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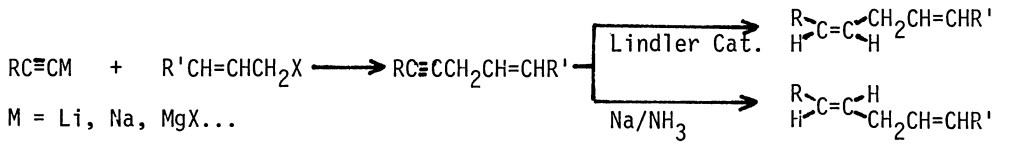
LITHIUM IODIDE MEDIATED REGIOSELECTIVE COUPLING OF LITHIUM ACETYLIDES WITH ALLYLIC HALIDES

Hidetaka YATAGAI, Yoshinori YAMAMOTO,* and Kazuhiro MARUYAMA
Department of Chemistry, Faculty of Science, Kyoto University
Kyoto 606

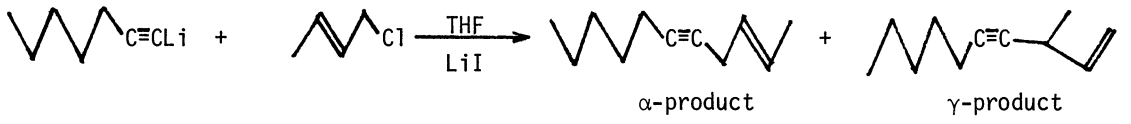
Regioselective coupling between lithium acetylides and allylic halides is realized by using lithium iodide as an additive.

The stereoselective synthesis of 1,4-diene units of natural products, such as insect sex pheromones[1] and arachidonic acid derivatives,[2] is a problem of pressing concern in organic synthesis. Among the many procedures, one of the most popular and easily accessible methods is to use the stereoselective reduction of 1,4-enynes which are produced from the coupling reaction between metal acetylides and allylic halides (eq 1).[3]



(1)

In connection with a synthetic project, we required an efficient methodology for regioselective coupling between lithium acetylides and crotyl chloride under mild conditions. Unfortunately, despite the availability of this array of approaches, the known procedures are frequently unsatisfactory either as a result of low yield or the lack of regio- and stereoselectivity.[4] We now wish to report that the coupling *in the presence of LiI* provides a solution to this problem (eq 2). The results are summarized in the Table I.



(2)

The representative procedure is as follows. In a 100 ml flask, equipped with a magnetic stirrer and maintained under N_2, were placed dry THF (10 ml) and 1-heptyne (10 mmol, 1.30 ml). BuLi in hexane (10 mmol) was added at 0°C and the resulting mixture was stirred for 30 min. In another flask, equipped with a magnetic stirrer and maintained under N_2, BuLi in hexane (20 mmol)

Table 1. Regioselective Coupling between Lithium Heptylide and Crotyl Chloride[a]

LiI (equiv)	Crotyl Chloride (equiv)	Reaction Conditions	Yield, %[b]	α-Product/γ-Product[c]
0	2	THF, room temperature	0	-
0.5	2	THF, room temperature	21	95/5
1	2	THF, room temperature	40	95/5
2	2	THF, reflux	84 (75)	95/5
3	2	THF, reflux	60	95/5

[a] All reactions were performed on a 10 mmol scale. LiI was in situ prepared, *since a commercially available material inherently contained water of crystallization.* [b] By Glpc (isolated yield). The crotyl unit in 2-undecen-5-yne retained the trans geometry. [c] By Glpc.

was placed. To this solution, MeI (20 mmol, 1.25 ml) was slowly added at 0°C and LiI soon precipitated. Hexane was removed under vacuum and then dry THF (20 ml) was added. The THF solution of LiI was added to the solution of lithium heptylide at 0°C and then crotyl chloride (20 mmol, 1.97ml) was added. The resulting mixture was refluxed for 1 hr. The usual work-up gave (E)-2-undecen-5-yne in 75 % yield.

This procedure was also applicable to other allylic halides, such as crotyl bromide, prenyl chloride, and prenyl bromide, and to other lithium acetylides, such as octylide and hexylide. We are now extending this method to the synthesis of some insect sex pheromones.

References and Notes

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2) a) K. C. Nicolaou, G. P. Gasic, W. E. Barnette, Angew. Chem. int. Ed. Engl., 17, 293 (1978); b) J. F. G. Vliegenthart, Chem. & Ind., 241 (1979).
3) a) See ref. 1a, p. 1868-1869. b) W. H. Kunau, Chem. Phys. Lipids, 11, 254 (1973).
4) The results of the coupling reactions via reported procedures are as follows; (M, X, additives and reaction conditions, yield of 1,4-enynes, the ratio of α-product and γ-product): a)(Li, Br, dioxane, 29 %, -) M. Jacobson, R. E. Redfern, W. A. Jones, and M. H. Aldrige, Science, 170, 542 (1970): b)(Na, Cl, liq NH_3, complex mixture, -) R. Köster, A. Bussmann, and G. Schroth, Ann. Chem., 2130 (1975): c)(MgBr, Br, CuCl-THF reflux, 75 %, 91/9) L. Brandsma, "Preparative Acetylenic Chemistry," Elsevier, p. 30, New York (1971); J. P. Danehy, D. B. Killian, and J. A. Nieuwland, J. Am. Chem. Soc., 58, 611 (1936); C. C. Leznoff and F. Sondheimer, ibid., 89, 4247 (1967); L. Heslinga, H. J. J. Pabon, and D. A. van Dorp, Rec. Trav. Chim. Pays. Bas, 92, 287 (1973); M. deGaudemaris and P. Arnaud, Bull. Soc. Chim. Fr., 315 (1962): d) (MgBr, Cl, Li_2CuCl_4-THF, 72 %, 95.6/4.4) R. L. Carney and J. W. Baum, Zoecon Corp., unpublished results (1975); see also ref. 1a: e) (Cu, Br, NaCN, 76 %, 75/25) J.-F. Normant, M. Bourgain, and A. M. Rone, C. R. Acad. Sci. Ser. C, 270, 354 (1970); M. Bourgain and J.-F. Normant, Bull. Soc. Chim. Fr., 1777 (1973).

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