup afforded **29** and **30** (74%) in a 2:1 ratio; IR (CCl_4) 3595, 3260 cm^{-1}; NMR (CCl_4) δ 8.6 (m, NOH), 4.25 (m, CHCl of **29**), 3.50 (m, CH_2Cl of **30**), 3.0–1.4 (m); GC–MS *m/e* (relative intensity) (**29**) 149 (isotopic), 147 (parent), 66 (base peak); (**30**) 149 (isotopic), 147 (parent), 55 (base peak).

In addition, these oximes were identified by standard deoximation to the corresponding ketones.[3]

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Registry No. **1**, 4160-49-0; **2**, 66980-41-4; **3**, 21299-26-3; **4**, 71987-94-5; **5**, 31053-10-8; **6**, 5771-58-4; **7**, 57719-96-7; **8**, 72003-75-9; **9**, 16335-43-6; **10**, 67052-06-6; **11**, 7434-01-7; **12**, 71987-95-6; **13**, 29773-67-9; **14**, 71987-96-7; **15**, 71987-97-8; **16**, 71987-98-9; **17**, 71987-99-0; **18**, 71988-00-6; **19**, 2862-90-0; **20**, 66980-42-5; **21**, 71988-01-7; **22**, 765-43-5; **23**, 5891-21-4; **24**, 3695-29-2; **25**, 3481-02-5; **26**, 939-52-6; **27**, 65488-05-3; **28**, 66386-25-2; **29**, 4500-22-5; **30**, 71988-02-8; pyridinium chloride, 628-13-7; pyridinium iodide, 18820-83-2; 1-acetylcyclopentene, 16112-10-0.

Conjugate Addition of RMgX to Nitroarenes: A Very Useful Method of Alkylation of Aromatic Nitro Compounds

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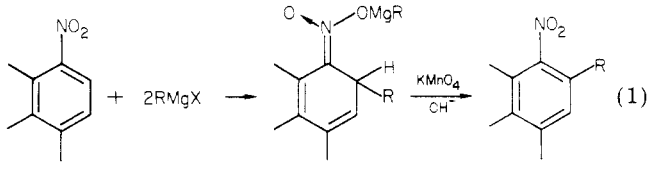
We recently reported[1a] that conjugate addition of alkyl Grignard compounds to nitroarenic systems in THF yields *o*- or *p*-alkylnitronate adducts. This reaction provides a series of general methods of synthesizing aromatic alkyl compounds containing different nitrogen functional groups. When the reactions were carried out with a 2:1 RMgX/substrate molar ratio and the adducts were decomposed with Lewis acids (BF_3 or concentrated HCl) alkylnitroso compounds were obtained in fair to good yields.[1b] Conversely, the use of a large excess of RMgX, in the presence of catalytic amounts of CuI, yielded amino derivatives.[2] More recently, other authors[3] reported a method of alkylation of nitrobenzenes and -naphthalenes by treatment of an equimolar solution of RLi or RMgX in THF for 1 h at 0 °C to give nitronate adducts, which were converted in situ to aromatic alkylnitro derivatives with DDQ or bromine and triethylamine. However, in our opinion, the use of a 1:1 RMgX/substrate molar ratio can be disadvantageous in most instances. We have found, for example, that the alkylation of 6-nitrobenzothiazole under the aforementioned experimental conditions leads to a crude product which contains large amounts of unreacted material. As a consequence of this there are considerable difficulties in purification with a decrease in the yields of the pure 6-nitro-7-alkylbenzothiazoles.

In previous work[1b] we discovered that an excess of metalloorganic reagent is required for the adduct formation to proceed to completion, since part of the RMgX is displaced from the reaction, being bound to the nitro or nitronate function. A 2:1 RMgX/substrate molar ratio ensures that reaction will proceed to completion in a short time for any given substrate. There are a few exceptions. Nitroindole, for instance, contains an acidic hydrogen, which can protonate RMgX. In this case a larger excess (3:1) is necessary. Since the presence of a large excess of RMgX in the reaction mixture prevents the use of oxidizing agents like DDQ or bromine in dry THF, we devised a method compatible with these experimental restrictions. In addition, the present method utilizes a procedure which has proven to be more advantageous in the time of reaction as well as in the choice of reagents. A 1 M solution of a nitroarene in THF was treated with a 2 M solution of RMgX in the same solvent at 0 °C for few minutes. The subsequent addition of an acetone–water solution of 0.67 mol of $KMnO_4$ immediately leads to the formation of alkynitroarenes (eq 1). The wide range of applicability



(1)

of this method is substantiated by good yields obtained for a large number of mono- and bicyclic aromatic systems. Investigated reactions, products, and yields are reported in Table I. Unsatisfactory results were exclusively obtained with 6-nitroquinoline. It is worth remembering, however, that the quinoline system gave analogous results during the synthesis of nitroso compounds.[1b] Chloro, methoxy, and methyl substituents as well as thiazole, pyrrole, and oxazole heterocondensed rings do not interfere with the reaction. In all cases alkylnitroarenes isolated after work up of the reaction mixture are chromatographically pure: particularly, only 7-alkylnitro derivatives from 6-nitrobenzothiazoles and 6-nitrobenzoxazole and the 4-alkyl derivative from 5-nitroindole are obtained, as expected from high regioselectivity previously observed in alkylation orientation of these substrates.[1a,b] These methods of in situ conversion of nitro to alkylnitro derivatives are of great utility, since a two-step procedure, involving the synthesis of nitroso compounds[4] and subse-

(1) (a) G. Bartoli, R. Leardini, M. Lelli, and G. Rosini, *J. Chem. Soc., Perkin Trans. 1*, 884 (1977); (b) G. Bartoli, R. Leardini, A. Medici, and G. Rosini, *ibid.*, 692 (1978).

(2) G. Bartoli, A. Medici, and G. Rosini, *Synthesis*, 436 (1978).
(3) F. Kienzle, *Helv. Chim. Acta*, 61, 449 (1978).

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