5,10,15,20-Tetraphenylporphyrinato-rhodium(III) Iodide Catalyzed Cyclopropanation Reactions of Alkenes Using Glycine Ester Hydrochloride

Anthony G. M. Barrett,* D. Christopher Braddock, Isabelle Lenoir, and Hitoshi Tone

Department of Chemistry, Imperial College of Science, Technology and Medicine, South Kensington, London SW7 2AY, UK

agmb@ic.ac.uk

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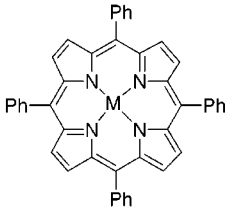
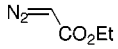
The metal complex catalyzed reaction of an alkene with an α-diazo ester is an efficient method for the preparation of cyclopropane derivatives.[1] However, since diazo compounds are unstable intermediates, the use of this method for the preparation of cyclopropanecarboxylates is fraught with hazards on a large scale. In consequence, we sought to explore the possibility of generating cyclopropanecarboxylate esters from glycine by diazotization using sodium nitrite and a Brønsted acid in the presence of a cyclopropanation catalyst. We sought to mediate the formation of the metallocarbene and its reaction with an alkene to provide the target cyclopropanecarboxylate in situ as the diazoester was formed. Herein we report the use of 5,10,15,20-tetraphenylporphyrazinatorhodium(III) iodide **1b** (TPPRhI) as such a catalyst for the direct conversion of glycine ethyl ester into cyclopropane derivatives.



1a M = 2H
1b M = RhI



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Initially we examined the conversion of styrene (**3a**) and glycine ethyl ester hydrochloride **4** into ethyl 2-phenylcyclopropanecarboxylate (**5a**) by reaction with sodium nitrite, a Brønsted or Lewis acid, and a copper(I), copper(II), rhodium(II), or rhodium(III) catalyst. We expected that such catalysts should mediate the (formal) carbene transfer from ethyl diazoacetate (**2**) to styrene **3a**. Conversion to provide **5a** using most copper(I), copper(II), rhodium(II), or rhodium(III) catalysts was at best inefficient. However, the use of the rhodium(III) porphyrin complex **1b**[2] provided the ester **5a** (62%) as a 1:1 mixture of *syn*- and *anti*-isomers. Optimally, the reaction was carried out using sodium nitrite (1.2 equiv), sulfuric acid (5 mol %), and iodide **1b** (0.5 mol %) in water and dichloromethane at room temperature. Excess styrene (10 equiv) was necessary for good conversions to provide **5a**. The cyclopropanation reaction was carried out using a range of alkenes (Table 1). The procedure was effective for simple aromatic and aliphatic compounds (entries 1−4 and 6−8). The poor yield of cyclopropane **5e** (entry 5) was most probably due to the volatility of 1-hexene. Both *trans*- and *cis*-1,2-disubstituted alkenes gave the corresponding cyclopropanes in good yields (entries 9, 10, and 13−17) except for *cis*- and *trans*-stilbene (entries 11 and 12) which failed to react at a significant rate. Both 1,1-disubstituted alkenes **3r** and **3s** gave the corresponding esters **5r** and **5s** (entries 18 and 19). While methyl 3-butenoate (**3t**) and *tert*-butyl vinyl ether (**3u**) gave rise to the cyclopropanes **5t** and **5u**, the allylic alcohol **3v**, allyl acetate (**3w**), and methyl vinyl ketone (**3x**) failed to provide the cyclopropane esters (entries 22−24).

Typically, rhodium-catalyzed reactions between diazoesters and olefins give *anti* cyclopropanes as the major product.[1,3] However, Callot has previously shown that the use of TPPRhI **1b** with diazoesters reverses this selectivity to give the *syn* product—although the selectivity is modest.[4,5] An optically pure binaphthyl-modified "chiral wall" porphyrin described by Kodadek also shows *syn* selectivity.[6] Recent work by Katsuki has shown that high *syn* selectivity (and excellent enantiomeric excesses) can also be obtained by the application of a chiral ruthenium salen complex.[7] We were therefore surprised to find that in general there was little *syn*/*anti* selectivity in our system using TPPRhI and the cyclopropyl adducts **5a**,[8] **5b**,[9] **5c**,[9] **5d**,[6] **5e**,[10] **5f**,[11] **5g**,[11] **5n**, **5p**, **5r**,[6] **5s**,[12] **5t**, and **5u** were obtained as an approximate 1:1 mixture of isomers.[13] Possibly this difference is the result of a different intimate coordination sphere at rhodium during the catalytic cycle under the nitrosation reaction conditions.[14] For the cyclopropanation of 1,2-dihydronaphthalene (**3i**), the *endo* (i.e., *syn*) isomer[15] was found to predominate (3.5:1). The *endo* configuration was assigned

(1) (a) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic methods for Organic synthesis with Diazo Compounds*; Wiley: New York, 1998. (b) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. (c) Davies, H. M. L. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, pp 1031−1067.

(2) Callot, H. J.; Schaeffer, E. *Nouv. J. Chim.* **1980**, *4*, 311.

(3) For recent examples, see: (a) Simkhovich, L.; Mahammed, A.; Goldberg, I.; Gross, Z. *Chem. Eur. J.* **2001**, 1041−1055. (b) Dias, E. L.; Brookhart, M.; White, P. S. *Chem. Commun.* **2001**, 423−424. (c) Davies, H. M. L.; Panaro, S. A. *Tetrahedron* **2000**, *56*, 4871−4880. (d) Demonceau, A.; Simal, F.; Noels, A. F.; Vinas, C.; Nunez, R.; Teixidor, F. *Tetrahedron Lett.* **1997**, *38*, 7879−7882 and references therein.

(4) Callot, H. J.; Piechcocki, C. *Tetrahedron Lett.* **1980**, *21*, 3489−3492.

(5) Callot, H. J.; Metz, F.; Piechocki, C. *Tetrahedron* **1982**, *38*, 2365−2369.

(6) O'Malley, S.; Kodadek, T. *Tetrahedron Lett.* **1991**, *32*, 2445−2447.

(7) Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron* **2000**, *56*, 3501−3509.

(8) Solladié-Cavallo, A.; Isarno, T. *Tetrahedron Lett.* **1999**, *40*, 1579−1582.

(9) Hixson, S. S.; Franke, L. A.; Gere, J. A.; Xing, Y.-d. *J. Am. Chem. Soc.* **1988**, *110*, 3601−3610.

(10) Cho, D.-J.; Jeon, S.-J.; Kim, H.-S.; Cho, C.-S.; Shim, S.-C.; Kim, T.-J. *Tetrahedron: Asymmetry* **1999**, *10*, 3833−3848.

(11) Simal, F.; Jan, D.; Demonceau, A.; Noels, A. F. *Tetrahedron Lett.* **1999**, *40*, 1653.

(12) Konzelman, L. M.; Conley, R. T. *J. Org. Chem.* **1968**, *33*, 3828−3838.

(13) In general, the very similar R_f values of the *syn*:*anti*-isomers precluded efficient chromatographic separation, and the cyclopropane adducts were best characterized as a mixture.

(14) The reaction of styrene and ethyl diazoacetate catalyzed by TPP*Ru*(CO) has been reported to give the *anti* ester as the major product: Galardon, E.; Le Maux, P.; Simonneaux, G. *Tetrahedron* **2000**, *56*, 615−621 and references therein.

(15) Huisgen, R.; Juppe, G. *Chem Ber.* **1961**, *94*, 2332−2349.

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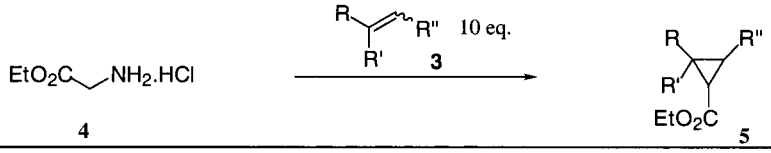
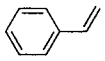
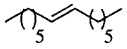
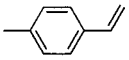
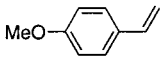
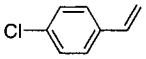
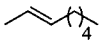
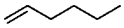
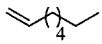
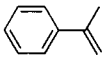
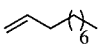
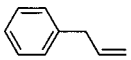
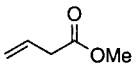
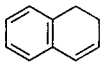
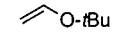
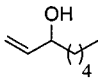
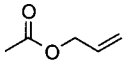
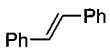
Table 1. Conversion of Hydrochloride 4 into Cyclopropane Esters 5



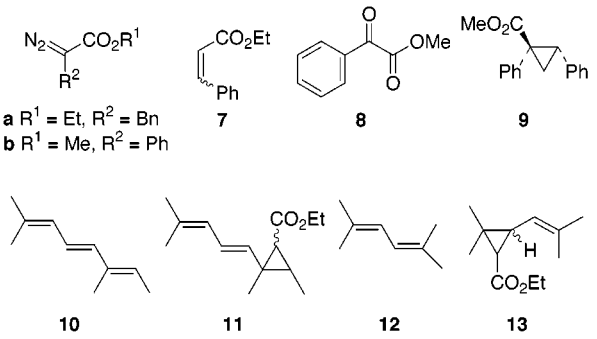
Entry	Alkene		Yield 5 (%)[a]	Entry	Alkene		Yield 5 (%)[a]
1		**3a**	**5a** (62)	13		**3m**	**5m** (55)
2		**3b**	**5b** (72)	14		**3n**	**5n** (52)
3		**3c**	**5c** (69)	15		**3o**	**5o** (49)
4		**3d**	**5d** (54)	16		**3p**	**5p** (59)
5		**3e**	**5e** (20)	17		**3q**	**5q** (57)
6		**3f**	**5f** (59)	18		**3r**	**5r** (60)
7		**3g**	**5g** (54)	19		**3s**	**5s** (64)
8		**3h**	**5h** (53)	20		**3t**	**5t** (40)
9		**3i**	**5i** (53)	21		**3u**	**5u** (64)
10		**3j**	**5j** (50)	22		**3v**	**5v** (0)
11		**3k**	**5k** (0)	23		**3w**	**5w** (0)
12		**3l**	**3l** (0)	24		**3x**	**5x** (0)

[a] Isolated combined yield of *cis*- and *trans*-isomers after chromatography.

on the basis of the ^{1}H NMR spectrum, where the aryl group shields the neighboring ethyl ester group (*endo* $CO_2CH_2CH_3$ δ_H = 1.07 ppm; *exo* $CO_2CH_2CH_3$ δ_H = 1.29 ppm) as delineated by Solladié-Cavallo and Isarno.[8] Interestingly, cyclohexene, cyclopentene, and cyclooctene displayed good *exo* selectivity (>9:1). These isomers are readily distinguished from their *endo* counterparts by inspection of the coupling constant of the characteristic triplet in the ^{1}H NMR spectrum for the α-ester proton (**5j**,[16] δ_H = 1.40 ppm, J = 4.3 Hz; **5o**,[16] δ_H = 1.40 ppm, J = 2.8 Hz; **5q**,[17] δ_H = 1.11 ppm, J = 4.3 Hz). Finally, allylbenzene-derived cyclopropane **5h**[6] was obtained predominately as the *anti*-isomer. This selectivity may be due to favorable π-stacking interactions of the phenyl group with the porphyrin unit.

An attempt was made to extend the methodology by replacement of glycine ethyl ester hydrochloride with the corresponding ester salts of alanine, cysteine, serine, phenylalanine, and phenylglycine. All these reactions failed to provide cyclopropanecarboxylates from styrene. In a control experiment, isolated diazoester **6a**[18] was allowed to react under the standard cyclopropanation procedure with or without sulfuric acid and water. In

(16) Hagan, M.; Lüning, U. *Chem. Ber.* **1997**, *130*, 231−234.
(17) Casey, C. P.; Miles, W. H.; Tukada, H. *J. Am. Chem. Soc.* **1985**, *107*, 2924−2931.
(18) Aitken, R. A.; Armstrong, J. M.; Drysdale, M. J.; Ross, F. C.; Ryan, B. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 593−604.



both cases, only ethyl cinnamate **7**[19] was isolated. Presumably this was formed via the diazonium salt and β-elimination. Reaction of the isolated diazoester **6b**[20] with TPPRhI **1b** and styrene gave only methyl benzoylformate (**8**)[21] on chromatography. This reaction was repeated with rigorous exclusion of oxygen and under anhydrous conditions, giving only the *trans*-cyclopropane **9**[22] (27%).

To understand how the cyclopropanation of styrene (**3a**) with glycine ethyl ester hydrochloride (**4**) proceeded, the course of reaction was followed by IR spectroscopy. Ethyl diazoacetate **2** (2114 cm^{-1}) was formed shortly after the start of the reaction. Its concentration was highest after 2 h when the mixture contained approximately 40−50% of **4** converted into diazo ester **2**. The concentration of **2** then decreased gradually, and after 9 h, no further diazo ester **2** was present. The cyclopropane (1721 cm^{-1}) **5a** was steadily formed from 2 to 3 h after the start of the reaction.

Finally, pyrethroids are a class of compounds with excellent insecticidal activity and are noteworthy in not being persistent in the environment.[23] Among other methods, these valuable agrochemicals have been prepared via rhodium-catalyzed cyclopropanation of olefins with α-diazo esters.[24] In consequence, we sought to prepare a representative pyrethroid from the glycine derivative **4**. Under the standard procedure, triene **10** provided cyclopropane ester **11** (59%) as a 1:1 *syn*:*anti* mixture. Reaction of diene **12** gave ethyl chrysanthemate (**13**)[25] (52%) as a 1:1 mixture of *syn:anti* diastereoisomers.

In conclusion, the one-pot synthesis of cyclopropanes from glycine ethyl ester hydrochloride (**4**) described in this paper avoids the need to isolate ethyl diazoacetate (**2**). The quantity of rhodium catalyst utilized was low (0.5 mol %), and the cyclopropane derivatives were generally obtained in good yield.

Experimental Section

General. CH_2Cl_2 was distilled from CaH_2. All other compounds were purchased from commercial sources and used as supplied. Analytical thin-layer chromatography was performed on precoated glass-backed plates (Merck Kieselgel 60 F254) and visualized with UV light or potassium permanganate as appropriate. Column chromatography was performed under medium pressure using Merck Kieselgel 60 (230−400) mesh (eluants are given in parentheses).

5,10,15,20-Tetraphenylporphyrinatorhodim(III) Iodide (1b).[2] A suspension of tetracarbonyl di-μ-chlorodirhodium (250 mg, 0.64 mmol) in dry CH_2Cl_2 (35 mL) under N_2 was added to Na_2CO_3 (860 mg, 8.0 mmol) and 5,10,15,20-tetraphenyl-21*H*,23*H*-porphyrin **1a** (170 mg, 0.28 mmol). The mixture was stirred for 12 h and washed with distilled H_2O (2 × 30 mL), dried ($MgSO_4$), and filtered. I_2 (110 mg, 0.44 mmol) was added, and the mixture was stirred for 1.5 h and concentrated in vacuo. Chromatography of the residue (4:1 hexanes:EtOAc) afforded **1b** (151 mg, 64%) as purple solid that was washed with hexanes (3 mL) and a drop of CH_2Cl_2: mp >350 °C; TLC R_f 0.25 (4:1 hexanes:EtOAc); MS (FAB+) *m/z* 842 $(M)^{+\bullet}$ 715 (M − I).

General Procedure for the Preparation of Cyclopropane Derivatives. An alkene (6.0 mmol) and TPPRh(III)I **1b** (2.5 mg, 30 μmol) were added in one portion to glycine ethyl ester hydrochloride (**4**) (84 mg, 0.60 mmol) in distilled H_2O (1 mL), and CH_2Cl_2 (10 mL) was added. The biphasic reaction mixture was cooled to −10 °C, and $NaNO_2$ (50 mg, 0.72 mmol) in distilled H_2O (0.50 mL) and aqueous H_2SO_4 (57.0 μL of a 5% w/w solution) were added in one portion. The mixture was allowed to warm to room temperature and stirred for 4 days. The mixture was diluted with CH_2Cl_2 (50 mL), dried ($MgSO_4$), rotary evaporated, and chromatographed.

Ethyl 2-Phenylcyclopropane-1-carboxylate (5a). Reaction of glycine ethyl ester hydrochloride (**4**) (84 mg, 0.60 mmol) and styrene (**3a**) (700 μL, 6.0 mmol) afforded *cis*-**5a** (35 mg, 31%) as a colorless oil: TLC R_f 0.35 (10:1 hexanes:Et_2O); IR (film) 1728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29−7.19 (m, 5H), 3.89 (q, 2H, J = 7.0 Hz), 2.60 (app. q, 1H, J = 8.5 Hz), 2.10 (ddd, 1H, J = 9.3, 8.6, 5.0 Hz), 1.73 (ddd, 1H, J = 6.5, 5.0, 4.6 Hz), 1.35 (ddd, 1H, J = 8.6, 8.3, 4.6 Hz), 0.99 (t, 3H, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 136.6, 129.3, 127.9, 126.6, 60.1, 25.4, 21.8, 14.0, 11.1; MS (CI) *m/z* 208 $(M + NH_4)^+$, 191 $(M + H)^+$; HRMS (CI) calcd for $C_{12}H_{15}O_2$ $(M + H)^+$, 191.1072; found $(M + H)^+$, 191.1063; and *trans*-**5a** (35 mg, 31%) as a colorless solid: TLC R_f 0.30 (10:1 hexanes:Et_2O); mp 29 °C; IR (film) 1723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.11 (m, 5H), 4.19 (q, 2H, J = 7.0 Hz), 2.54 (ddd, 1H, J = 9.2, 6.5, 4.0 Hz),1.92 (ddd, 1H, J = 8.2, 5.2, 4.0 Hz), 1.62 (ddd, 1H, J = 9.2, 5.3, 4.6 Hz), 1.33 (ddd, 1H, J = 8.2, 6.6, 4.6 Hz), 1.30 (t, 3H, J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 140.1, 128.5, 126.5, 126.2, 60.7, 26.2, 24.2, 17.1, 14.3; MS (CI) *m/z* 208 $(M + NH_4)^+$, 191 $(M + H)^+$; HRMS (CI) calcd for $C_{12}H_{15}O_2$ $(M + H)^+$, 191.1072; found $(M + H)^+$, 191.1068.

Ethyl 2,3-Dimethyl-2-(4-methyl-1,3-pentadienyl)-1-cyclopropanecarboxylate (11). Reaction of glycine ethyl ester hydrochloride (**4**) (84 mg, 0.60 mmol) and 2,6-dimethyl-2,4,6-octatriene **10** (1.0 mL, 6.0 mmol) afforded **11** (78 mg, 59%) as a 1:1 mixture of diastereoisomers as a colorless oil: TLC R_f 0.40 (10:1 hexanes:Et_2O); IR (film) 1725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.34−6.31 (m, 2H), 6.07 (d, 1H, J = 15.5 Hz, 1 isomer), 5.91 and 5.82 (d, 2H, J = 10.5 Hz, 1 isomer), 5.40 (d, 1H, J = 15.5 Hz, 1 isomer), 4.16−4.10 (m, 4H), 1.80−1.64 (m, 10H), 1.60−1.38 (m, 4H), 1.34−1.02 (m, 20H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 170.9, 139.0, 133.0, 132.8, 128.8, 126.5, 126.4, 125.6, 124.8, 60.2, 59.8, 35.0, 32.9, 32.0, 30.3, 29.7, 28.5, 25.9, 25.8, 24.6, 18.3, 18.2, 16.9, 16.8, 14.3, 13.2, 8.3; MS (CI) *m/z* 223 $(M + H)^+$; HRMS (CI) calcd for $C_{14}H_{23}O_2$ $(M + H)^+$, 223.1698; found $(M + H)^+$, 223.1695.

Ethyl Chrysanthemate (13). Reaction of glycine ethyl ester hydrochloride (**4**) (84 mg, 0.60 mmol) and 2,5-dimethylhexa-2,4-diene (**12**) (855 μL, 6.0 mmol) afforded **13** (61 mg, 52%) as a 1:1 mixture of diastereoisomers as a colorless oil: TLC R_f 0.40 (10:1 hexanes:Et_2O); IR (film) 1725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.40 (d, 1H, J = 8.5 Hz, 1 isomer), 4.90 (d, 1H, J = 8.0 Hz, 1 isomer), 4.19−4.06 (m, 4H), 2.08−1.63 (m, 16 H), 1.40−1.15 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 171.1, 135.3, 134.5, 121.2, 118.2, 60.1, 59.7, 34.8, 32.5, 32.1, 31.2, 28.8, 28.4, 26.2, 25.9, 25.5, 25.0, 22.1, 20.3, 18.4, 18.2, 14.7, 14.3; MS (CI) *m/z* 197 $(M + H)^+$; HRMS (CI) calcd for $C_{12}H_{21}O_2$ $(M + H)^+$, 197.1541; found $(M + H)^+$, 197.1535.

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Supporting Information Available: Experimental procedures and data for cyclopropane derivatives **5b**−**5j**, **5m**−**5u**, and **9**, diazoesters **6a** and **6b**, and esters **7** and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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