X-ray powder diffraction data for 1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxopiperidin-1-yl)phenyl]-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxylic acid ethyl ester, $C_{27}H_{28}N_4O_5$

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1-(4-methoxyphenyl)-7-oxo-6-[4-(2-oxopiperidin-1-yl)phenyl]-4,5,6,7- tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxylic acid ethyl ester is an important intermediate in the synthesis of the anticoagulant, apixaban. X-ray powder diffraction data for this compound are reported [$a = 14.101(4)$ Å, $b = 10.105(6)$ Å, $c = 9.532(7)$ Å, $\alpha = 72.774(1)°$, $\beta = 97.356(3)°$, $\gamma = 108.237(3)°$, unit-cell volume $V = 1231.45$ Å^3, $Z = 2$, and space group P-1]. No detectable impurities were observed. © *2017 International Centre for Diffraction Data*. [doi:10.1017/S0885715617000574]

Key words: pharmaceutical intermediate, anticoagulant, apixaban

I INTRODUCTION

Apixaban (Eliquis®) is a novel oral pyrazole-based direct FXa inhibitor; this drug was developed by Bristol-Myers Squibb and Pfizer to treat and prevent thrombotic disorder (Watson *et al*., 2011). Since May 2011, apixaban has been approved for venous thrombus embolism prevention in adult elective hip or knee replacement patients in various countries, such as the USA, China, Brazil, Australia, New Zealand and some European countries (Deeks, 2012). The title compound (Figure 1) is an important intermediate in the synthesis of the anticoagulant, Apixaban. We have reported the crystal structures of other intermediates in our previous work (Wang *et al*., 2015a, 2015b, 2015c, 2015d, 2015e, 2016a, 2016b). Crystallographic data for some intermediates were deposited

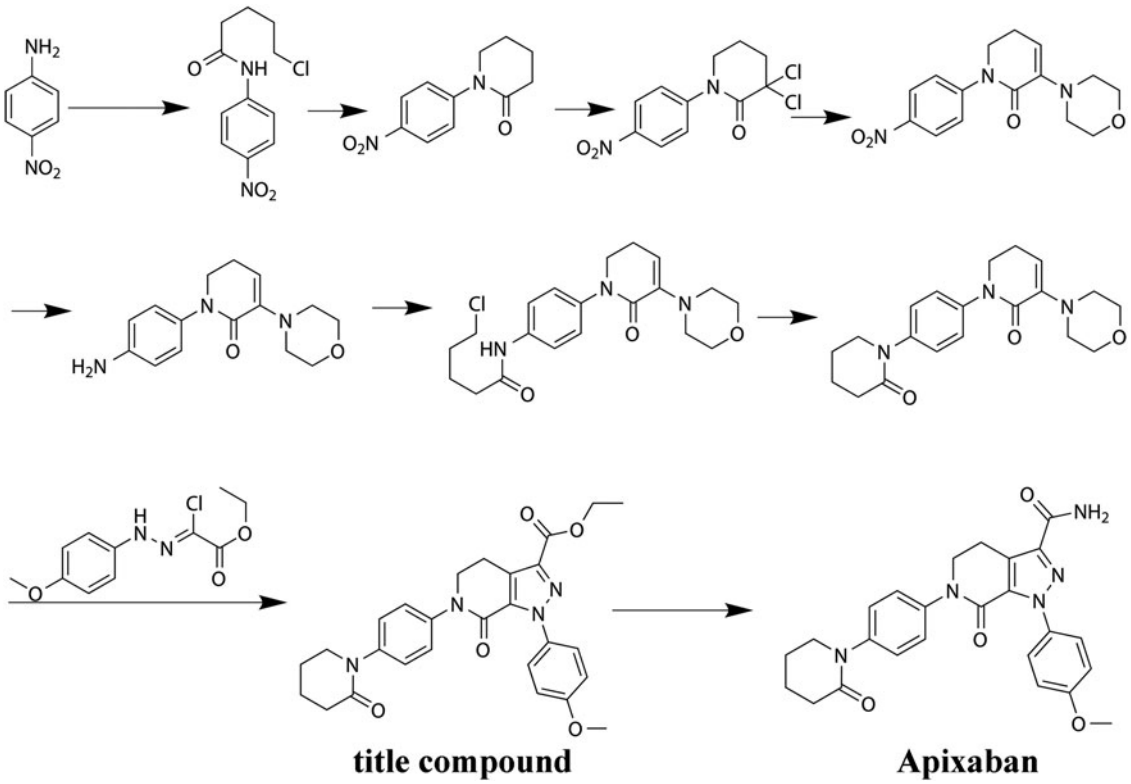

Figure 1. Synthesis of the title compound.

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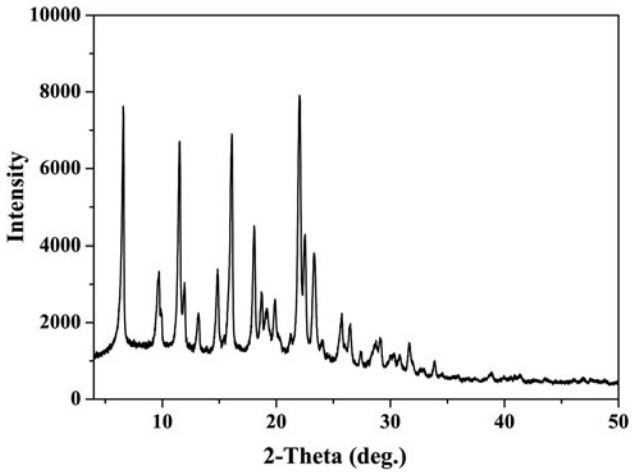

Figure 2. X-ray powder diffraction (XRD) pattern of the title compound using Cu$K\alpha$ radiation.

with the Cambridge Crystallographic Data Center (CCDC) with a supplementary publication number of CCDC-1504960, 148511, 1504963, 1505268, 1505270. Presently, the crystal structure of the title compound has not been reported.

II. EXPERIMENTAL

A. Sample preparation

The title compound was prepared according to the literatures (Anon, 2013; Singh *et al.*, 2015; Ye and Wang, 2015). The melting point and measured density of the title compound are 177-178 °C and 1.33 g cm^{-3}, respectively. The title compound was recrystallized in ethyl acetate and dried. The sample was then ground into powder and mounted on a flat zero background plate.

B. Diffraction data collection and reduction

X-ray powder diffraction (XRD) measurement was performed at room temperature using an X'Pert PRO

TABLE I. Indexed X-ray powder diffraction data for the title compound. The *d*-values were calculated using Cu$K\alpha_1$ radiation (λ = 1.540 56 Å).

$2\theta_{obs}$(°)	d_{obs}(Å)	I_{obs}	h	k	l	$2\theta_{cal}$(°)	d_{cal}(Å)	$\Delta 2\theta$
6.5732	13.4357	96	1	0	0	6.5990	13.3833	−0.0258
9.7114	9.1000	42	0	0	1	9.7133	9.0982	−0.0019
9.9215	8.9078	29	1	−1	0	9.9231	8.9063	−0.0016
11.5233	7.6728	85	1	0	−1	11.5361	7.6643	−0.0128
11.9698	7.3876	37	1	0	1	11.9636	7.3914	0.0062
13.1384	6.7330	28	1	1	0	13.1213	6.7418	0.0171
13.2172	6.6931	27	2	0	0	13.2200	6.6916	−0.0029
14.8847	5.9468	41	1	1	1	14.8782	5.9494	0.0065
15.3968	5.7501	21	0	1	−1	15.4038	5.7476	−0.0070
15.7907	5.6076	34	1	−1	1	15.7896	5.6079	0.0010
16.1058	5.4986	87	2	0	−1	16.1199	5.4938	−0.0141
16.7361	5.2929	18	2	0	1	16.7355	5.2931	0.0005
17.6814	5.0120	20	1	1	−1	17.7044	5.0055	−0.0229
18.0622	4.9072	57	1	−2	−1	18.0722	4.9045	−0.0099
18.6925	4.7431	35	2	−1	1	18.7008	4.7410	−0.0083
19.2046	4.6178	30	0	2	0	19.2021	4.6184	0.0025
19.4146	4.5683	23	3	−1	0	19.4062	4.5702	0.0084
19.4934	4.5500	22	0	0	2	19.4973	4.5491	−0.0039
19.9005	4.4578	33	3	0	0	19.8857	4.4611	0.0147
19.9005	4.4578	33M	2	−2	0	19.9215	4.4532	−0.0211
20.1368	4.4060	22	3	−1	−1	20.1478	4.4037	−0.0110
20.3600	4.3582	20	1	0	−2	20.3557	4.3592	0.0044
21.3185	4.1644	21	2	−1	−2	21.2845	4.1710	0.0341
21.8306	4.0679	46	3	0	−1	21.8261	4.0687	0.0045
22.0407	4.0296	100	1	2	1	22.0509	4.0277	−0.0102
22.0801	4.0225	98	1	2	0	22.0905	4.0206	−0.0104
22.5134	3.9460	54	1	−2	−2	22.5158	3.9456	−0.0024
23.2224	3.8271	41	3	−1	1	23.2350	3.8251	−0.0126
23.3275	3.8101	48	3	−2	0	23.3382	3.8084	−0.0107
23.4063	3.7975	43	0	2	2	23.4033	3.7979	0.0030
24.0890	3.6914	19	2	0	2	24.0602	3.6957	0.0288
25.3889	3.5052	17	2	1	2	25.3893	3.5052	−0.0004
25.5334	3.4857	21	4	−1	0	25.5268	3.4866	0.0066
25.7434	3.4578	28	3	1	1	25.7360	3.4587	0.0074
25.9929	3.4251	18	4	−1	−1	26.0039	3.4237	−0.0109
26.0454	3.4183	18	1	2	2	26.0464	3.4182	−0.0009
26.3868	3.3749	24	2	2	0	26.4187	3.3709	−0.0319
26.4919	3.3617	25	2	2	1	26.4830	3.3628	0.0089
26.6100	3.3471	17	4	0	0	26.6202	3.3458	−0.0102
26.8726	3.3150	13	2	−3	−1	26.8769	3.3145	−0.0042
27.4110	3.2511	16	3	0	−2	27.4283	3.2491	−0.0173
28.0019	3.1838	13	4	−2	0	27.9992	3.1841	0.0026
28.3432	3.1462	15	0	1	3	28.3453	3.1460	−0.0020

Continued

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TABLE I. Continued

$2\theta_{obs}$(°)	d_{obs}(Å)	I_{obs}	h	k	l	$2\theta_{cal}$(°)	d_{cal}(Å)	$\Delta 2\theta$
28.5533	3.1235	18	3	0	2	28.5414	3.1248	0.0119
28.6978	3.1082	18	4	−1	1	28.6778	3.1103	0.0200
28.9078	3.0860	17	1	−3	−2	28.9362	3.0831	−0.0284
29.1311	3.0629	19	2	−3	−2	29.1291	3.0631	0.0020
29.7482	3.0008	12	1	−2	−3	29.7486	3.0007	−0.0005
29.9583	2.9802	14	4	−1	−2	29.9486	2.9811	0.0097
30.0896	2.9675	14	3	−3	0	30.0761	2.9688	0.0134
30.3128	2.9461	15	0	3	2	30.2833	2.9489	0.0294
30.7855	2.9020	15	1	−2	2	30.7602	2.9043	0.0253
30.8249	2.8983	15	3	−3	−2	30.8357	2.8974	−0.0108
31.6389	2.8256	19	1	3	0	31.6279	2.8266	0.0111
31.6389	2.8256	19M	3	2	0	31.6475	2.8249	−0.0086
31.9672	2.7973	12	5	−1	0	31.9694	2.7971	−0.0022
32.6631	2.7393	10	3	−2	−3	32.6413	2.7411	0.0218
32.8732	2.7223	10	2	0	3	32.8683	2.7227	0.0049
32.9520	2.7160	10	5	−2	−1	32.9345	2.7174	0.0175
33.4903	2.6735	8	0	1	−3	33.4842	2.6740	0.0061
33.8580	2.6453	12	4	−3	−2	33.8492	2.6460	0.0087
34.1993	2.6197	8	1	−3	−3	34.1804	2.6211	0.0189
34.3700	2.6071	8	3	−2	2	34.3535	2.6083	0.0165
34.5276	2.5955	9	3	2	−1	34.5248	2.5957	0.0028
34.5276	2.5955	9M	5	0	−1	34.5298	2.5954	−0.0022
34.9084	2.5681	7	3	2	2	34.9050	2.5683	0.0033
35.0922	2.5551	7	3	0	−3	35.0961	2.5548	−0.0039
35.2892	2.5412	7	5	0	1	35.2903	2.5412	−0.0012
35.4205	2.5321	8	1	3	−1	35.4261	2.5317	−0.0057
35.4992	2.5267	7	2	−1	3	35.4989	2.5267	0.0004
35.6699	2.5150	7	3	−3	−3	35.6813	2.5142	−0.0114
35.8800	2.5007	8	1	−4	−1	35.8784	2.5009	0.0017
36.0770	2.4875	7	2	2	3	36.0939	2.4864	−0.0169
36.3658	2.4684	7	4	−1	−3	36.3403	2.4701	0.0255
36.5497	2.4564	7	3	−4	−1	36.5465	2.4566	0.0032
36.6153	2.4522	7	2	−4	−2	36.6145	2.4522	0.0008
36.8123	2.4395	7	2	3	2	36.8166	2.4392	−0.0044
37.3244	2.4072	7	4	−3	1	37.3165	2.4077	0.0079
38.6243	2.3291	8	0	4	2	38.5987	2.3306	0.0256
38.8343	2.3170	9	6	−1	−1	38.8375	2.3168	−0.0032
39.9373	2.2555	7	4	2	−1	39.9045	2.2573	0.0328
40.1342	2.2449	7	3	1	−3	40.1352	2.2449	−0.0010
40.5019	2.2254	7	2	−2	3	40.4903	2.2260	0.0116
40.6069	2.2199	7	3	−2	−4	40.5933	2.2206	0.0137
40.7776	2.2110	7	3	−3	2	40.7650	2.2116	0.0127
40.9221	2.2035	8	4	0	3	40.8995	2.2047	0.0225
41.0927	2.1947	7	3	−1	−4	41.0931	2.1947	−0.0004
41.2897	2.1847	7	6	0	−1	41.2609	2.1862	0.0288
41.3685	2.1808	8	2	−3	−4	41.3575	2.1813	0.0109
42.0381	2.1475	6	6	0	1	42.0468	2.1471	−0.0087
42.1563	2.1418	6	4	−1	3	42.1650	2.1414	−0.0087
42.3795	2.1241	7	5	−2	2	42.3685	2.1316	0.0110
42.5239	2.1160	6	6	−3	0	42.5535	2.1227	−0.0295
43.1148	2.0964	6	3	3	−1	43.1190	2.0962	−0.0042
43.4693	2.0801	7	0	1	−4	43.4470	2.0811	0.0223
43.6794	2.0706	7	5	2	0	43.6980	2.0697	−0.0186
45.6883	1.9841	6	3	3	3	45.7121	1.9831	−0.0237
46.0035	1.9712	7	6	−3	1	45.9951	1.9716	0.0084
46.0691	1.9686	6	6	−4	−1	46.0793	1.9682	−0.0102
46.4236	1.9544	6	1	−4	−4	46.3986	1.9554	0.0250
46.5812	1.9481	6	3	−4	−4	46.5828	1.9481	−0.0016
46.7782	1.9404	7	1	−3	3	46.8022	1.9394	−0.0240
46.9226	1.9347	7	4	−5	−2	46.9005	1.9356	0.0221
47.2115	1.9236	6	2	−3	3	47.2276	1.9230	−0.0162
47.5003	1.9041	6	6	−2	2	47.5010	1.9125	−0.0007
48.1174	1.8895	6	4	3	−1	48.1182	1.8894	−0.0007
49.0234	1.8566	6	7	0	1	49.0265	1.8565	−0.0031
49.2992	1.8469	5	5	1	−3	49.3127	1.8464	−0.0135
49.7062	1.8327	5	4	1	4	49.6861	1.8334	0.0201
49.7981	1.8296	5	1	−3	−5	49.7978	1.8296	0.0003

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diffractometer (PANalytical Co., Ltd., Netherlands) with a PIXcel 1D detector and Cu$K\alpha$ radiation (generator setting: 40 kV and 40 mA). The diffraction data were collected over the angular range from 4° to 50°2θ with a step size of 0.013 13°2θ and a counting time of 50 ms step^{-1}. Figure 2 shows the powder X-ray diffraction pattern of the title compound.

The software package Material Studio 8.0 (Accelrys Co., Ltd., CA, USA) was used to process the data in the Analytical & Testing Center (Sichuan University, Chengdu, China). The XRD pattern was pre-treated by subtracting the background, smoothing, and stripping off the $K\alpha_2$ component. Automatic indexing results were obtained by X-Cell method (Neumann, 2003). The preliminary cell from indexing was refined using the Pawley method (Pawley, 1981), which involves assigning the Miller indices (h, k, l) to each observed peak in the experimental powder XRD pattern.

III. RESULTS

Based on the characteristic peaks, the detected form of the title compound in the present study could be classified as Form A (Anon, 2013). Pawley refinement results confirmed that the title compound is triclinic with space group P-1 and unit-cell parameters: $a = 14.101(4)$ Å, $b = 10.105(6)$ Å, $c = 9.532(7)$ Å, $\alpha = 72.774(1)°$, $\beta = 97.356(3)°$, $\gamma = 108.237(3)°$, unit-cell volume $V = 1231.45$ Å^3, $Z = 2$ and $\rho_x = 1.318$ g cm^{-3}. The values of $2\theta_{obs}$, d_{obs}, I_{obs}, h, k, l, $2\theta_{cal}$, d_{cal}, $\Delta 2\theta$ are listed in Table I.

SUPPLEMENTARY MATERIAL

The supplementary material for this article can be found at https://doi.org/10.1017/S0885715617000574

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