

Cyclopropanation of Electron-deficient Alkenes and Wideqvist-type Synthesis of Cyclopropanes mediated by Indium Metal

Shuki Araki* and Yasuo Butsugan

Department of Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466, Japan

Cyclopropanation of electron-deficient alkenes and Wideqvist-type transformation of carbonyl compounds to cyclopropanes have been achieved by the action of active methylene dibromides and metallic indium.

Heteroatom elements have been attracting growing interest in their use in synthetic organic chemistry. Among them, less common metals including Ga,¹ Sb,² Bi,³ and some lanthanides⁴ have recently proved to be useful for organic transformations; however, indium is still rarely used. We have shown recently that indium metal is effective for Barbier allylation of carbonyl compounds⁵ and for the Reformatsky reaction.⁶ We describe here a novel cyclopropanation of electron-deficient alkenes and Wideqvist-type transformation of carbonyl compounds to tetracyanocyclopropanes, mediated by indium metal.⁷

Cyclopropanation of alkenes (Table 1) was carried out in *N,N*-dimethylformamide (DMF) using active methylene dibromides and indium metal in the presence of lithium iodide (Scheme 1). Electron-deficient alkenes gave good to moder-

ate yields of products, but non-activated and electron-rich alkenes such as cyclohexene and butyl vinyl ether did not give any trace of cyclopropanes. Without lithium iodide, the yields were lower. DMF is the solvent of choice; no reaction occurred in diethyl ether or tetrahydrofuran.

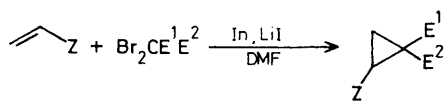
When aldehydes and ketones were treated with dibromomalononitrile, indium, and lithium iodide, tetracyanocyclopropanes were obtained (Scheme 2). Ketones are less reactive than aldehydes, giving lower yields (Table 2). This Wideqvist-type reaction⁸ is considered to proceed *via* alkylidenemalononitrile, which was actually isolated in the reaction with *p*-anisaldehyde. Interestingly, ethyl dibromocynoacetate in place of dibromomalononitrile gave exclusive formation of the corresponding oxiranes (Scheme 3).

The present indium-mediated cyclopropanation of alkenes and Wideqvist-type synthesis of tetracyanocyclopropanes provide easy access to cyclopropanes bearing more than three

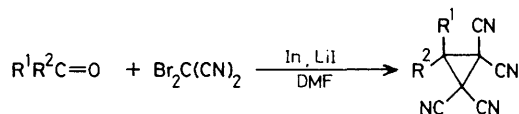
Table 1. Cyclopropanation of electron-deficient alkenes.^a

Alkene	Br ₂ CE ¹ E ²	Yield/% ^b
CH ₂ =CHCOMe	Br ₂ C(CN) ₂	94 ^c (78)
CH ₂ =CHCO ₂ Et		70 ^c
CH ₂ =CHCN		53 ^c
CH ₂ =CHPh		20
PhCH=C(CN) ₂		96
EtCH=C(CN)CO ₂ Et		100 ^{c,d}
CH ₂ =CHCOMe	Br ₂ C(CN)CO ₂ Et	88 ^e (70)
CH ₂ =CHCO ₂ Et		32 ^e (0)
CH ₂ =CHCN		46 ^e
CH ₂ =CHCHO		36 ^{c,e} (43)
CH ₂ =CHCOMe	Br ₂ C(CO ₂ Et) ₂	75
CH ₂ =CHCHO		74

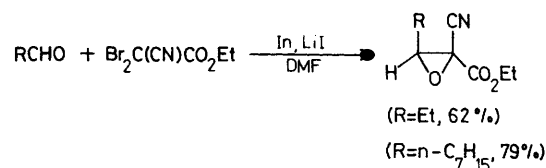
^a All reactions were carried out with alkene (1.5 mmol), Br₂CE¹E² (0.5 mmol), indium powder (0.5 mmol), and lithium iodide (1 mmol) in DMF (1 ml) at room temperature for 1 h. All products gave spectral (¹H n.m.r., i.r., and mass) data and, in the case of new compounds, microanalytical data in agreement with the proposed structures. ^b Isolated yield based on Br₂CE¹E². Figures in parentheses refer to the yields without lithium iodide. ^c New compound. ^d *trans*-Isomer only. ^e Mixture of stereoisomers.



Scheme 1



Scheme 2



Scheme 3. Reaction conditions: RCHO (1.5 mmol), Br₂C(CN)CO₂Et (0.5 mmol), indium powder (0.5 mmol), and lithium iodide (1 mmol) in DMF (1 ml) at 0°C for 1 h.

Table 2. Transformation of carbonyl compounds to tetracyanocyclopropanes.^a

R ¹ R ² C=O		Yield/ % ^b
R ¹	R ²	
Et	H	87
n-C ₇ H ₁₅	H	72 ^c
Ph	H	94
<i>p</i> -MeOC ₆ H ₄	H	47 ^d
2-furyl	H	62
Et	Et	9
	-(CH ₂) ₄ -	39
	-(CH ₂) ₅ -	57
Ph	Me	5

^a All reactions were carried out with carbonyl compound (0.25 mmol), dibromomalononitrile (0.5 mmol), indium powder (0.5 mmol), and lithium iodide (1 mmol) in DMF (1 ml) at 0°C for 1 h. All products gave spectral (¹H n.m.r., i.r., and mass) data and, in the case of new compounds, microanalytical data in agreement with the proposed structures. ^b Isolated yield. ^c New compound. ^d *p*-Methoxybenzylidenemalononitrile was also isolated in 43% yield.

J. CHEM. SOC., CHEM. COMMUN., 1989

electron-withdrawing substituents,⁹ which are known to show interesting and synthetically useful reaction behaviour¹⁰ but are normally difficult to obtain.

Received, 18th April 1989; Com. 9/01652J

References

- 1 S. Araki, H. Ito, and Y. Butsugan, *Appl. Organomet. Chem.*, 1988, **2**, 475.
- 2 Y. Butsugan, H. Ito, and S. Araki, *Tetrahedron Lett.*, 1987, **28**, 3707; Y. Z. Huang, C. Chen, and Y. Shen, *ibid.*, 1988, **29**, 5275, and references cited therein.
- 3 D. H. R. Barton and J-P. Finet, *Pure Appl. Chem.*, 1987, **59**, 937; H. Ohki, M. Wada, and A-y. Akiba, *Tetrahedron Lett.*, 1988, **29**, 4719, and references cited therein.
- 4 H. B. Kagan and J. L. Namy, *Tetrahedron*, 1986, **42**, 6573.
- 5 S. Araki, H. Ito, and Y. Butsugan, *J. Org. Chem.*, 1988, **53**, 1831.
- 6 S. Araki, H. Ito, and Y. Butsugan, *Synth. Commun.*, 1988, **18**, 453.
- 7 For a recent review of cyclopropanation, see: 'The Chemistry of the Cyclopropyl Group,' ed. Z. Rappoport, Wiley, New York, 1987.
- 8 S. Wideqvist, *Arkiv. Kemi. Mineral. Geol.*, 1945, **20B**, 8; H. Hart and F. Freeman, *J. Org. Chem.*, 1963, **28**, 1220.
- 9 For recent synthesis of such cyclopropanes, see: C. Chen, Y. Z. Huang, and Y. Shen, *Tetrahedron Lett.*, 1988, **29**, 1033.
- 10 S. Danishefsky, *Acc. Chem. Res.*, 1979, **12**, 66.