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Reaction of magnesium cyclopropylidene with *N*-lithio arylamines: a method for generation of α-amino-substituted cyclopropylmagnesiums and a study for their reactivity with electrophiles

Tsuyoshi Satoh,[a,*] Mariko Miura,[a] Ken Sakai[b] and Yoshimi Yokoyama[b]

[a]*Department of Chemistry, Faculty of Science, Tokyo University of Science, Kagurazaka, Shinjuku-ku, Tokyo 162-8601, Japan*
[b]*Department of Chemistry, Faculty of Science, Kyushu University, Hakozaki 6-10-1, Higashi-ku, Fukuoka 812-8581, Japan*

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Abstract—Magnesium cyclopropylidene was generated from 1-chlorocyclopropyl phenyl sulfoxide with *i*-PrMgCl in THF at −78 °C in high yield by a sulfoxide–magnesium exchange reaction. The generated magnesium cyclopropylidene was found to be reactive with *N*-lithio arylamines to give α-amino-substituted cyclopropylmagnesiums. The reaction of the α-amino-substituted cyclopropylmagnesiums with several electrophiles was examined and a new method for a synthesis of cyclopropane amino acid derivatives was realized.

1. Introduction

Carbenes and carbenoids have long been recognized as highly reactive carbon species and are frequently used as useful intermediates in organic synthesis.[1] In the synthetic viewpoint, however, many carbenes are relatively short-lived and are too reactive to control. Recently, carbene–metal complexes (metal carbenes or metallocarbenes) were found to be controllable and highly effective carbenoids and are used widely in organic synthesis.[1b]

Cyclopropylidenes (carbenacyclopropanes) are the carbenes or carbenoids of cyclopropanes and are also known as interesting reactive intermediates. Cyclopropylidenes are usually known as the fleeting intermediates of the reaction of 1,1-dihalocyclopropanes with alkylmetals giving allenes.[2] These reactions are called the Doering–Moore–Skattebol reaction or the Doering–LaFlamme allene synthesis.[3]

Recently, we are interested in the chemistry of the magnesium carbenoids derived from α-haloalkyl sulfoxides[4] or α-haloalkenyl sulfoxides[5] by the sulfoxide–magnesium exchange reaction.[6] In the studies, we have found that the magnesium cyclopropylidenes **2**, which were derived from 1-chlorocyclopropyl phenyl sulfoxides **1** with a Grignard reagent by the sulfoxide–magnesium exchange reaction, are much more stable and controllable compared to the corresponding lithium cyclopropylidenes and could be used in organic synthesis.[7]

In continuation of our interest in the use of the magnesium cyclopropylidenes in organic synthesis we investigated the reaction of the magnesium cyclopropylidenes **2** with several nucleophiles and found that the reaction with *N*-lithio arylamines gave α-amino-substituted cyclopropylmagnesiums **3**. We also investigated the reaction of the cyclopropylmagnesiums **3** with several electrophiles and developed this chemistry to a new method for a synthesis of cyclopropane amino acid derivatives **4** (E=$COOCH_3$) (Scheme 1).

Cyclopropane amino acids (1-aminocyclopropane-1-carboxylic acid) and their derivatives have recently received considerable attention.[8] The reaction described below is worth noting as a unique way for the synthesis of cyclopropane amino acid derivatives.

Keywords: Sulfoxide; Sulfoxide–magnesium exchange; Magnesium cyclopropylidene; α-Amino-substituted cyclopropylmagnesium; Cyclopropane amino acid.
* Corresponding author. Tel.: +81 3 5228 8272; fax: +81 3 3235 2214; e-mail: tsatoh@ch.kagu.tus.ac.jp

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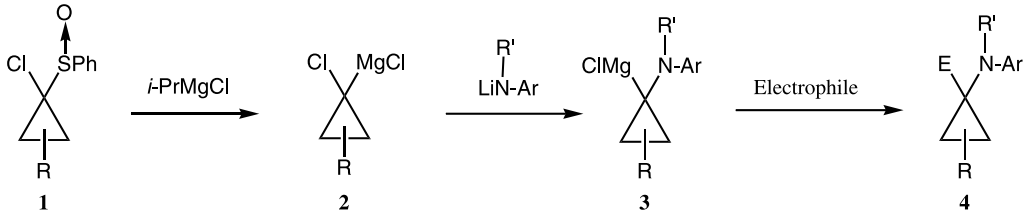


Scheme 1.

2. Results and discussion

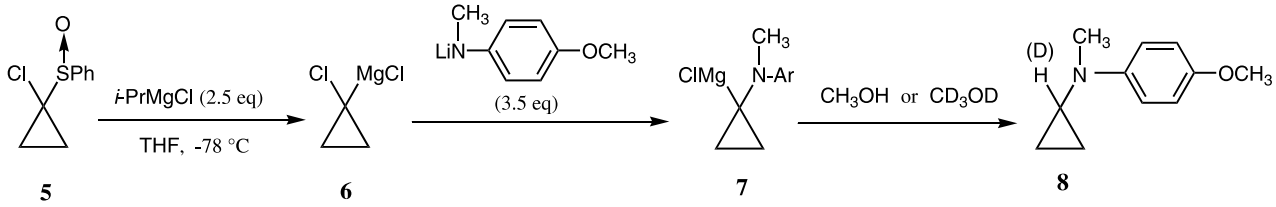
2.1. Generation of magnesium cyclopropylidene 6 from 1-chlorocyclopropyl phenyl sulfoxide 5 by the sulfoxide–magnesium exchange reaction and their reaction with *N*-lithio arylamines

First, 1-chlorocyclopropyl phenyl sulfoxide **5** was synthesized from commercially available cyclopropyl phenyl sulfide[7b] and it was treated with 2.5 equiv of *i*-PrMgCl in THF at −78 °C. The sulfoxide–magnesium exchange reaction took place instantaneously to afford 1-chlorocyclopropyl magnesium chloride **6** in high yield.[7] To this reaction mixture, 3.5 equiv of *N*-lithio *N*-methyl *p*-anisidine (prepared from *N*-methyl *p*-anisidine with *n*-BuLi in THF) was added through a cannula and the reaction mixture was slowly allowed to warm to −50 °C (Scheme 2, entry 1).

Fortunately, the desired *N*-cyclopropyl *N*-methyl *p*-anisidine **8** was obtained in 42% yield. When the temperature of the reaction was allowed to warm to −40 °C, the yield of **8** was improved to 82% (entry 2). Interestingly, quenching of this reaction with CD_3OD gave the deuterated compound **8** (D) and the deuterium incorporation was measured to be 98% by ^1H NMR. This result indicated that the intermediate of this reaction is α-amino-substituted cyclopropylmagnesium **7**.

The temperature of the reaction mixture was further allowed to warm to room temperature (entries 3–5); however, the yields were the same within experimental error. The results in entries 2–5 implied that the reaction of **6** with *N*-lithio *N*-methyl *p*-anisidine was almost completed at about −40 °C and the resulting α-amino-substituted cyclopropylmagnesium **7** is stable at room temperature. When this reaction was conducted with 2 equiv of *N*-lithio *N*-methyl *p*-anisidine, the same yield of **8** was obtained (entry 6). It is noted that the reaction with 1.5 equiv of the amine gave a diminished yield (61%) of **8**.

Encouraged by these results, we investigated the reaction of magnesium cyclopropylidene **6** with other *N*-lithioamines and the results are summarized in Table 1. *N*-Methylaniline, 4-chloro-*N*-methylaniline, and *N*-benzyl-*p*-anisidine gave 60–67% yield of the desired *N*-cycloproyl aryl amines (**9a**–**9c**) and quenching with CD_3OD gave the deuterated compounds with high deuterium content (entries 1–3). Diphenylamine gave the desired cyclopropyl amine **9d**; however, the yield was not satisfactory (entry 4). Interestingly, dibenzylamine did not afford any

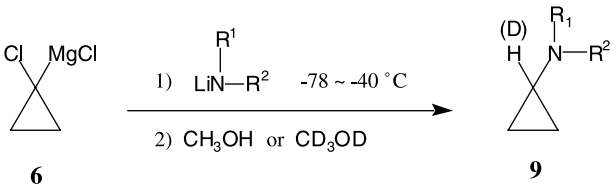


Entry	Temperature	Electrophiles	**8**	
			Yield / %	D-content / %
1	-78 ~ -50 °C	CH_3OH	42	--
2	-78 ~ -40 °C	CD_3OD	82	98
3	-78 ~ -30 °C	CH_3OH	76	--
4	-78 ~ 0 °C	CH_3OH	79	--
5	-78 ~ room temp.	CD_3OD	82	98
6[a]	-78 ~ -40 °C	CH_3OH	82	--

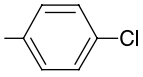
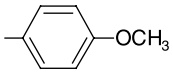
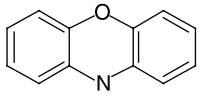
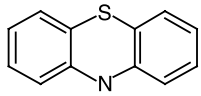
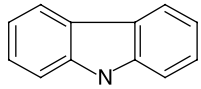
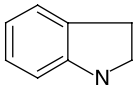
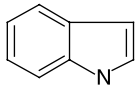
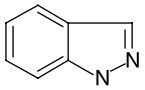
[a] The reaction was carried out with 2.0 equivalents of *N*-lithio *N*-methyl *p*-anisidine.

Scheme 2. Generation of magnesium cyclopropylidene **6** and reation with *N*-lithio *N*-methyl *p*-anisidine followed by CH_3OH or CD_3OD.

Table 1. Reaction of magnesium cyclopropylidene **6** with *N*-lithio amines followed by CH_3OH or CD_3OD



6 **9**

Entry	R^1	R^2	Equiv of amine	**9**		
					Yield (%)	D-content (%)
1	CH_3		3.5	**9a**	67	93
2	CH_3		3.5	**9b**	60	90
3	CH_2Ph		3.5	**9c**	60	98
4			3.5	**9d**	42	92
5	CH_2Ph	CH_2Ph	3.5	**9e**	0	
6[a]			2.0	**9f**	87	99
7[a]			2.0	**9g**	55	—[b]
8[a]			2.0	**9h**	43	—[b]
9[a]			2.0	**9i**	75	—[b]
10[a]			2.0	**9j**	21	—[b]
11[a]			2.0	**9k**	12	—[b]

[a] Temperature of the reaction mixture was allowed to warm to room temperature.
[b] The reaction was quenched with methanol.

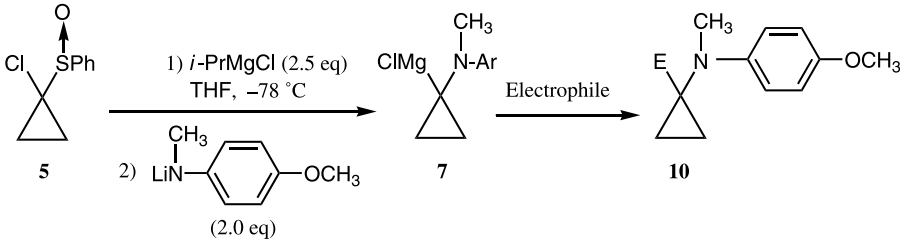
cyclopropylamine at all (entry 5). Only isopropyl phenyl sulfoxide and dibenzylamine were observed from the reaction mixture. This result indicated that the magnesium cyclopropylidene **6** only reacts with *N*-lithio arylamines. This result consistents with that of the reaction of *N*-lithio amines with the magnesium carbenoids generated from 1-chloroalkyl phenyl sulfoxides reported before.[4c]

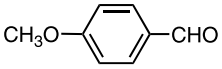
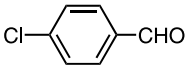
Further, we investigated the reaction of **6** with *N*-lithio nitrogen-containing heterocyclic compounds. In these cases, we used 2 equiv of the nucleophiles. Phenoxazine gave excellent yield of **9f** with perfect deuterium incorporation (entry 6). Phenothiazine and carbazole gave moderate yields of the desired compounds **9g** and **9h** (entries 7 and 8). Indoline gave good yield of the desired compound **9i**; however, indole and indazole gave very poor yields (entries 10 and 11). These results implied that the yields of the reaction of **6** with *N*-lithio nitrogen-containing heterocyclic compounds are fairly variable with the used heterocyclic compounds.

2.2. Investigation of the reactivity of the α-amino-substituted cyclopropylmagnesiums 7 with electrophiles and a new synthesis of cyclopropane amino acid derivatives

As described above, the reaction of the magnesium cyclopropylidene **6** with *N*-lithio arylamines gave α-amino-substituted cyclopropylmagnesiums, which were deuterated with high deuterium incorporation. If these

Table 2. Generation of α-amino-substituted cyclopropylmagnesium **7** and reaction with several electrophiles



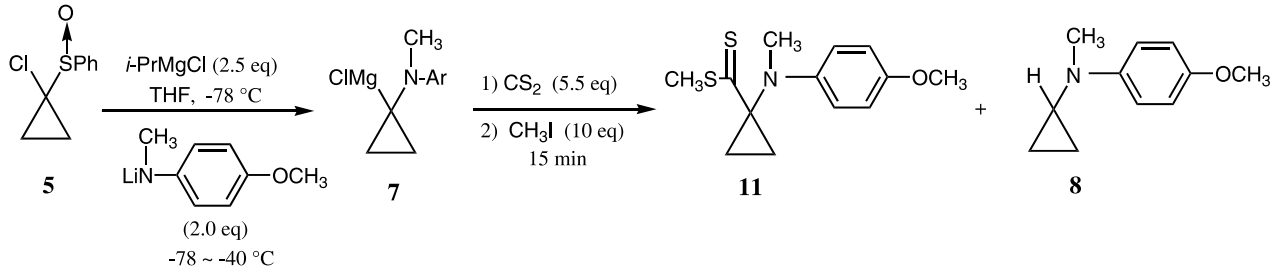
Entry	Electrophile	Equiv	Conditions	**10**	
					Yield (%)
1	PhCHO	5.5	−40 to −20 °C, 1 h	**10a**	40
2		5.5	−40 to −20 °C, 1 h	**10b**	53
3		5.5	−40 to −20 °C, 1 h	**10c**	0[a]
4	CH_3CH_2CHO	5.5	−40 to −20 °C, 1 h		0[a]
5	$ClCOOC_2H_5$	3.0	−40 °C, 10 min	**10d**	10
6[b]	$ClCOOC_2H_5$	5.5	−40 °C, 10 min	**10d**	20
7[b]	$ClCOOCH_3$	5.5	−40 °C, 10 min	**10e**	11
8[b]	$NCCOOC_2H_5$	5.5	−40 °C, 10 min		0[a]
9[b]	CO_2	5.5	−40 °C, 10 min		Complex

[a] No reaction was observed.
[b] 3.5 equiv of *N*-lithio *N*-methyl *p*-anisidine was used in this reaction.

cyclopropylmagnesiums have enough nucleophilicity to several electrophiles, addition of the electrophiles to the reaction mixture was expected to give *N*-cyclopropylamines having a substituent at the α-position **10** (Table 2). We tried to trap the α-amino-substituted cyclopropylmagnesium **7** with several electrophiles and the results are summarized in Table 2.

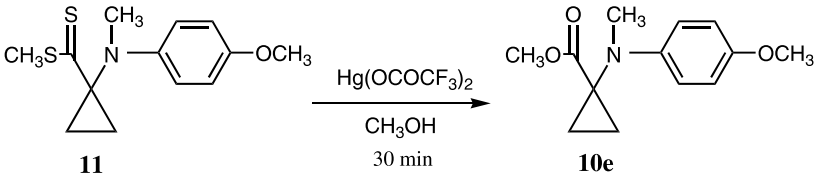
Benzaldehyde and *p*-anisaldehyde gave the desired adduct **10a** and **10b** in moderate yield; however, *p*-chlorobenzaldehyde and propionaldehyde gave none of the desired adduct (entries 1–4). These results implied that the nucleophilicity of **7** is quite low. Next, with great anticipation, we investigated the reaction of **7** with ethyl chloroformate; however, only maximum 20% yield of the desired cyclopropane amino acid derivative **10d** was obtained. Methyl chloroformate, ethyl cyanoformate, and carbon dioxide were not effective (entries 7–9).

Finally, we investigated the reaction of **7** with carbon disulfide (Scheme 3).[9] α-Chlorocyclopropyl phenyl sulfoxide **5** was treated with 2.5 equiv of *i*-PrMgCl followed by *N*-lithio *N*-methyl *p*-anisidine (2.0 equiv) and the



Entry	Conditions for the treatment with CS_2	**11** / yield %	**8** / yield %
1	-40 °C, 10 min	Trace	75
2	-40 °C, 1 h	17	61
3	-40 ~ -20 °C, 1 h	72	10
4	-40 ~ room temp., 2 h	91	0

Scheme 3. Generation of α-amino-substituted cyclopropylmagnesium chloride **7** and reaction with CS_2 followed by iodomethane.



Entry	Conditions	$Hg(OCOCF_3)_2$ (equiv)	**10e** / yield %
1	Room temperature	2	40[a]
2	Room temperature	3	53
3	0 °C	3	71
4	-20 °C	3	92

[a] Dithioester **11** was recovered in 16% yield.

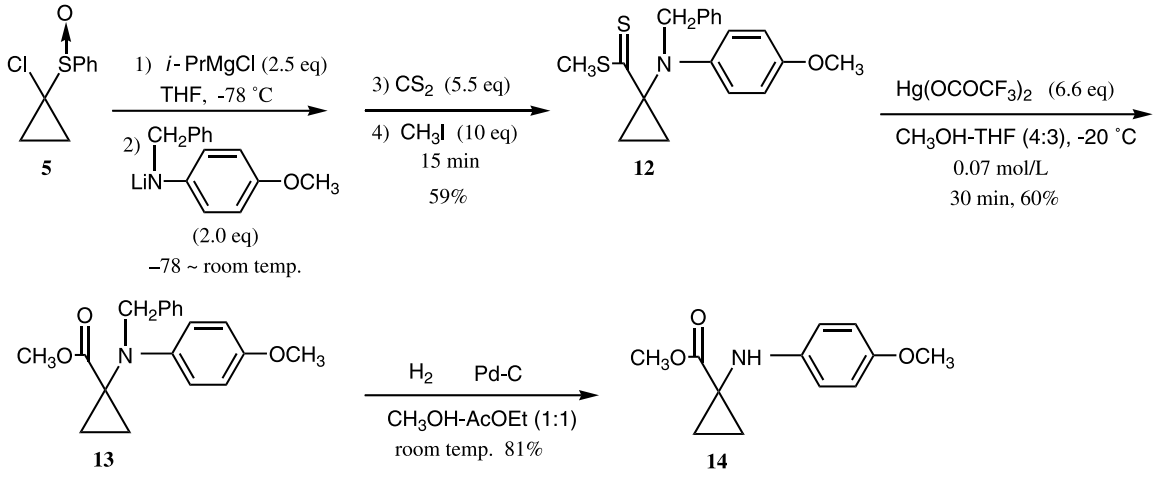
Scheme 4. Methanolysis of the dithioester **11** with $Hg(OCOCF_3)_2$ in methanol.

temperature of the reaction mixture was allowed to warm to −40 °C. To this reaction mixture was added 5.5 equiv of carbon disulfide and the reaction mixture was stirred at −40 °C for 10 min. Iodomethane (10 equiv) was added finally to this reaction mixture (Scheme 3, entry 1). From this reaction the desired dithioester **11** was obtained; however, cyclopropylamine **8** was found to be the main product.

The reaction time for the treatment with carbon disulfide was prolonged to 1 h (entry 2) or the reaction temperature was allowed to warm to −20 °C and stirred 1 h (entry 3) to give the desired dithioester **11** in up to 72% yield. The best yield was obtained when the reaction with carbon disulfide was warmed to room temperature and stirred for 2 h (entry 4).

Methanolysis of the dithioester **11** was successfully carried out with mercury(II) trifluoroacetate in methanol[10] at the concentration of 0.2 mol/L and the results are summarized in Scheme 4. The reaction did not complete with 2 equiv of $Hg(OCOCF_3)_2$ at room temperature (entry 1). The reaction completed with 3 equiv of $Hg(OCOCF_3)_2$; however, the reaction gave some byproducts and the yield was not satisfactory (entry 2). The reaction was conducted with 3 equiv of $Hg(OCOCF_3)_2$ at 0 and −20 °C, and the best yield (92%) of the cyclopropane amino acid derivatives **10e** was obtained at −20 °C (entry 4).

As the generality of this reaction, we further investigated the reaction of **5** with *N*-benzyl-*p*-anisidine (Scheme 5). Treatment of **5** with *i*-PrMgCl followed by *N*-lithio *N*-benzyl-*p*-anisidine gave the α-amino-substituted cyclopropylmagnesium. Carbon disulfide followed by iodomethane was added to the reaction mixture as above to afford the desired dithioester **12** in 59% overall yield from **5**. As the solubility of **12** was found to be low in methanol, methanolysis of the dithioester **12** was carried out in a mixture of CH_3OH–THF with excess $Hg(OCOCF_3)_2$ to give the methylester **13** in 60% yield. Finally, the benzyl group was hydrogenolized with hydrogen in the presence of Pd–C to give cyclopropane amino acid derivative **14** in 81% yield.



Scheme 5. A synthesis of cyclopropane amino acid derivative **14** from **5** with *N*-benzyl-*p*-anisidine.

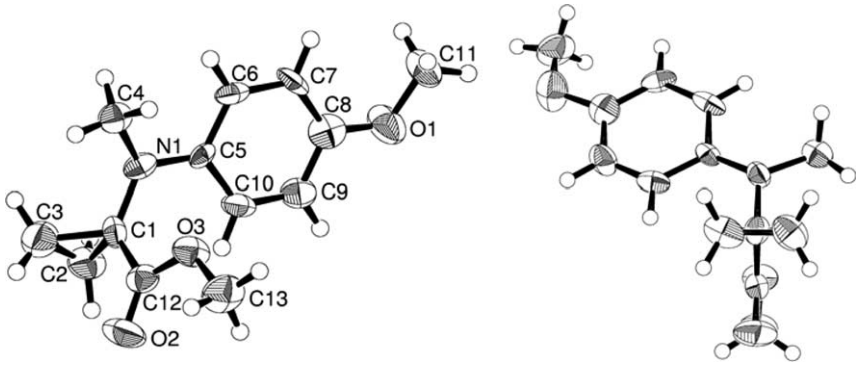


Figure 1. An ORTEP view for the structure of **10e** showing the atom labeling diagram (left), together with a view perpendicular to the cyclopropane ring showing the location of the (4-methoxyphenyl)methylamino group with regard to the cyclopropane ring (right).

2.3. X-ray crystallographic analysis of the cyclopropane amino acid derivative 10e

During the course of this work, we encountered an unusual phenomenon in the ^{1}H NMR spectrum measured in a $CDCl_3$ solution of the cyclopropane amino acid derivative **10e**. If the rotational motion of the (4-methoxyphenyl)methylamino moiety about the N–C(cyclopropane) bond axis is undertaken very rapidly within a timescale much shorter than the timescale of ^{1}H NMR, the structure of **10e** should be regarded as symmetrical leading to the observation of two sets of magnetically non-equivalent protons on the cyclopropane ring. In spite of the fact that three methyl groups of **10e** showed quite sharp signals, four protons on the cyclopropane ring are observed at δ 1.20 with a broad signal (two protons) and at δ 1.47 and 1.81 as two very broad signals (each one proton), indicating that the two carbon atoms on its 2- and 3-positions are not equivalent magnetically. In order to better understand the structure of **10e** and to elucidate the unusual observation described above, the crystal structure of **10e** has been determined by X-ray diffraction. The ORTEP diagram of **10e** is shown in Figure 1.[11]

Obviously, the crystal structure is not symmetrical with regard to the cyclopropane ring. The result also indicates that the methoxycarbonyl moiety is so bulky that the fast rotation of the (4-methoxyphenyl)methylamino moiety around the N–C (cyclopropane) bond is prohibited. The molecular modeling studies using either the crystal structure or a computed structure (density functional method) also showed that such a rotation mode is not favored due to the steric contacts between these bulky moieties. It is also noteworthy that compound **8** whose structure is given by the substitution of the methoxycarbonyl unit in **10e** by a proton shows two sets of symmetrical signals in its ^{1}H NMR. As a whole, the unexpected ^{1}H NMR signals of **10e** can be understood from the structure in Figure 1.

3. Experimental

3.1. General

^{1}H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 300 and 500 spectrometer. Electron-impact mass spectra (MS) were obtained at 70 eV by direct insertion. Silica gel 60 (MERCK) containing 0.5% fluorescence reagent 254 and a quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry solvent, THF was distilled from benzophenone ketyl.

3.1.1. 1-Chlorocyclopropyl phenyl sulfoxide (5). To a solution of cyclopropyl phenyl sulfide (3 g; 19.9 mmol) in CH_2Cl_2 (80 mL) was added *m*-chloroperbenzoic acid (about 70% purity; 5.4 g; 21.9 mmol) with stirring at 0 °C. The reaction mixture was stirred at 0 °C for 30 min. To the reaction mixture was added aq Na_2SO_3 to reduce excess *m*-chloroperbenzoic acid and the solution was diluted with CH_2Cl_2 and the organic layer was washed with 5% NaOH followed by satd aq NH_4Cl. The organic layer was dried over $MgSO_4$ and the solvent was evaporated to give an oil, which was purified by silica gel column chromatography to afford 3.3 g (99%) of cyclopropyl phenyl sulfoxide as a cololess oil; IR (neat) 3007, 1652, 1478, 1444, 1087, 1044, 1022 (SO), 880, 750, 692 cm^{-1}.

A solution of the cyclopropyl phenyl sulfoxide (2.14 g; 13 mmol) in CCl_4 (26 mL) was stirred with *N*-chlorosuccinimide at room temperature for 13 h. The precipitate was filtered off and the solvent was evaporated to give an oil, which was purified by silica gel column chromatography to afford 2.5 g (96%) of **5** as a colorless crystals; mp 49–50 °C (AcOEt–hexane); IR (KBr) 3084, 1477, 1443, 1089 (SO), 1059 (SO), 754, 691 cm^{-1}; ^{1}H NMR δ 1.21–1.27 (1H, m), 1.36–1.42 (1H, m), 1.65–1.72 (2H, m), 7.52–7.59 (3H, m), 7.70–7.73 (2H, m). MS *m*/*z* (%) 200 (M^+, 8), 125 (100), 97 (19), 77 (20), 51 (13). Calcd for C_9H_9ClOS: M, 200.0061. Found: *m*/*z* 200.0054. Anal. Calcd for C_9H_9ClOS; C, 53.86; H, 4.52; Cl, 17.67; S, 15.98. Found: C, 53.94; H, 4.17; Cl, 17.58; S, 15.97.

3.1.2. *N*-Cyclopropyl-*N*-(4-methoxyphenyl)methylamine (8). To a solution of *i*-PrMgCl (0.75 mmol) in THF (1.5 mL) at −78 °C was added a solution of **5** (60 mg; 0.3 mmol) in 1.5 mL of THF dropwise with stirring. After 10 min, a solution of *N*-lithio *N*-methyl *p*-anisidine (prepared from *N*-methyl *p*-anisidine (1.05 mmol) and *n*-BuLi (1.16 mmol) in 1.5 mL of THF at 0 °C) was added to a solution of the magnesium cyclopropylidene **6** through a cannula and the reaction mixture was slowly allowed to warm to −40 °C over 1 h. The reaction was quenched with MeOH and the

whole was extracted with $CHCl_3$ and the organic layer was washed with satd aq NH_4Cl and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **8** (43.6 mg; 82%) as a light yellow oil; IR (neat) 3004, 2933, 1513, 1455, 1361, 1245, 1040, 818 cm^{-1}; ^1H NMR δ 0.58 (2H, m), 0.77 (2H, m), 2.27 (1H, m), 2.92 (3H, s), 3.77 (3H, s), 6.84 (2H, d, J=9.2 Hz), 6.97 (2H, d, J=9.2 Hz). MS m/z (%) 177 (M^+, 100), 176 (60), 162 (80), 146 (18), 134 (16), 121 (57). Calcd for $C_{11}H_{15}NO$: M, 177.1154. Found: m/z 177.1135.

3.1.3. *N*-Cyclopropyl-*N*-methylphenylamine (9a). Light yellow oil; IR (neat) 2933, 1601, 1503, 1363, 751, 692 cm^{-1}; ^1H NMR δ 0.61 (2H, m), 0.81 (2H, m), 2.37 (1H, m), 2.97 (3H, s), 6.76 (1H, t, J=7.3 Hz), 6.99 (2H, d, J=8.0 Hz), 7.21–7.26 (2H, m). MS m/z (%) 147 (M^+, 100), 146 (89), 132 (46), 120 (20), 104 (23), 91 (40), 77 (42). Calcd for $C_{10}H_{13}N$: M, 147.1048. Found: m/z 147.1057.

3.1.4. *N*-(4-Chlorophenyl)-*N*-cyclopropylmethylamine (9b). Colorless amorphous; IR (neat) 2935, 1599, 1497, 1360, 1115, 813, 668 cm^{-1}; ^1H NMR δ 0.60 (2H, m), 0.81 (2H, m), 2.36 (1H, m), 2.95 (3H, s), 6.89 (2H, d, J=8.9 Hz), 7.17 (2H, d, J=8.9 Hz). MS m/z (%) 181 (M^+, 100), 180 (86), 166 (67), 146 (50), 144 (50), 140 (68), 125 (47), 111 (59), 91 (39). Calcd for $C_{10}H_{12}ClN$: M, 181.0659. Found: m/z 181.0659.

3.1.5. *N*-Benzyl-*N*-cyclopropyl(4-methoxyphenyl)amine (9c). Colorless amorphous; IR (neat) 2943, 1513, 1454, 1366, 1243, 1043, 818, 729 cm^{-1}; ^1H NMR δ 0.65 (2H, m), 0.78 (2H, m), 2.52 (1H, m), 3.74 (3H, s), 4.55 (2H, s), 6.79 (2H, d, J=9.2 Hz), 6.87 (2H, d, J=9.2 Hz), 7.15–7.30 (5H, m). MS m/z (%) 253 (M^+, 84), 252 (44), 162 (99), 147 (26), 134 (54), 132 (70), 91 (100). Calcd for $C_{17}H_{19}NO$: M, 253.1465. Found: m/z 253.1463.

3.1.6. *N*-Cyclopropyldiphenylamine (9d). Colorless oil; IR (neat) 3022, 1590, 1491, 1358, 1298, 1267, 1025, 748, 693 cm^{-1}; ^1H NMR δ 0.64 (2H, m), 0.85 (2H, m), 2.75 (1H, m), 6.99 (2H, m), 7.07 (4H, m), 7.28 (4H, m). MS m/z (%) 209 (M^+, 100), 208 (82), 193 (19), 167 (28), 117, (88), 104 (63), 91 (38), 77 (91). Calcd for $C_{15}H_{15}N$: M, 209.1203. Found: m/z 209.1203.

3.1.7. 10-Cyclopropyl-10*H*-phenoxazine (9f). To a solution of *i*-PrMgCl (0.5 mmol) in THF (1.0 mL) at −78 °C was added a solution of **5** (40 mg; 0.2 mmol) in 1.0 mL of THF dropwise with stirring. After 10 min, a solution of *N*-lithio phenoxazine (prepared from phenoxazine (0.4 mmol) and *n*-BuLi (0.44 mmol) in 0.6 mL of THF at 0 °C) was added to the solution of the magnesium cyclopropylidene **6** through a cannula and the reaction mixture was slowly allowed to warm to room temperature over 2 h. The reaction was quenched with MeOH and the whole was extracted with $CHCl_3$ and the extract was washed with aq NH_4Cl and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **9f** (38.9 mg; 87%) as colorless crystals; mp 111–112 °C (AcOEt–hexane); IR (KBr) 2956, 1590, 1483, 1338, 1268, 745 cm^{-1}; ^1H NMR δ 0.72 (2H, m), 1.10 (2H, m), 2.38 (1H, m), 6.75 (4H, m), 6.86–6.91 (2H, m), 6.98 (2H, d, J=8.0 Hz). MS m/z (%) 223 (M^+, 65), 222 (100), 207 (10), 182 (41), 127, (10). Calcd for $C_{15}H_{13}NO$: M, 223.0996. Found: m/z 223.0998.

3.1.8. 10-Cyclopropyl-10*H*-phenothiazine (9g). Colorless crystals; mp 118–121 °C (AcOEt–hexane); IR (KBr) 3055, 1572, 1459, 1313, 1243, 1023, 755 cm^{-1}; ^1H NMR δ 0.72 (2H, m), 1.15 (2H, m), 2.79 (1H, m), 6.93 (2H, t, J=5.5 Hz), 7.11 (2H, dd, J=1.2, 7.6 Hz), 7.14–7.25 (4H, m). MS m/z (%) 239 (M^+, 86), 238 (100), 223 (17), 210 (12), 198 (35), 154 (9). Calcd for $C_{15}H_{13}NS$: M, 239.0768. Found: m/z 239.0770. Anal. Calcd for $C_{15}H_{13}NS$: C, 75.28; H, 5.47; N, 5.85; S, 13.40. Found: C, 74.93; H, 5.83; N, 5.58; S, 12.98.

3.1.9. 9-Cyclopropyl-9*H*-carbazole (9h). Colorless crystals; mp 118–120 °C (AcOEt–hexane); IR (KBr) 3063, 1596, 1480, 1457, 1375, 1317, 1233, 1158, 1034, 753, 748, 723 cm^{-1}; ^1H NMR δ 1.11 (2H, m), 1.26 (2H, m), 3.30 (1H, m), 7.23 (2H, ddd, J=0.9, 7.4, 7.5 Hz), 7.46 (2H, ddd, J=1.3, 7.4, 8.6 Hz), 7.65 (2H, d, J=8.3 Hz), 8.06 (2H, d, J=7.6 Hz). MS m/z (%) 207 (M^+, 63), 206 (100), 204 (18), 180 (15), 166 (12), 140 (10). Calcd for $C_{15}H_{13}N$: M, 207.1046. Found: m/z 207.1041.

3.1.10. 1-Cyclopropyl-2,3-dihydro-1*H*-indole (9i). Colorless oil; IR (neat) 2926, 2822, 1607, 1488, 1453, 1368, 1277, 1021, 869, 748 cm^{-1}; ^1H NMR δ 0.64 (2H, m), 0.67 (2H, m), 2.11 (1H, m), 2.90 (2H, t, J=8.3 Hz), 3.36 (2H, t, J=8.3 Hz), 6.70 (1H, dt, J=0.9, 7.3 Hz), 6.83 (1H, dd, J=0.9, 7.3 Hz), 7.08 (2H, m). MS m/z (%) 159 (M^+, 87), 158 (100), 144 (66), 130 (48), 117 (27), 91 (24), 77 (18). Calcd for $C_{11}H_{13}N$: M, 159.1047. Found: m/z 159.1043.

3.1.11. 1-Cyclopropyl-1*H*-indole (9j). Colorless oil; IR (neat) 3013, 2925, 1509, 1476, 1464, 1370, 1314, 1235, 765, 741 cm^{-1}; ^1H NMR δ 0.99–1.09 (4H, m), 3.34 (1H, m), 6.42 (1H, dd, J=0.6, 3.0 Hz), 7.08–7.13 (2H, m), 7.19–7.25 (1H, m), 7.55–7.61 (2H, m). MS m/z (%) 157 (M^+, 75), 156 (100), 130 (21), 128 (10). Calcd for $C_{11}H_{11}N$: M, 157.0891. Found: m/z 157.0886.

3.1.12. 1-Cyclopropyl-1*H*-indazole (9k). Colorless oil; IR (neat) 2925, 1615, 1466, 1425, 1218, 768, 743 cm^{-1}; ^1H NMR δ 1.17 (2H, m), 1.24 (2H, m), 3.59 (1H, m), 7.16 (1H, t, J=7.4 Hz), 7.39 (1H, t, J=7.4 Hz), 7.61 (1H, d, J=8.2 Hz), 7.71 (1H, d, J=7.4 Hz), 7.94 (1H, s). MS m/z (%) 158 (M^+, 82), 157 (58), 131 (100), 130 (60), 104 (37), 103 (24), 77 (21), 76 (28). Calcd for $C_{10}H_{10}N_2$: M, 158.0844. Found: m/z 158.0847.

3.1.13. {1-[(4-Methoxyphenyl)methylamino]cyclopropyl}-phenylmethanol (10a). To a solution of *i*-PrMgCl (0.75 mmol) in THF (1.5 mL) at −78 °C was added a solution of **5** (60 mg; 0.3 mmol) in 1.5 mL of THF dropwise with stirring. After 10 min, a solution of *N*-lithio *N*-methyl-*p*-anisidine (prepared from *N*-methyl-*p*-anisidine (0.6 mmol) and *n*-BuLi (0.66 mmol) in 0.9 mL of THF at 0 °C) was added to a solution of the magnesium cyclopropylidene **6** through a cannula and the reaction mixture was slowly allowed to warm to −40 °C for 1 h. Benzaldehyde (1.65 mmol) was added to the reaction mixture dropwise with stirring and the solution was slowly allowed to warm to −20 °C over 1 h. The reaction was

quenched with MeOH and the whole was extracted with $CHCl_3$ and the extract was washed with aq NH_4Cl and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **10a** (34.5 mg; 40%) as a colorless oil; IR (neat) 3446 (OH), 2904, 1512, 1453, 1242, 1039, 818, 745, 702 cm^{-1}; ^1H NMR δ 0.80 (2H, s), 0.94 (1H, br s), 1.11 (1H, br s), 2.62 (3H, br s), 3.77 (3H, s), 5.01 (1H, s), 6.78–6.84 (4H, m), 7.26–7.35 (5H, m). MS *m/z* (%) 283 (M^+, 21), 177 (21), 176 (100), 146 (13), 145 (17), 144 (15), 121 (75). Calcd for $C_{18}H_{21}NO_2$: M, 283.1571. Found: *m/z* 283.1577.

3.1.14. *N*-(4-Methoxyphenyl)-*N*-[1-{(4-methoxyphenyl)-hydroxymethyl}cyclopropyl]methylamine (10b). Colorless oil; IR (neat) 3469 (OH), 2934, 1514, 1464, 1243, 1036, 818 cm^{-1}; ^1H NMR δ 0.77–0.80 (2H, m), 0.93 (1H, br s), 1.07–1.12 (1H, m), 2.62 (3H, br s), 3.76 (3H, s), 3.80 (3H, s), 4.97 (1H, s), 6.77–6.85 (6H, m), 7.22 (2H, d, J=8.6 Hz). MS *m/z* (%) 313 (M^+, 14), 176 (100), 145 (22), 144 (17), 135 (12), 121 (71), 77 (11). Calcd for $C_{19}H_{23}NO_3$: M, 313.1676. Found: *m/z* 313.1669.

3.1.15. Ethyl 1-[(4-methoxyphenyl)methylamino]cyclopropanecarboxylate (10d). To a solution of *i*-PrMgCl (0.75 mmol) in THF (1.5 mL) at −78 °C was added a solution of **5** (60 mg; 0.3 mmol) in 1.5 mL of THF dropwise with stirring. After 10 min, a solution of *N*-lithio *N*-methyl-*p*-anisidine (prepared from *N*-methyl-*p*-anisidine (1.05 mmol) and *n*-BuLi (1.16 mmol) in 1.5 mL of THF at 0 °C) was added to a solution of the magnesium cyclopropylidene **6** through a cannula and the reaction mixture was slowly allowed to warm to −40 °C for 1 h. Ethyl chloroformate (1.65 mmol) was added to the reaction mixture dropwise with stirring and the reaction mixture was stirred for 10 min. The reaction was quenched with MeOH and the whole was extracted with $CHCl_3$ and the extract was washed with aq NH_4Cl and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **10d** (14.8 mg; 20%) as a colorless oil; IR (neat) 2936, 1723 (CO), 1513, 1294, 1245, 1186, 1143, 1039, 818 cm^{-1}; ^1H NMR δ 1.14 (3H, t, J=7.0 Hz), 1.19 (2H, br s), 1.45 (1H, br s), 1.78 (1H, br s), 3.03 (3H, s), 3.75 (3H, s), 4.09 (2H, q, J=7.0 Hz), 6.74 (2H, d, J=9.2 Hz), 6.81 (2H, d, J=9.2 Hz). MS *m/z* (%) 249 (M^+, 43), 220 (59), 176 (68), 175 (27), 144 (18), 135 (21), 121 (100). Calcd for $C_{14}H_{19}NO_3$: M, 249.1363. Found: *m/z* 249.1368.

3.1.16. Methyl 1-[(4-methoxypenyl)methylamino]cyclopropanecarboxylate (10e). Colorless crystals; mp 59–61 °C (AcOEt–hexane); IR (KBr) 2958, 1722 (CO), 1512, 1433, 1301, 1248, 1195, 1035, 817 cm^{-1}; ^1H NMR δ 1.20 (2H, br s), 1.47 (1H, br s), 1.81 (1H, br s), 3.03 (3H, s), 3.63 (3H, s), 3.75 (3H, s), 6.74 (2H, d, J=8.9 Hz), 6.82 (2H, d, J=8.9 Hz). MS *m/z* (%) 235 (M^+, 49), 220 (42), 176 (72), 175 (49), 121 (100). Calcd for $C_{13}H_{17}NO_3$: M, 235.1208. Found: *m/z* 235.1213. Anal. Calcd for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.93. Found: C, 66.29; H, 7.33; N, 5.88.

3.1.17. 1-[*N*-Methyl-(4-methoxylphenyl)amino]cyclopropanecarbodithioic acid methyl ester (11). To a solution of *i*-PrMgCl (0.75 mmol) in THF (1.5 mL) at −78 °C was added a solution of **5** (60 mg; 0.3 mmol) in 1.5 mL of THF dropwise with stirring. After 10 min, a solution of *N*-lithio *N*-methyl-*p*-anisidine (prepared from *N*-methyl-*p*-anisidine (0.6 mmol) and *n*-BuLi (0.66 mmol) in 0.9 mL of THF at 0 °C) was added to solution of the magnesium cyclopropylidene **6** through a cannula and the reaction mixture was slowly allowed to warm to −40 °C over 1 h. Carbon disulfide (1.65 mmol) was added to the reaction mixture dropwise with stirring and the solution was slowly allowed to warm to room temperature over 2 h. Iodomethane (3.0 mmol) was added to the reaction mixture dropwise with stirring and the reaction mixture was stirred for 15 min. The reaction was quenched with MeOH and the whole was extracted with $CHCl_3$ and the extract was washed with aq NH_4Cl and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **11** (72.8 mg; 91%) as a colorless light yellow amorphous; IR (KBr) 2910, 1516, 1343, 1278, 1246, 1175, 1030, 814 cm^{-1}; ^1H NMR δ 1.32 (1H, br s), 1.55 (1H, br s), 2.03 (1H, br s), 2.44 (1H, br s), 2.51 (3H, s), 3.08 (3H, s), 3.76 (3H, s), 6.66 (2H, d, J=9.2 Hz), 6.84 (2H, d, J=9.2 Hz). MS *m/z* (%) 267 (M^+, 100), 252 (47), 219 (27), 174 (19), 122 (22), 121 (27). Calcd for $C_{13}H_{17}NOS_2$: M, 267.0751. Found: *m/z* 267.0757.

3.1.18. Methyl 1-[(4-methoxypenyl)methylamino]cyclopropanecarboxylate (10e). To a solution of **11** (80 mg; 0.3 mmol) in MeOH (1.5 mL) at −20 °C was added mercury (II) trifluoroacetate (0.9 mmol) with stirring and the reaction mixture was stirred for 30 min. The reaction mixture was diluted with $CHCl_3$ and the solution was washed with 10% NaOH and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **10e** (65 mg; 92%) as colorless crystals. Melting point and all the spectral data were identical with the product described above.

3.1.19. 1-[*N*-Benzyl-*N*-(4-methoxyphenyl)amino]cyclopropanecarbodithioic acid methyl ester (12). Light yellow amorphous; IR (neat) 3000, 2930, 1511, 1440, 1353, 1278, 1236, 1186, 1147, 1036, 955, 817, 757 cm^{-1}; ^1H NMR δ 1.59 (2H, m), 1.84 (1H, m), 2.55 (3H, s), 2.66 (1H, m), 3.72 (3H, s), 4.75 (1H, d, J=18.0 Hz), 4.95 (1H, d, J=18.0 Hz), 6.60 (2H, d, J=9.2 Hz), 6.77 (2H, d, J=9.2 Hz), 7.11 (2H, d, J=8.0 Hz), 7.21–7.34 (3H, m). MS *m/z* (%) 343 (M^+, 52), 252 (100), 218 (27), 205 (19), 204 (34), 160 (55), 91 (89). Calcd for $C_{19}H_{21}NOS_2$: M, 343.1064. Found: *m/z* 343.1071.

3.1.20. Methyl 1-[*N*-Benzyl-(4-methoxyphenyl)amino]-cyclopropanecarboxylate (13). To a solution of **12** (34 mg; 0.1 mmol) in MeOH (0.82 mL) and THF (0.61 mL) at −20 °C was added mercurry (II) trifluoroacetate (0.66 mmol) and the reaction mixture was stirred for 30 min. The reaction mixture was diluted with $CHCl_3$ and the solution was washed with 10% NaOH and dried over $MgSO_4$. After removal of the solvent, the product was purified by silica gel column chromatography to give **13** (18.6 mg; 60%) as a colorless amorphous; IR (neat) 2950, 2832, 1726 (CO), 1509, 1451, 1291, 1244, 1163, 1044, 819 cm^{-1}; ^1H NMR δ 1.25–1.43 (3H, m), 1.91 (1H, br s), 3.69 (3H, s), 3.72 (3H, s), 4.66 (2H, d, J=14.4 Hz), 6.63 (2H, d, J=9.5 Hz), 6.75 (2H, d, J=9.5 Hz), 7.16 (2H, d, J=7.6 Hz), 7.22 (1H, t, J=7.6 Hz), 7.30 (2H, t, J=7.6 Hz). MS *m/z* (%) 311 (M^+, 30), 252 (27), 220 (43), 190 (55), 160

(24), 92 (22), 91 (100). Calcd for $C_{19}H_{21}NO_3$: M, 311.1519. Found: *m/z* 311.1517.

3.1.21. Methyl 1-(4-methoxyphenylamino)cyclopropanecarboxylate (14). To a solution of **13** (21 mg; 0.07 mmol) in MeOH (0.7 mL) and AcOEt (0.7 mL) at room temperature was added 10%-Pd/C (21 mg). The reaction mixture was stirred for 5 h under hydrogen atmosphere. The catalyst was filtered off and the solvent was removed. The product was purified by silica gel column chromatography to give **14** (13 mg; 81%) as a colorless oil; IR (neat) 3380 (NH), 2953, 1725 (CO), 1512, 1236, 1038, 822, 754 cm^{-1}; ^1H NMR δ 1.16 (2H, m), 1.56 (2H, m), 3.65 (3H, s), 3.74 (3H, s), 4.32 (1H, br s), 6.65 (2H, d, $J=8.9$ Hz), 6.77 (2H, d, $J=8.9$ Hz). MS *m/z* (%) 221 (M^+, 53), 190 (56), 162 (100), 161 (55), 160 (52), 146 (49), 130 (42), 121 (29). Calcd for $C_{12}H_{15}NO_3$: M, 221.1051. Found: *m/z* 221.1059.

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11. $C_{13}H_{17}NO_3$, $M=235.28$, Orthorhombic, space group *Pbca* (#61), $a=12.8035(12)$, $b=7.7201(8)$, $c=24.955(2)$ Å, $V=2466.7(4)$ Å^3, $Z=8$, $F(000)=1008$, $D_{calc}=1.267$ g cm^{-3}, μ(Mo K_α)$=0.9$ cm^{-1}, $T=296$ K, radiation$=0.71073$ Å, $R1=0.2567$ for $I>2.0\sigma(I)$, $wR2=0.3582$ for all data (2824 reflections), GOF$=1.508$ (157 parameters), crystal dimensions $0.3\times0.08\times0.08$ mm^3. A quality single crystal of the compound (colorless prism) was mounted on a glass fiber. Diffraction data were measured on a Bruker APEX CCD-Detector X-ray diffractometer with monochromated Mo K_α radiation. The data reduction, structure solution and refinement, and all the necessary computational data processes were performed using SMART, SAINT, SHELXTL, KENX, and TEXSAN programs. Data deposited at the Cambridge Crystallographic Data Centre; deposition number CCDC 285997.