Ethyl Iodide[1]

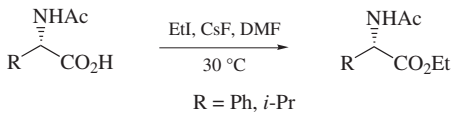
EtI

[75-03-6] C_2H_5I (MW 155.97)
InChI = 1/C2H5I/c1-2-3/h2H2,1H3
InChIKey = HVTICUPFWKNHNG-UHFFFAOYAT

(esterification of carboxylic acids;[1] alkylation of amines,[6,8] alkoxides, thiolates[9] and enolates;[17,21] preparation of Grignard reagents[22])

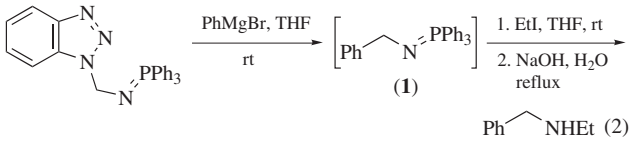
Alternate Name: iodoethane.
Physical Data: mp −108 °C; bp 70–73 °C, *d* 1.941 g cm^{-3}.
Solubility: sol water (with decomposition), alcohol, most organic solvents.
Form Supplied in: heavy, clear, very refractive liquid; colorless when pure, becomes red on exposure to light and air due to iodine liberation; common impurities are ethanol and iodine.
Preparative Methods: prepared by reaction of ethanol and iodine in the presence of red phosphorus.
Purification: purified by shaking with dilute solution of sodium bisulfite or sodium thiosulfate until colorless; wash with water, dry ($CaCl_2$), and distill. May also be purified by passing through a column of silica gel or alumina followed by distillation.
Handling, Storage, and Precautions: store colorless solution over silver leaf or copper wire in brown bottle away from light. Avoid storing over mercury as ethylmercury(II) iodide, the byproduct of decomposition, is extremely poisonous. Harmful if swallowed, inhaled, or absorbed through the skin. Extremely harmful to mucous membranes, upper respiratory tract, eyes, and skin. Exposure can cause spasms, inflammation of contact area, coughing, nausea, and vomiting. Use in a fume hood.

Esterifications. Ethyl iodide has seen widespread use as a reagent for conversion of carboxylic acids to ethyl esters.[1] The procedure involves treatment of a carboxylic acid with base followed by addition of ethyl iodide. The method is particularly useful with substrates containing acid-sensitive protecting groups. Conditions are varied: HMPA/NaOH (yields >95%),[2] DMSO/KOH (>90%),[3] $NaHCO_3$/DMF (>95%),[4] CsF/DMSO or DMF (92–100%).[5] The latter method was particularly useful in the direct conversion of organotin carboxylates, commonly employed to protect carboxylic acids in the presence of amines in peptide synthesis, to esters. The conversion proceeds in excellent yields (85–91%) at mild temperatures with no racemization (eq 1).



(1)

Heteroatom Alkylation. Various heteroatoms react with ethyl iodide. *N*-Ethylamines, hydrazines,[6] and amides have been prepared. Secondary *N*-ethylamines were prepared by Katritzky et al. in 55–65% yield via the reaction of (**1**) with ethyl iodide followed by treatment with NaOH/H_2O (eq 2).[7]

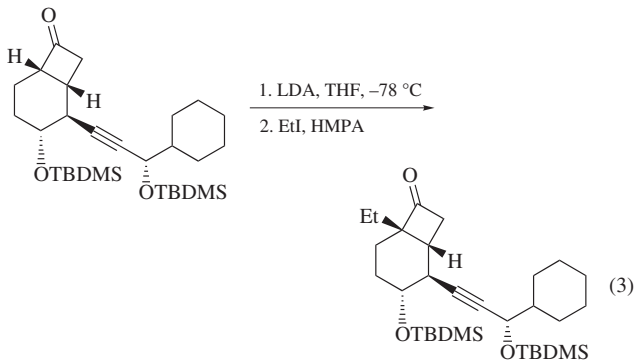


(2)

Pyrroles were *N*-ethylated (DMSO, KOH, 60% yield) during the synthesis of novel 2-azafulvenes.[8]

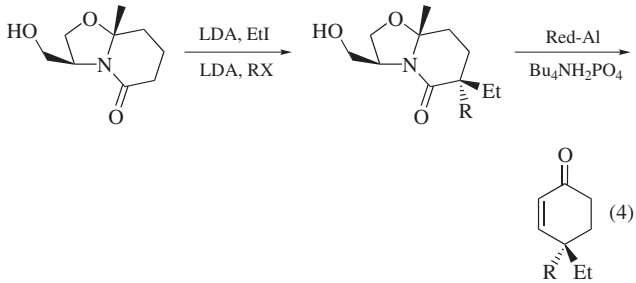
In a related reaction, thioethers were prepared in the presence of a Pt^{II} catalyst in 80–90% yield.[9] This reaction was developed as an alternative to the more traditional method demonstrated by Ono (DBU/benzene).[10] In a similar fashion, alcohols can be converted to the corresponding ethyl ethers.

***C*-Alkylations.** Alkylation of carbon nucleophiles with ethyl iodide is a convenient method for introducing an ethyl group at a carbon center. The substrates are treated with base (*t*-BuOK,[11] NaOEt,[12] *n*-BuLi,[13] NaHMDS,[14] LiHMDS,[15] LDA,[16] etc.) followed by quenching with ethyl iodide. The solvent is usually, but not limited to, THF or diethyl ether. Temperatures and reaction times vary depending on the specific substrate. Yields also vary but most appear to be good to excellent (>80%). A variety of compounds have been prepared including introduction of quaternary chiral centers at bridgehead positions (eq 3).[17]



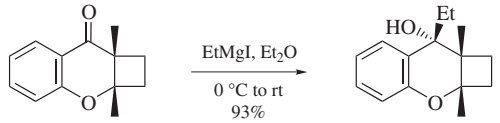
(3)

Asymmetric alkylation reactions have also taken advantage of the versatility of this reagent. Such chiral enolate systems as oxazolidinones,[18] dihydropyrimidinones,[19] camphorsulfonamides,[20] and chiral lactams[21] have been alkylated in high chemical and optical yields. Meyers et al. utilized chiral lactams in a general preparation of cyclohexenones bearing a tertiary or quaternary chiral center at the C-4 position (eq 4).[21]



(4)

Grignard Reagent. Conversion of ethyl iodide to its Grignard reagent proceeds easily (Mg, Et_2O, 0 °C). An example of the utilization of this reagent can be found in the synthesis of a debromoaplysin analog (eq 5).[22]



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1. Haslam, E., *Tetrahedron* **1980**, *36*, 2409.
2. (a) Shaw, J. E.; Kunerth, D. C.; Sherry, J. J., *Tetrahedron Lett.* **1973**, 689. (b) Shaw, J. E.; Kunerth, D. C., *J. Org. Chem.* **1974**, *39*, 1968.
3. Johnstone, R. A. W.; Rose, M. E., *Tetrahedron* **1979**, *35*, 2169.
4. Sato, T.; Otura, J.; Nozaki, H., *J. Org. Chem.* **1992**, *57*, 2166.
5. Knapp, S.; Gibsen, F. S., *J. Org. Chem.* **1992**, *57*, 4802.
6. Barluenga, J.; Merino, I.; Vina, S.; Palacious, F., *Synthesis* **1990**, 398.
7. Katritzky, A. R.; Jiang, J.; Urozdi, L., *Synthesis* **1990**, 565.
8. Taheri, S. A. N.; Jones, R. A.; Badesha, S. S.; Harria, M. M., *Tetrahedron* **1989**, *45*, 7717.
9. Page, C. B.; Klair, S. S.; Brown, M. P.; Smith, C. S.; Maginn, J. J.; Mulley, S., *Tetrahedron* **1992**, *48*, 5933.
10. Ono, N.; Miyake, H.; Saito, T.; Kaji, A., *Synthesis* **1980**, 952.
11. Curran, D. P.; Liu, H., *J. Am. Chem. Soc.* **1992**, *114*, 5863.
12. Bishop, J. E.; Nagy, J. O.; O'Connell, J. F.; Rapoport, H., *J. Am. Chem. Soc.* **1991**, *113*, 8024.
13. Golec, J. M. C.; Hedgecock, C. J. R.; Kennewell, P. D., *Tetrahedron Lett.* **1992**, *33*, 547.
14. Chu, K. S.; Negrete, G. R.; Konopelski, J. P.; Labner, F. J.; Woo, N.-T.; Olmstead, M. M., *J. Am. Chem. Soc.* **1992**, *114*, 1800.
15. Amoroso, R.; Cardillo, G.; Tomasini, C., *Tetrahedron Lett.* **1992**, *33*, 2725.
16. deJong, J. C.; Feringa, B. L., *Tetrahedron Lett.* **1989**, *30*, 7239.
17. Wu, H. Y.; Walker, K. A. M.; Nelson, J. T., *J. Org. Chem.* **1990**, *55*, 5074.
18. Yan, T. H.; Chu, V. V.; Lin, T. C.; Wu, C. H.; Liu, L. H., *Tetrahedron Lett.* **1991**, *32*, 4959.
19. Negrete, G. R.; Konopelski, J. P., *Tetrahedron: Asymmetry* **1991**, *2*, 105.
20. Yen, K. F.; Uang, B. J., *Tetrahedron: Asymmetry* **1992**, *3*, 697.
21. (a) Wunsch, T.; Meyers, A. I., *J. Org. Chem.* **1990**, *55*, 4233. (b) Meyers, A. I.; Berney, D., *Org. Synth.* **1990**, *69*, 55.
22. Nath, A.; Ghosh, A.; Venkateswaran, R. V., *J. Org. Chem.* **1992**, *57*, 1467.

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