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Regio- and site-selective cycloadditions

I. The reaction of aryl azides and of ethyl diazoacetate with the bis(trimethylsilyl)polyynes, $Me_3Si(C{\equiv}C)_nSiMe_3$ ($n = 2$ or 3) *

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Abstract

Phenyl azide and ethyl diazoacetate add '*endo*' to $Me_3Si(C{\equiv}C)_2SiMe_3$. 4-Nitrophenyl azide reacts exclusively with the triple bond adjacent to silicon in $Me_3Si(C{\equiv}C)_3SiMe_3$, also in the '*endo*' sense. The regio- and site-specificity exhibited in these cycloadditions is attributed to orbital rather than to steric control.

Introduction

The behaviour of extended conjugated substrates towards (Diels–Alder) dienes and dipoles constitutes a fruitful, yet hitherto unsystematically investigated, area for research, of interest to the experimental Chemist and theorist alike, seeking to consolidate rules governing the orientation (regioselection) and site of cycloaddition [1,2]. Emphasis on novel diene and dipole design, and on catalysis, coupled with difficulties in preparing appropriate model conjugated systems (enynes, polyenes, polyynes, etc.) capable of surviving prolonged reaction times and elevated temperatures, are in part responsible for this uneven approach to the subject.

Two decades ago, we [3] and others [4], devised practicable routes to a series of bis(trialkylsilyl)polyynes, $R_3Si(C{\equiv}C)_nSiR_3$, whose potential in synthesis has been part-realized [5]. The utility of these compounds lies in the stabilizing influence of the protecting silyl groups (reminescent of CMe_3), coupled with their ease of displacement under mild conditions which can, if desired, be monitored accurately by UV spectroscopy [3]. During the intervening period, we have gradually accumulated information on the behaviour of these and allied silyl-ended acyclic conjugated systems in cycloadditions, and we disclose here the first results of our

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* For my teacher, Colin Eaborn, on the occasion of his 65th birthday, with affection and respect.

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studies, which demonstrate that the commonly encountered '*exo*' mode of cycloaddition can be reversed by effective deployment of silyl groups.

Results

Phenyl azide and ethyl diazoacetate react slowly with bis(trimethylsilyl)butadiyne at elevated temperatures (110–130 °C) to yield the 1,2,3-triazole (Fig. 1a) and

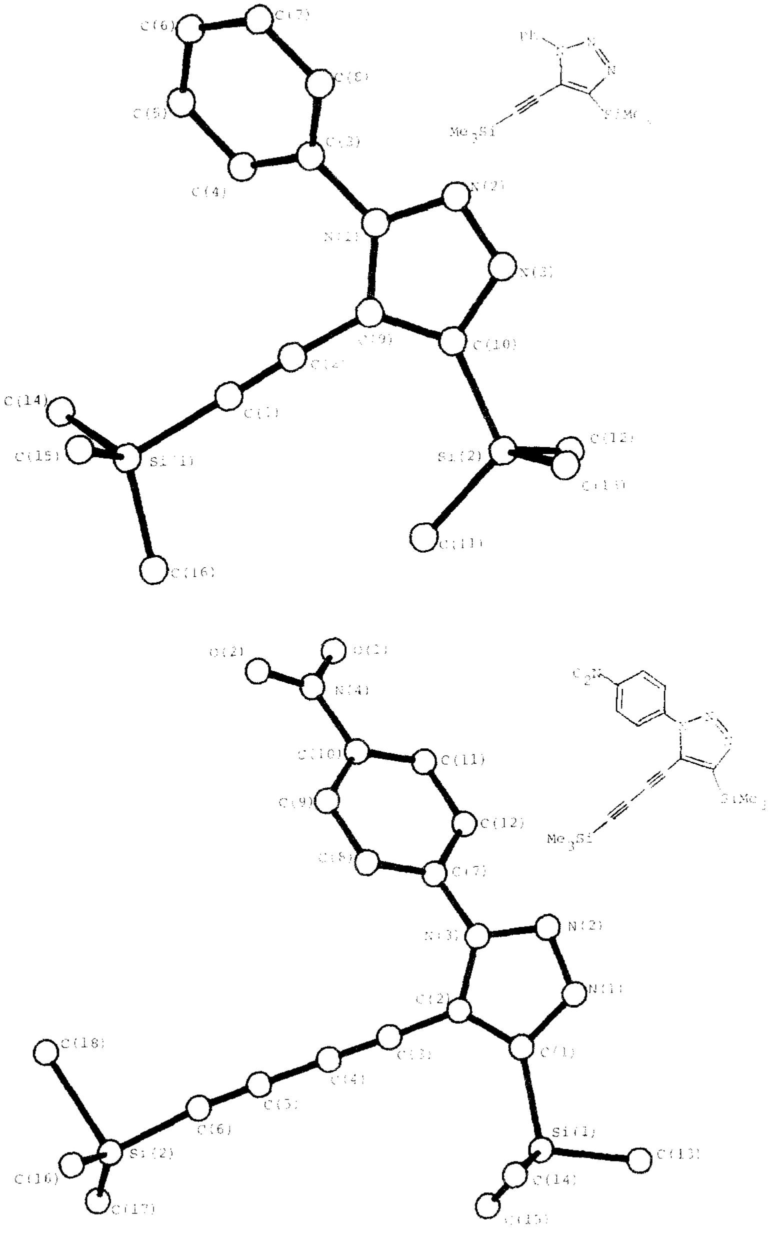

Fig. 1. (a) The molecular structure of 1-phenyl-4-trimethylsilyl-5-trimethylsilylethynyl-1,2,3-triazole and (b) 1-(4-nitrophenyl)-4-trimethylsilyl-5-trimethylsilylbutadiynyl-1,2,3-triazole.

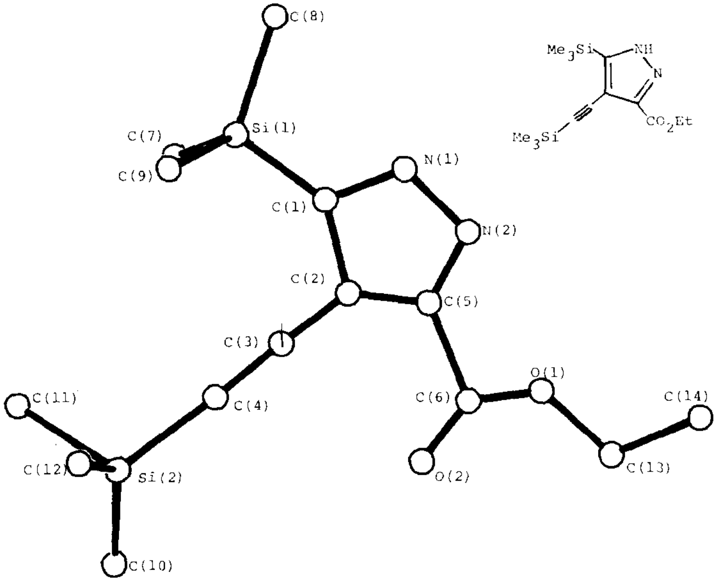

Fig. 2. The molecular structure of 3-ethoxycarbonyl-4-trimethylsilylethynyl-5-trimethylsilyl-1,2-pyrazole.

Table 1A

1-Phenyl-4-trimethylsilyl-5-trimethylsilylethynyl-1,2,3-triazole. Fractional atomic coordinates ($\times 10^4$), with estimated standard deviations in parentheses

	x	*y*	*z*		*x*	*y*	*z*
Si(1)	−2042(2)	−3627(2)	1094(2)	Si(1a)	−7204(2)	1858(2)	−4285(2)
Si(2)	3304(2)	−4847(2)	2026(2)	Si(2a)	−1980(3)	2930(2)	−5668(2)
N(1)	2388(5)	−2307(5)	154(4)	N(1a)	−2545(6)	1009(5)	−3383(4)
N(2)	3604(6)	−2306(6)	211(4)	N(2a)	−1269(7)	1080(6)	−3504(5)
N(3)	3966(6)	−3092(6)	827(4)	N(3a)	−996(6)	1695(6)	−4226(5)
C(1)	−362(7)	−3411(6)	937(5)	C(1a)	−5542(8)	1822(7)	−4164(5)
C(2)	706(7)	−3280(6)	824(5)	C(2a)	−4436(7)	1729(7)	−4103(5)
C(3)	1777(7)	−1526(6)	−510(5)	C(3a)	−3088(7)	360(7)	−2649(5)
C(4)	1174(8)	−1873(7)	−967(5)	C(4a)	−3680(9)	−361(7)	−2732(6)
C(5)	580(9)	−1097(8)	−1574(6)	C(5a)	−4214(9)	−981(7)	−2015(7)
C(6)	630(9)	−29(8)	−1726(6)	C(6a)	−4139(9)	−927(8)	−1235(7)
C(7)	1238(9)	295(7)	−1267(6)	C(7a)	−3557(10)	−205(9)	−1153(6)
C(8)	1820(8)	−466(7)	−647(6)	C(8a)	−3013(8)	435(7)	−1851(6)
C(9)	1976(7)	−3114(6)	728(5)	C(9a)	−3065(7)	1613(6)	−4064(5)
C(10)	3008(7)	−3644(6)	1167(5)	C(10a)	−2077(7)	2054(7)	−4605(5)
C(11)	1884(9)	−5410(8)	2364(6)	C(11a)	−3293(11)	3017(11)	−6136(8)
C(12)	4974(9)	−5942(8)	1569(7)	C(12a)	−285(12)	2250(12)	−6402(8)
C(13)	3394(11)	−4312(9)	2935(6)	C(13a)	−2023(20)	4239(11)	−5534(8)
C(14)	−2165(9)	−3729(10)	56(7)	C(14a)	−7167(9)	412(8)	−4145(8)
C(15)	−3464(10)	−2449(10)	1605(8)	C(15a)	−8694(9)	2715(9)	−3485(7)
C(16)	−1939(11)	−4932(10)	1773(8)	C(16a)	−7261(11)	2495(11)	−5398(7)

Table 1B

1-(4-Nitrophenyl)-4-trimethylsilyl-5-trimethylsilylbutadiynyl-1,2,3-triazole fractional atomic coordinates ($\times 10^4$), with estimated standard deviations in parentheses

	x	*y*	*z*		*x*	*y*	*z*
Si(1)	3573(1)	1595(1)	1352(1)	C(6)	302(4)	4052(7)	1905(8)
Si(2)	− 775(1)	4207(3)	2105(3)	C(7)	3755(3)	5404(3)	1607(4)
O(1)	3485(4)	8771(3)	734(5)	C(8)	3311(3)	5773(4)	2496(5)
O(2)	3039(3)	8650(3)	2538(4)	C(9)	3173(3)	6733(4)	2505(5)
N(1)	4652(2)	3181(3)	1476(4)	C(10)	3490(3)	7295(3)	1618(5)
N(2)	4683(2)	4112(3)	1526(4)	C(11)	3934(3)	6938(4)	726(5)
N(3)	3921(2)	4424(3)	1596(4)	C(12)	4074(3)	5975(3)	717(5)
N(4)	3318(3)	8312(3)	1634(5)	C(13)	4366(4)	1025(4)	553(6)
C(1)	3863(3)	2874(3)	1498(4)	C(14)	3591(4)	1133(4)	3055(6)
C(2)	3390(3)	3673(3)	1572(4)	C(15)	2501(4)	1468(4)	309(7)
C(3)	2543(3)	3777(3)	1600(5)	C(16)	− 845(7)	3806(12)	3713(12)
C(4)	1826(3)	3871(4)	1669(6)	C(17)	− 1467(5)	3820(8)	674(10)
C(5)	1007(3)	3981(5)	1774(7)	C(18)	− 969(7)	5556(11)	2203(15)

1,2-pyrazole (Fig. 2), respectively, as the sole isolable products. The structures were proved conclusively by X-ray diffraction (relevant bond angles and lengths are given in Tables 1a and 2), and are commensurate with regiospecific '*endo*' cycloaddition. Since the silyl groups can be removed in turn and without difficulty [6], preparative sequences of this kind, i.e. cycloaddition followed by deprotection, provide a useful pathway to 4-ethynyl-1,2,3-triazoles and 3-ethynyl-1,2-pyrazoles, with added poten-

Table 2

3-Ethoxycarbonyl-4-trimethylsilylethynyl-5-trimethylsilyl-1,2-pyrazole. Fractional atomic coordinates ($\times 10^4$), with estimated standard deviations in parentheses

	x	*y*	*z*
Si(1)	8487(5)	539(5)	8268(4)
Si(2)	5905(9)	708(8)	6191(5)
O(1)	4725(10)	2092(12)	9443(9)
O(2)	4631(14)	1856(12)	8329(9)
N(1)	7425(10)	1250(10)	9306(8)
N(2)	6539(12)	1559(11)	9518(6)
C(1)	7471(13)	942(12)	8654(8)
C(2)	6504(16)	1220(14)	8459(7)
C(3)	6326(14)	1029(14)	7811(12)
C(4)	6119(21)	864(20)	7155(10)
C(5)	6047(13)	1524(13)	8986(8)
C(6)	4973(19)	1878(14)	8891(8)
C(7)	8224(21)	− 714(18)	7943(14)
C(8)	9377(18)	390(20)	8997(14)
C(9)	8792(20)	1351(20)	7509(14)
C(10)	4834(30)	156(33)	5942(16)
C(11)	6727(49)	− 492(36)	5858(20)
C(12)	6455(39)	1548(31)	5781(13)
C(13)	3768(22)	2332(44)	9711(25)
C(14)	3871(43)	3076(55)	10388(18)

tial for introducing functionality on the alkyne or heterocycle by selective displacement of the silyl groups [7].

4-Nitrophenyl azide reacts with bis(trimethylsilyl)hexatriyne to yield the '*endo*' product (Fig. 1b, Table 1b) in analogous fashion, with cycloaddition taking place exclusively at the triple bond adjacent to silicon.

Frontier molecular orbital (FMO) Analysis

Interpretation of the regioselectivity exhibited in most diazoalkane cycloadditions is relatively straightforward [1,8]; reactions are usually of Type I [9], i.e. dipole(HOMO) – dipolarophile(LUMO) controlled, $\Delta\epsilon$ (9–10 eV) being less than the difference (11–13 eV) between the high energy dipole(LUMO) (actually the NLUMO, 1.8 eV) and the energy range (-9 to -11 eV) commonly associated with dipolarophile HOMOs. Type II [9] cycloadditions involving ambiphilic azides are often less regioselective [9] because the lower energy LUMO (e.g. -0.2 eV for phenylazide) reduces the dipole(LUMO) – dipolarophile(HOMO) energy separation and, as a consequence, the latter interaction may compete effectively with dipole(HOMO) – dipolarophile(LUMO) control, especially when electron-rich dipolarophiles are used in conjunction with electron-deficient dipoles. Since the (diazoalkane) HOMO coefficient on carbon (1.57 for diazomethane itself) is much greater than the terminal nitrogen coefficient (0.85 for diazomethane) [1], '*exo*' orientation is commonly observed in cycloadditions to substrates bearing large terminal coefficients. The reactions of diazomethane [11] and of phenyl azide [12] with butadiyne conform to this pattern and yield mono or bis '*exo*' products.

Reactions with $Me_3Si(C{\equiv}C)_nSiMe_3$ (n = 2 or 3)

Introduction of a carbethoxy substituent on to diazomethane will lower both HOMO and LUMO energies [1]; however, the $Me_3Si(C{\equiv}C)_2SiMe_3$ LUMO (esti-

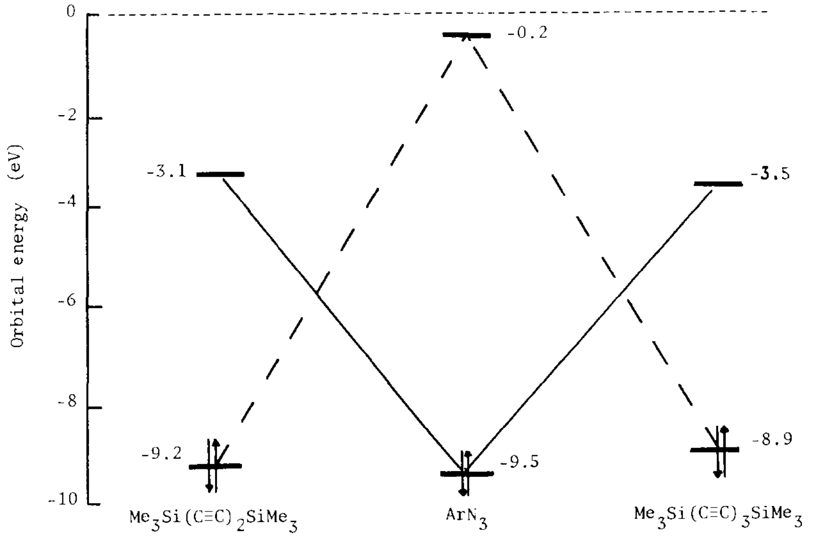

Fig. 3. An FMO energy level diagram for ArN_3 and $Me_3Si(C{\equiv}C)_nSiMe_3$ ($n = 2$ or 3).

mated as −3.1 eV from the UV spectrum [13]) and HOMO (−9.2 eV) energies compensate for this lowering so that in the cycloaddition the dipole (HOMO) – dipolarophile(LUMO) ($\Delta\epsilon$ ca. 7–9 eV) interaction predominates. The interaction between aryl azides and $Me_3Si(C{\equiv}C)_2SiMe_3$ or $Me_3Si(C{\equiv}C)_3SiMe_3$ (HOMO −8.9 eV, LUMO −3.5 eV [13]) is illustrated in Fig. 3 and demonstrates clearly that the azide(HOMO) – diyne(LUMO) ($\Delta\epsilon$ 6.4 eV) or azide(HOMO) – triyne(LUMO) ($\Delta\epsilon$ 6.0 eV) separations are less than the corresponding azide(LUMO) – diyne(HOMO) ($\Delta\epsilon$ 9.0 eV) or azide(LUMO) – triyne(HOMO) ($\Delta\epsilon$ 8.7 eV) separations, so that the former interactions are favoured.

It is tempting, at first sight, to attribute the preference for '*endo*' orientation exhibited in all three cycloadditions involving the bis(trimethylsilyl)polyynes to steric factors. However, if these were to be significant, one might reasonably expect 4-nitrophenyl azide to react with the central triple bond of $Me_3Si(C{\equiv}C)_3SiMe_3$ rather than with one of the terminal sites. We prefer to discount the steric argument and to interpret our results in terms of π-donation from the alkynyl system to silicon. This effect is known to be enhanced [13] in the $Me_3Si(C{\equiv}C)_nSiMe_3$ LUMOs and will reduce the coefficient on the alkynyl carbon α to silicon whilst augmenting the coefficient on the β carbon. Pairing of the carbon atoms in dipole and polyyne substrate bearing the greater coefficients will result in '*endo*' orientation, as realised in practice.

Experimental

*1-Phenyl-4-trimethylsilyl-5-trimethylsilylethynyl-1,2,3-triazole (**1a**)*

A toluene (60 cm^3) solution of phenyl azide [14] (4.2 g, 0.035 mol) and bis(trimethylsilyl)butadiyne [15] (6.7 g, 0.035 mol) was heated under a dinitrogen atmosphere at the reflux temperature for 40 h. Solvent was then removed in vacuo and the brown residue was vacuum sublimed to yield a small forerun of $Me_3Si(C{\equiv}C)_2SiMe_3$ (75.80 °C/0.05 mmHg), followed by a white solid (120–130 °C/0.03 mmHg) which was recrystallised from MeOH to yield **1a** (41%) m.p. 47–48 °C. IR (KBr disc): 2170 cm^{-1} ($\nu(C{\equiv}C)$. ^1H NMR: $(CCl_4)(\delta)$: $(CH_3)_3SiC{\equiv}C$ 0.22s (9H), $(CH_3)_3Si$ 0.40s (9H), C_6H_5 7.55m (3H) + 7.85m (2H).

*1-(4-Nitrophenyl)-4-trimethylsilyl-5-trimethylsilylbutadiynyl-1,2,3-triazole (**1b**)*

An analogous reaction between 4-nitrophenyl azide [16] (3.44 g, 0.021 mol) and bis(trimethylsilyl)hexatriyne [17] (4.6 g, 0.021 mol) in xylene (30 cm^3) (24 h reflux period) followed by removal of solvent and vacuum sublimation gave a minute quantity of unreacted $Me_3Si(C{\equiv}C)_3SiMe_3$ (85 °C/0.5 mmHg) followed by a yellow gum (150–200 °C/0.05 mmHg), which was recrystallised from MeOH to yield **1b** as pale yellow plates (43%) m.p. 133–134 °C. IR: 2111 cm^{-1} ($\nu(C{\equiv}C)_2$). ^1H NMR $(CCl_4)(\delta)$: $(CH_3)_3Si(C{\equiv}C)_2$ 0.26s (9H), $(CH_3)_3Si$ 0.45s (9H), 4-C_6H_4 8.21q (4H).

*3-Ethoxycarbonyl-4-trimethylsilylethynyl-5-trimethylsilyl-1,2-pyrazole (**2**)*

Ethyl diazoacetate [18] (5.7 g, 0.05 moles) and $Me_3Si(C{\equiv}C)_2SiMe_3$ (9.7 g, 0.05 mol) were dissolved in a minimum of toluene and the mixture was stirred and heated at reflux for 50 h. Removal of solvent in vacuo left a dark crystalline mass which was sublimed to give traces of $Me_3Si(C{\equiv}C)_2SiMe_3$, followed by oily impurities (90–100 °C/0.05 mmHg) and the desired cycloaddition product (180–200 °C/0.05 mmHg), which was recrystallized from ethyl ethanoate to yield white crystals of **2** (25%) m.p. 205.2–205.5 °C. IR: 2164 cm^{-1} (ν(C≡C)). ^{1}H NMR (CCl_4)(δ): $(CH_3)_3SiC\equiv C$ 0.20s (9H), $(CH_3)_3Si$ 0.25s (9H), CH_3CH_2 1.20t (3H), CH_3CH_2 4.26q (2H), N*H* 13.16s (1H).

X-ray structure determinations

A summary of the data collection and structure refinement parameters is given in Table 3. In each case, diffraction data were measured with monochromated Mo-K_α radiation (λ 0.71069 Å) out to θ_{max} of 22° on an Enraf-Nonius CAD4 diffractometer in the θ–2θ mode, and with a maximum scan time of 1 minute. No crystal decay was observed during the data collections and no absorption corrections were applied. The structures were solved by direct methods using MULTAN [19] and refined by full matrix least-squares with non-hydrogen atoms anisotropic and with a weighting scheme of $w = 1/\sigma^2(F)$. In **1a**, the two independent molecules are essentially the same and have been given equivalent numbering: only one is shown in Fig. 1. The programs used were from the Enraf-Nonius SDP-Plus package and were run on a PDP11/34 computer. Tables of bond lengths and angles, temperature factors, hydrogen atom coordinates, and structure factors are available from one of the authors (PBH).

Crystals of **2** diffracted extremely weakly, and only a very limited data set was available. This means that although the gross stereochemistry of the molecule has been determined, individual bond lengths are not reliable.

Table 3

Data collection and structure refinement parameters for the cycloadducts

Compound	**1a**	**1b**	**2**
Formula	$C_{16}H_{23}N_3Si_2$	$C_{18}H_{22}N_4O_2Si_2$	$C_{14}H_{24}N_2O_2Si_2$
M	313.6	382.6	308.5
Crystal system	triclinic	monoclinic	tetragonal
Space group	$P\bar{1}$	$P2_1/c$	$P4/n$
a (Å)	10.727(5)	16.341(3)	14.476(9)
b (Å)	12.873(5)	14.194(5)	14.476(9)
c (Å)	16.450(7)	10.298(4)	19.690(9)
α (°)	77.60(3)	90	90
β (°)	70.95(3)	102.01(2)	90
γ (°)	66.68(4)	90	90
U (Å^3)	1962.3	2336.3	4125.9
Z	4	4	8
D_{calc} (g cm^{-3})	1.06	1.09	0.96
μ(Mo-K_α)/(cm^{-1})	1.7	1.6	1.7
Total unique reflections	4822	3178	2869
Observed reflections	2172, $I > 3\sigma(I)$	2208, $I > \sigma(I)$	898, $I > \sigma(I)$
Hydrogen atoms	Fixed, B 4.0 Å^2	omitted	omitted
$R = \Sigma \|\|F_0\| - \|F_c\|\|/\Sigma\|F_0\|$	0.073	0.077	0.17
$R' = \{\Sigma w(\|F_0\| - \|F_c\|)^2/\Sigma w\|F_0\|^2)$	0.078	0.113	0.19

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