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Efficient cyclopropanation of active methylene compounds. A serendipitous discovery

Veera Reddy Arava,[a,*] Udaya Bhaskara Rao Siripalli[a] and Pramod Kumar Dubey[b]

[a]*Research and Development Laboratories, Suven Life Sciences Ltd, # 18, Phase-III, Jeedimetla, Hyderabad 500055, India*
[b]*Department of Chemistry, J.N.T. University, Hyderabad 500072, India*

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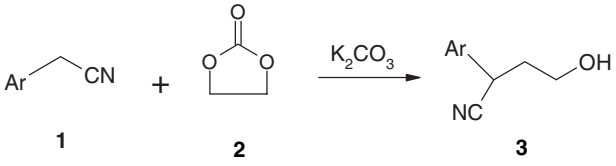
Abstract—Cyclopropanation of active methylene compounds has been achieved in good yields with ethylene carbonate as the cyclopropanating agent in the presence of a simple base.

1. Introduction

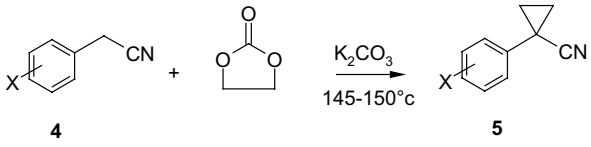
Cyclopropanation of active methylene compounds is a very useful reaction in organic synthesis.[1,2] In general, it is carried out using either ethylene dichloride or ethylene dibromide[3] as the alkylating agent in the presence of a strong base like sodium hydride or 50% aqueous sodium hydroxide in the presence of a phase transfer catalyst (PTC), and the yields are moderate to good. During the course of our investigations on the monomethylation of arylacetonitriles **1** with dimethyl carbonate (DMC) as a selective alkylating agent,[4,5] we explored the reaction of arylacetonitriles **1** with ethylene carbonate[6,7] for generating hydroxyethyl substituted compounds **3** (Eq. 1).



1 2 3

(1)

The treatment of arylacetonitriles **1** with ethylene carbonate **2** in the presence of potassium carbonate at 140–150 °C, to our surprise, generated the cyclopropane derivatives **5** (Eq. 2). A possible mechanism is shown in Scheme 1.



4 5

a) X = H, b) 3-phenoxy, c) X = 3,4-dimethoxy, d) X = 4-chloro,

e) X = 3,4-dichloro f) X = 4-bromo, g) X = 4-fluoro, h) X = 4-methylthio

i) X = 4-methoxy, j) X = 3-methoxy, k) X = 4-methyl, l) X = 3-chloro.

(2)

To check the versatility of this reaction, a series of arylacetonitriles were subjected to the cyclopropanation reaction, and the results are summarized in Table 1. All the cyclopropanes were characterized by spectral data (^{1}H and ^{13}C NMR and IR).

2. Typical experimental procedure

2.1. 1-Arylcyclopropanecarbonitriles (5a–l)

To a magnetically stirred solution of the nitrile (**4a**–**l**, 42.7 mmol) and ethylene carbonate (0.284 mol) was added potassium carbonate (36.2 mmol) at room temperature. The reaction temperature was raised to 145–150 °C and maintained for 1 h. After the consumption of the starting material (by TLC), the reaction mixture

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* Corresponding author. Tel.: +91 40 30923856; fax: +91 40 23193541; e-mail: reddyvenis@rediffmail.com

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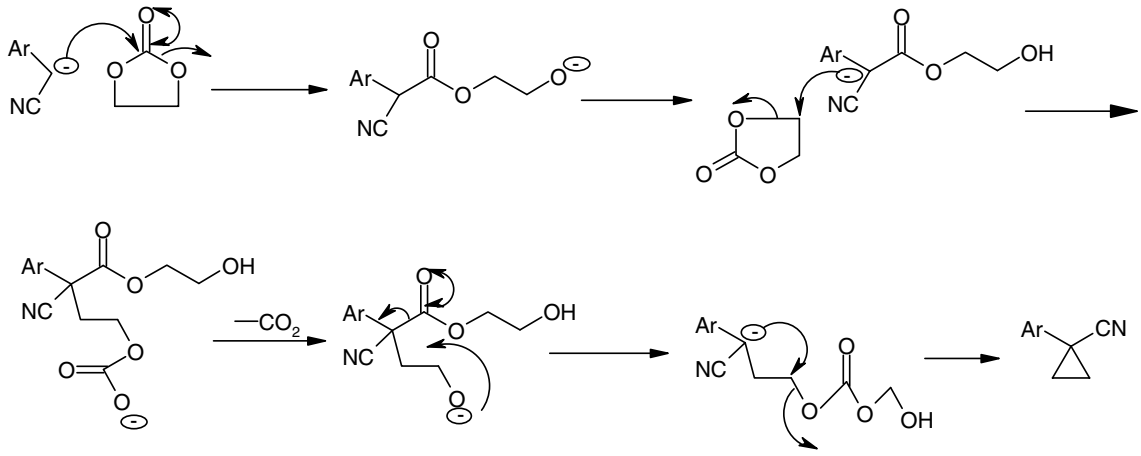

Scheme 1.

Table 1.

Starting material	Yield (%)	^{1}H and ^{13}C NMR data
(a) X = H	46	^{1}H NMR ($CDCl_3$) δ, 1.37–1.40 (2H), 1.68–1.71 (2H), 7.24–7.36 (5H). ^{13}C NMR ($CDCl_3$) δ, 13.4, 17.73, 122, 125.15, 127.3, 128.65, 135.6
(b) X = 3-phenoxy	54	^{1}H NMR ($CDCl_3$) δ, 1.37–1.41 (2H), 1.68–1.72 (2H), 6.89–7.36 (9H). ^{13}C NMR ($CDCl_3$) δ, 13.54, 18.17, 122.05, 115.81, 117.43, 118.82, 120.33, 123.50, 129.69, 130.03, 137.96, 156.42, 157.65
(c) X = 3,4-dimethoxy	56	^{1}H NMR ($CDCl_3$) δ, 1.33–1.36 (2H), 1.64–1.67 (2H), 3.86 (3H), 3.90 (3H), 6.81–6.86 (3H). ^{13}C NMR ($CDCl_3$) δ, 13.00, 16.88, 55.452, 109.49, 110.875, 118.05, 122.46, 127.93, 148.19, 148.69
(d) X = 4-chloro	53	^{1}H NMR ($CDCl_3$) δ, 1.36–1.39 (2H), 1.72–1.75 (2H), 7.20–7.34 (4H). ^{13}C NMR ($CDCl_3$) δ, 13.25, 18.11, 121.98, 127.04, 128.89, 133.38, 134.49
(e) X = 3,4-dichloro	53	^{1}H NMR ($CDCl_3$) δ, 1.38–1.42 (2H), 1.75–1.80 (2H), 7.12–7.44 (3H). ^{13}C NMR ($CDCl_3$) δ, 13.04, 18.36, 121.33, 124.88, 127.51, 130.56, 131.53, 132.79, 136.2
(f) X = 4-bromo	53	^{1}H NMR ($CDCl_3$) δ, 1.36–1.40 (2H), 1.73–1.76 (2H), 7.14–7.49 (4H). ^{13}C NMR ($CDCl_3$) δ, 13.3, 18.13, 121.34, 121.85, 127.27, 131.79, 135.0
(g) X = 4-fluoro	27	^{1}H NMR ($CDCl_3$) δ, 1.34–1.37 (2H), 1.69–1.72 (2H), 7.01–7.29 (4H). ^{13}C NMR ($CDCl_3$) δ, 13.00, 17.57, 115.47, 115.69, 122.23, 127.71, 131.63, 160.64, 163.09
(h) X = 4-methylthio	47	^{1}H NMR ($CDCl_3$) δ, 1.34–1.37 (2H), 1.68–1.71 (2H), 2.47 (3H), 7.01–7.29 (4H). ^{13}C NMR ($CDCl_3$) δ, 12.9, 15.2, 17.6, 122.08, 125.57, 126.43, 132.27, 137.83
(i) X = 4-methoxy	46	^{1}H NMR ($CDCl_3$) δ, 1.30–1.33 (2H), 1.63–1.66 (2H), 3.78 (3H), 6.80–7.25 (4H). ^{13}C NMR ($CDCl_3$) δ, 12.6, 16.94, 54.8, 113.88, 122.49, 126.35, 127.41
(j) X = 3-methoxy	52	^{1}H NMR ($CDCl_3$) δ, 1.37–1.40 (2H), 1.67–1.71 (2H), 3.80 (3H), 6.79–7.27 (4H). ^{13}C NMR ($CDCl_3$) δ, 13.47, 17.89, 54.90, 111.51, 112.45, 117.38, 122.18, 129.65, 137.31, 159.67
(k) X = 4-methyl	43	^{1}H NMR ($CDCl_3$) δ, 1.27–1.29 (2H), 1.65–1.68 (2H), 2.31 (3H), 7.12–7.23 (4H). ^{13}C NMR ($CDCl_3$) δ, 13.07, 17.51, 20.46, 122.35, 125.4, 129.2, 132.67, 136.97, 137.27
(l) X = 3-chloro	53	^{1}H NMR ($CDCl_3$) δ, 1.39–1.42 (2H), 1.73–1.76 (2H), 7.17–7.30 (4H). ^{13}C NMR ($CDCl_3$) δ, 13.25, 18.08, 121.56, 123.6, 125.6, 127.45, 129.5, 137.85, 138.87

was cooled to 45–50 °C, treated with water (75 ml) and extracted with toluene (2 × 50 ml). The combined organic extract was washed with water (25 ml) and then dried over Na_2SO_4. Evaporation of the solvent and purification of the residue by column chromatography on silica gel furnished the 1-arylcyclopropanecarbonitriles **5a–l** (Table 1).

3. Conclusions

We have developed the use of the simple, cheap and versatile ethylene carbonate as an efficient cyclopropanating reagent of active methylene compounds.

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