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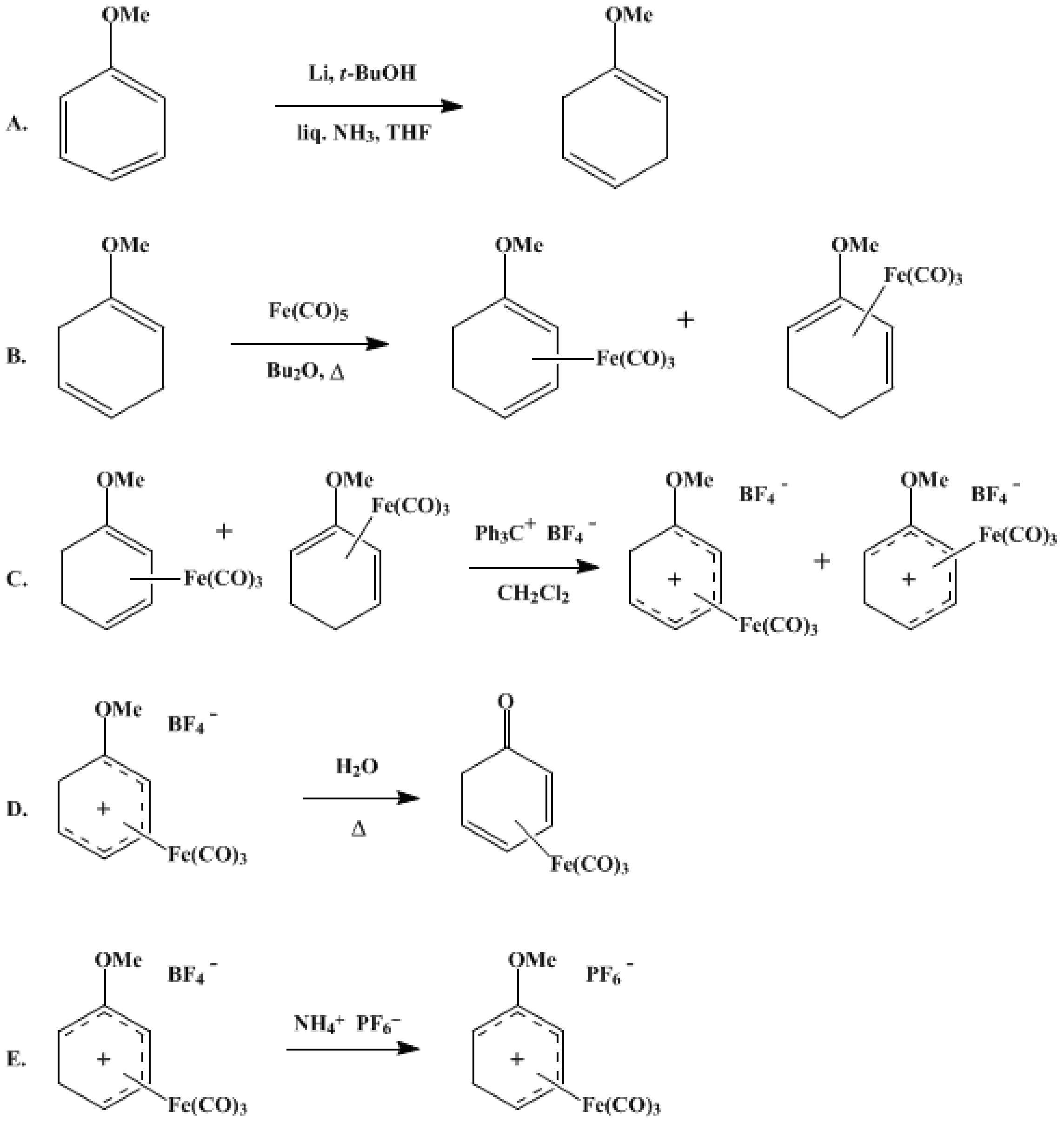
TRICARBONYL[(2,3,4,5-η)-2,4-CYCLOHEXADIEN-1-ONE]IRON AND TRICARBONYL[(1,2,3,4,5-η)-2-METHOXY-2,4-CYCLOHEXADIEN-1-YL]IRON(1+) HEXAFLUOROPHOSPHATE (1−) FROM ANISOLE

[Iron, tricarbonyl[(2,3,4,5-η)-2,4-cyclohexadien-1-one] and Iron(1+), tricarbonyl [(1,2,3,4,5-η)-2-methoxy-2,4-cyclohexadien-1-yl] hexafluorophosphate (1−)]



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1. Procedure

Caution! Parts A and B must be conducted in an efficient hood to prevent exposure to ammonia, *iron pentacarbonyl, and carbon monoxide.*

A. *1-Methoxy-1,4-cyclohexadiene.* A 3-l., three-necked, round-bottomed flask equipped with an inlet tube, mechanical stirrer, and an acetone–dry ice condenser fitted with a drying tube is charged with 150 ml. of tetrahydrofuran, 250 ml. of *tert*-butyl alcohol, and 50 g. (0.46 mole) of anisole (Note 1). About 1.5 l. of dried liquid ammonia (Note 2) is distilled into the reaction vessel from a steam bath. Lithium (11.5 g., 1.66 g.-atoms) (Note 3), (Note 4) is added cautiously with stirring and, when the addition is complete, the stirring is continued for 1 hour with refluxing. The blue color is discharged by cautiously adding methanol dropwise (about 100 ml. is required); 750 ml. of water is then added carefully. The excess ammonia is allowed to evaporate overnight, more water is added, dissolving the lithium salts, and the mixture is extracted three times with 100-ml. portions of petroleum ether (b.p. 30–40°) (Note 5). The combined extracts are washed four times with 75-ml. portions of water, removing *tert*-butyl alcohol and methanol, and dried over anhydrous magnesium sulfate, and the solvent is removed through a 30-cm. Vigreux column (Note 6) under reduced pressure (20 mm.). Distillation of the residue yields 1-methoxy-1,4-cyclohexadiene (38–40 g., about 75%) (Note 7), (Note 8), b.p. 40° (20 mm.).

B. *Tricarbonyl*[(1,2,3,4-η)-1- *and* 2-*methoxy*-1,3-*cyclohexadiene]iron.* A 500-ml., three-necked, round-bottomed flask equipped with a nitrogen-inlet tube, a condenser provided with a gas bubbler, and a stopper is flushed with nitrogen and charged with 39 g. (0.35 mole) of 1-methoxy-1,4-cyclohexadiene, 320 ml. of dibutyl ether (Note 9), and 95 g. (65 ml., 0.49 mole) of filtered iron pentacarbonyl (Note 10), (Note 11),(Note 12). Using a heating mantle, the mixture is refluxed for 18 hours (Note 13) under a slow nitrogen stream. After cooling, the reaction mixture is filtered by suction through Celite, removing iron particles (Note 14), the Celite is washed twice with 15-ml. portions of dibutyl ether, and the washings and filtrate are combined. The crude product (Note 15) is obtained by evaporating excess iron pentacarbonyl, unreacted diene, and the dibutyl ether using a rotary evaporator (in a fume hood), with a hot-water bath and ice cooling of the receiver. The distillate is again refluxed for 18 hours under nitrogen as before and worked up in the same manner. This procedure is then repeated again. Distillation of the combined residues using a nitrogen leak (Note 16) yields 54 g. of the product as a yellow oil, b.p. 66–68° (0.1 mm.) (Note 17). The distillation residue, after elution through a short acidic alumina column with light petroleum ether and solvent evaporation, yields an additional 5 g. of product, giving a total yield of 59–68 g. (67–78%) (Note 18), (Note 19).

C. *Tricarbonyl*[(1,2,3,4,5-η)-1- *and* 2-*methoxy*-2,4-*cyclohexadien*-1-*yl*]*iron*(1+) *tetrafluoroborate* (1−). Triphenylmethyl tetrafluoroborate (34 g., 0.10 mole) (Note 20) is dissolved in a minimum volume of dichloromethane, and 18 g. (0.072 mole) of tricarbonyl (1- and 2-methoxy-1,3-cyclohexadiene)iron dissolved in a like volume of dichloromethane is added. The resulting dark solution is left for 20–30 minutes and added with stirring to three times its volume of diethyl ether (Note 21). The precipitate is collected and washed with ether, yielding 21–22 g. (87–91%) of product as a yellow solid (Note 19).

D. *Tricarbonyl*[(2,3,4,5-η)-2,4-*cyclohexadian*-1-*one*]*iron.* The tetrafluoroborate mixture from Part C (21 g., 0.062 mole) is heated on a steam bath for 1 hour in 450 ml. of water, during which time orange crystals separate. After cooling, the mixture is extracted three times with 100-ml. portions of ether, into which most of the solid dissolves. (The aqueous layer is used in Part E.) The extracts are dried over anhydrous magnesium sulfate, and the ether is evaporated, yielding 7–7.5 g. (47–51%) of the yellow crystalline dienone complex (Note 22).

E. *Tricarbonyl*[(1,2,3,4,5-η)-2-*methoxy*-2,4-*cyclohexadien*-1-*yl*]*iron*(1+) *hexafluorophosphate*(1−). To the aqueous layer from Part D is added with swirling 7.1 g. (0.044 mole) of ammonium hexafluorophosphate (Note 23) in 30 ml. water. After 30 minutes, the light-yellow product is filtered, washed with water, and air dried, yielding 9–10 g. (35–44%) (Note 19), (Note 24).

2. Notes

1. Anisole (500 g.) was purified[2] by washing twice with 50 ml. of 2 *N* sodium hydroxide, twice with 50 ml. of water, drying over anhydrous magnesium sulfate, and distillation, b.p. 43–46° (20 mm.). The checkers used anisole obtained from Kanto Chemical Co., Ltd., Japan.
2. Liquid ammonia, from a cylinder, is purified by addition of 2–3 g. of sodium cut into small pieces and

distillation into the reaction vessel.

3. The submitters used lithium wire (Merck & Company, Inc.) (12 in. = 1 g.) cut into small pieces. The checkers used a block of lithium cut into small pieces.

4. The lithium pieces must be small and added to the ammonia solution cautiously. If too much is added at one time, the reaction becomes violent and froths.

5. Frequently not all of the ammonia evaporates; the first extraction should be by swirling in a separatory funnel without a stopper, and subsequent extractions should be done with frequent pressure release.

6. The solvent must be carefully removed; use of a rotary evaporator results in considerable loss of the product.

7. The IR spectrum of the 1-methoxy-1,4-cyclohexadiene shows the absence of strong aromatic absorption at 1600 cm.$^{-1}$; the UV spectrum shows absence of absorption at 270 nm., indicating absence of the conjugated isomer.

8. ^{1}H NMR spectrum, δ (number of protons): δ 2.5–2.9 (4H), 3.48 (3H), 3.50 (1H), 5.60 (2H).

9. Dibutyl ether must be dry and peroxide-free. This can be achieved by filtering it through a large column of basic alumina, or by leaving overnight over sodium wire and distillation. If these precautions are not observed, low yields result. The checkers purified dibutyl ether by distillation from a sodium hydride dispersion.

10. During the reaction the hood must be operating at all times, as carbon monoxide is evolved.

11. Iron pentacarbonyl is toxic and volatile; consequently, it should only be handled in a good hood, while wearing gloves.

12. The submitters used iron pentacarbonyl "pract." grade obtained from Fluka A G. The checkers used iron pentracarbonyl obtained from Merck, Germany.

13. When the reaction was followed by ^{1}H NMR spectroscopy, it was found that the yield reached a maximum after 18 hours; longer refluxing resulted in decomposition and lower yields. At that point as well, the maximum proportion of the 1-methoxy isomer was produced; this isomer is converted into the dienone complex.

14. Care should be exercised in filtering the reaction mixture. The solid collected is largely finely divided iron and pyrophoric; it should not be allowed to dry.

15. The crude product is unstable and should be stored under nitrogen with refrigeration.

16. Alternatively, rapid magnetic stirring will prevent bumping and allow distillation without a gas bleed.

17. For smaller batches, purification by elution of the product through a short column of acidic alumina with light petroleum ether and evaporation of the solvent is satisfactory.

18. In one of the checker's experiments almost all the material could be distilled, giving 68.14 g. (77.9%) of the product, b.p. 66–67° (0.3–0.4 mm.).

19. For ^{1}H NMR and IR spectra, see Birch and co-workers.[3]

20. Triphenylmethyl fluoroborate is prepared by dissolving 27 g. (0.10 mole) of triphenylmethanol ("purum," Fluka A G) in 260 ml. of propionic anhydride by warming on a steam bath. With an acetone–dry ice bath the solution is cooled to 10° and maintained between 10° and 20° while 31 ml. of 43% (w/w) fluoroboric acid is added portionwise with swirling. The yellow solid is collected, washed well with dry ether, and dried in a desiccator under vacuum, yielding 34 g. (90–99%). The product is very hygroscopic, taking up water with hydrolysis. It is desirable to prepare this reagent immediately before use.

21. The ether should be reagent grade but not sodium-dried. The traces of water present destroy excess reagent, leading to a cleaner product.

22. The product at this stage is sufficiently pure for most purposes. It can be recrystallized in small batches from water,[3] m.p. 104–104.5°; it can be chromatographed on silica or acidic alumina or sublimed at 80–90° (0.2 mm.). The checkers obtained the purified material (m.p. 104–105°) by recrystallization from dichloromethane-ether. The purified material has the following IR spectrum ($CHCl_3$) cm.$^{-1}$: 2070 strong, 2000 strong, 1665 strong; ^{1}H NMR spectra ($CDCl_3$), δ (multiplicity, number of protons): 2.28–2.45 (m, 2H), 3.1–3.46 (m, 2H), 5.6–6.1 (m, 2H).

23. Obtained from Ozark-Mahoning Chemical Co.

24. The complex can be stored for long periods under nitrogen in a refrigerator with only slight darkening. The purified material has the following IR spectrum (Nujol) cm^{-1}: 2110 strong, 2060 strong, 1515 weak, 1494 weak, 1253 medium strong.

3. Discussion

Anisole is reduced using the solvent of Dryden and collegues.[4] Iron pentacarbonyl and 1-methoxy-1,4-cyclohexadiene react as shown by Birch and co-workers,[3] although dibutyl ether has been found to be a superior solvent.[5] The tricarbonyl(methoxy-1,3-cyclohexadiene)iron isomers undergo hydride abstraction[3,6] with triphenylmethyl tetrafluoroborate, forming the dienyl salt mixture, of which the 1-methoxy isomer is hydrolyzed by water to the cyclohexadienone complex. The 2-methoxy isomer can be recovered by precipitation as the hexafluorophosphate salt. By this method the 3-methyl-substituted dienone complex has also been prepared[3] from 1-methoxy-3-methylbenzene. The use of the conjugated 1-methoxy-1,3-cyclohexadiene in Part B led to no increase in yield or rate and resulted chiefly in another product of higher molecular weight. An alternative route to the dienone is the reaction of tricarbonyl(1,4-dimethoxycyclohexadiene)iron with sulfuric acid.[7]

The dienone complex is an effective phenylating agent for aromatic amines; *e.g.*, aniline and tricarbonylcyclohexadienoneiron react in glacial acetic acid at 75° overnight, giving diphenylamine in 95% yield.[8] Under appropriate experimental conditions cyclohexadienone complexes react with lithium alkyls and, upon removal of iron tricarbonyl, the alkylbenzene is formed.[9] The 2-methoxy cation has now been resolved, *via* the menthoxy derivative.[10] This cation is equivalent to sterically directed 2-cyclohexen-1-one 4-cation.[9]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 1001

References and Notes

1. Research School of Chemistry, Australian National University, P.O. Box 4, Canberra, ACT 2600, Australia.
2. D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, "Purification of Organic Compounds," Pergamon Press, Oxford, 1966.
3. A. J. Birch, P. E. Cross, J. Lewis, D. A. White, and S. B. Wild, *J. Chem. Soc. A*, 332 (1968).
4. H. L. Dryden, Jr., G. M. Webber, R. R. Burtner, and J. A. Cella, *J. Org. Chem.*, **26**, 3237 (1961).
5. M. Cais and N. Maoz, *J. Organomet. Chem.*, **5**, 370 (1966).
6. E. O. Fischer and R. D. Fischer, *Angew. Chem.*, **72**, 919 (1960).
7. A. J. Birch, L. F. Kelly, and D. J. Thompson, *J. Chem. Soc., Perkin Trans. 1*, (1980).
8. A. J. Birch and I. D. Jenkins, *Tetrahedron Lett.*, 119 (1975).
9. A. J. Birch, B. M. R. Bandara, K. Chamberlain, B. Chauncy, P. Dahler, A. I. Day, I. D. Jenkins, L. F. Kelly, T.-C. Khor, G. Kretschmer, A. J. Liepa, A. S. Narula, W. D. Raverty, E. Rizzardo, C. Sell, G. R. Stephenson, D. J. Thompson, and D. H. Williamson, *Tetrahedron*, **37**, Suppl. 9, 289 (1981).
10. A. J. Birch and T.-C. Khor, unpublished work.

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

petroleum ether

Tricarbonyl[(2,3,4,5-η)-2,4-cyclohexadien-1-one]iron

TRICARBONYL[(1,2,3,4,5-η)-2-METHOXY-2,4-CYCLOHEXADIEN-1-YL]IRON(1+)
HEXAFLUOROPHOSPHATE(1−)

Iron, tricarbonyl[(2,3,4,5-η)-2,4-cyclohexadien-1-one]

Iron(1+), tricarbonyl[(1,2,3,4,5-η)-2-methoxy-2,4-cyclohexadien-1-yl] hexafluorophosphate (1−)

Tricarbonyl[(1,2,3,4-η)-1- and 2-methoxy-1,3-cyclohexadiene]iron

Tricarbonyl[(1,2,3,4,5-η)-1- and 2-methoxy-2,4-cyclohexadien-1-yl]iron(1+) tetrafluoroborate(1−)

tricarbonyl (1- and 2-methoxy-1,3-cyclohexadiene)iron

Tricarbonyl[(2,3,4,5-η)-2,4-cyclohexadian-1-one]iron

iron pentracarbonyl

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

ammonia (7664-41-7)

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

aniline (62-53-3)

sodium hydroxide (1310-73-2)

carbon monoxide (630-08-0)

iron (7439-89-6)

nitrogen (7727-37-9)

Anisole (100-66-3)

sodium (13966-32-0)

dibutyl ether (142-96-1)

dichloromethane (75-09-2)

diphenylamine (122-39-4)

triphenylmethanol (76-84-6)

lithium (7439-93-2)

magnesium sulfate (7487-88-9)

propionic anhydride (123-62-6)

Tetrahydrofuran (109-99-9)

sodium hydride (7646-69-7)

tert-butyl alcohol (75-65-0)

iron pentacarbonyl

fluoroboric acid (16872-11-0)

Triphenylmethyl tetrafluoroborate,
Triphenylmethyl fluoroborate

1-Methoxy-1,4-cyclohexadiene (2886-59-1)

ammonium hexafluorophosphate

1-methoxy-3-methylbenzene (100-84-5)

1-methoxy-1,3-cyclohexadiene