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ORIGINAL PAPER

Synthesis and Crystal Structure of [1,2,4]-Triazolo-annulated 3-Aza-A-homocholestane Derivative: A Novel Pentaheterocyclic Ring System

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Abstract A novel pentaheterocyclic ring system derived from (5α)-cholestan-3-one, i.e. [1*R*-[1α(*R**),3a*β*,3bα,5a-*β*,12aα,12b*β*,14aα]]-1-(1,5-dimethylhexyl)-1,2,3,3a,3b,4,5,11,12,12a,12b,13,14,14a-tetradecahydro-8,12a,14a-trimethyl-9-(2,4,6-trichlorophenyl)-cyclopenta[5,6]naphtho[2,1-*d*][1,2,4]triazolo[1,5-*a*]azepinium hexachloroantimonate (**6**) has been synthesized via the reverse-electron-demand 1,3-dipolar cycloaddition of the 1-aza-2-azoniaallene cation **4** to the triple bond of acetonitrile followed by ring enlargement. The structure of **6** was determined by NMR, IR and high-resolution mass spectra, and unequivocally confirmed by X-ray crystallographic analysis. The title compound crystallizes in monoclinic class under the space group P2-1 with a = 8.163(3) Å, b = 11.214(4) Å, c = 24.191(9) Å, $\alpha = 90°$, $\beta = 97.740(5)°$, and $\gamma = 90°$. The five-membered triazole ring is essentially planar and aromatic, while the seven-membered azepine ring is not planar, but adopts a chair-like conformation.

Keywords 1,2,4-Triazole · Azepine · 3-Aza-A-Homocholestane · Synthesis · Crystal Structure

Introduction

[1,2,4]-Triazoles and related fused heterocycles belong to a class of privileged structures in the design and discovery of new physiologically active compounds [1–7]. For instance, azepines with an additional triazole ring annulated to the seven-membered ring have been extensively investigated due to their ubiquitous feature of many pharmaceutical products [8–10]. In general, the incorporation of a triazole ring plays a fundamental role in enhancing the affinities for receptors.

On the other hand, many steroidal heterocycles with high biological activities have attracted widespread attention [11–13]. The replacement of one or more carbon atoms of a steroid molecule by a heteroatom, especially nitrogen often results in useful alterations to its biological activity [14]. The easily accessible steroidal ketone (5α)-cholestan-3-one **1** has been widely employed as a substrate for preparation of thiazolyl and thieno cholestane derivatives with potent antiinflammatory effects, [15], 3-aza-A-homocholestanes and 3-aza-A-homo-5α-cholestano[3,4-*d*]tetrazole analogues [16, 17]. It is therefore worth developing new routes to steroidal heterocyclic derivatives [18]. A literature survey revealed that methods for achieving the expansion of A-ring to azepine ring seem to be not as plentiful. The well exploited strategies are the Schmidt reaction [19, 20], Beckmann rearrangement [21, 22].

We are currently engaged in a program aimed at synthesizing novel triazolo annulated heterocycles. In this regard, we have established a reliable general synthetic pathway to attain [1,2,4]-triazoloazepines [23–25]. Working on this line, it appeared to us to be of interest to combine the triazole ring to the 3-aza-A-homo-cholestane motif. In this contribution, we report the synthesis and crystal structure of an unprecedented pentacyclic compound, [1*R*-[1α(*R**),3a*β*,3bα,5a*β*,12aα,12b*β*,14aα]]-1-(1,5-dimethylhexyl)-1,2,3,3a,3b,4,5,11,12,12a,12b,13,14,14a-tetradecahydro-8,12a,14a-trimethyl-9-(2,4,6-trichlorophenyl)-cyclopenta[5,6]naphtho[2,1-*d*][1,2,4]triazolo[1,5-*a*]azepinium hexachloroantimonate (**6**).

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Experimental

Instruments

The infrared spectrum IR spectra were recorded using KBr pellets on a Nicolet-360 IR spectrometer, and absorptions are given in wavenumbers (cm^{-1}). The ^{1}H and ^{13}C NMR spectra were measured on a JEOL ECA 400 spectrometer with TMS as an internal reference and $CDCl_3$ as the solution, and the chemical shifts are given in δ (ppm). Coupling constants (J) are reported in Hz. High-resolution mass spectrum was recorded on a SHIMADZU LCMS-IT-TOF mass spectrometer with ESI ionization. Melting points are uncorrected and expressed in °C.

Single crystal X-ray data were collected on a BRUKER SMART APEX-CCD diffractometer equipped with a graphite-monochromated Mo$K\alpha$ radiation. The structure was solved by direct Fourier methods. Full-matrix least-squares refinement was based on F^2 with SHELXL-97 [26].

Synthesis of the Compound

All chemicals used for this synthesis were of reagent grade quality and used as received. Solvents were dried by standard methods and distilled prior to use.

*(5α)-Cholestan-3-one (2,4,6-trichlorophenyl)hydrazone (**2**)*

A mixture of cholestan-3-one **1** (1.93 g, 5 mmol) and 2,4,6-trichlorophenylhydrazine (1.05 g, 5 mmol) containing 0.5 mL of glacial acetic acid were refluxed in ethanol for 3 h. After cooling, the precipitates were obtained by filtration, which was recrystallized from hot 95% ethanol to provide 2.50 g of the pure hydrazone **2** as a white solid. Yield: 86%. m.p. 118–120 °C. *Anal*. required for $C_{33}H_{49}Cl_3N_2$: C, 68.32; H, 8.51; N, 4.83%. Found: C, 68.23; H, 8.45; N, 4.95%. IR (KBr pellets, cm^{-1}): ν 3422, 3222, 2963, 2932, 2852, 1550, 1467, 1445, 1377. ^{1}H NMR ($CDCl_3$): δ 0.67–3.05 (m, 46H, steroidal H), 6.78 (s, 1H, NH), 7.28 (s, 2H, aromatic H).

*3-Chloro-3-(2,4,6-trichlorophenyl)azo-(5α)-cholestane (**3**)*

The reaction was performed in a nitrogen atmosphere. To a solution of hydrazone **2** (1.16 g, 2.0 mmol) in CH_2Cl_2 (20 mL) under external ice-water cooling was added dropwise over 15 min a solution of *t*-BuOCl (0.32 g, 3 mmol) in CH_2Cl_2 (5 mL). The mixture was stirred for 30 min, the progress of the reaction was monitored by TLC. Upon full conversion of the hydrazone **2**, the mixture was dried over $CaCl_2$, filtered and concentrated under reduced pressure to remove volatiles. Since the resulting product **3** was unstable, the crude material was used in the next step without further purification. Orange oil. Yield: 97%. IR (KBr pellets, cm^{-1}): ν 1720, 1552, 1382. ^{1}H NMR ($CDCl_3$): δ 0.66–2.70 (m, 46H, steroidal H), 7.20 (s, 2H, aromatic H).

[1R-[1α(R),3aβ,3bα,5aβ,12aα,12bβ,14aα]]-1-(1,5-dimethylhexyl)-1,2,3,3a,3b,4,5,11,12,12a,12b,13,14,14a-tetradecahydro-8,12a,14a-trimethyl-9-(2,4,6-trichlorophenyl)-cyclopenta[5,6]naphtho[2,1-d][1,2,4]triazolo[1,5-a]azepinium hexachloroantimonate (**6**)*

A mixture of compound **3** (0.61 g, 1 mmol) and acetonitrile (1 mL, ~19 mmol) was prepared and cooled to about −60 °C, to which a solution of $SbCl_5$ (0.45 g, 1.5 mmol) in dry CH_2Cl_2 (5 mL) was carefully dropped in a period of 30 min. The mixture was stirred at this temperature for 2 h, then allowed gradually to warm to 30 °C (bath temperature) and was stirred further for 1.5 h. After concentrating the mixture to about 2 mL by evaporating the volatiles, the crude product was precipitated by slow addition of cold Et_2O (20 mL). The crude product was purified by recrystallization from MeOH-MeCN-Et_2O (1:1:1) to afford 0.85 g of pure compound **6** as brownish crystals. Yield: 90%. m.p. 222–224 °C. *Anal.* Required for $C_{35}H_{51}Cl_9N_3Sb$: C: 44.04; H, 5.38; N, 4.40%. Found C: 43.84; H, 5.38; N, 4.80%. IR (KBr pellets, cm^{-1}): ν 2491, 2865, 1570, 1556, 1458, 1389. ^{1}H NMR ($CDCl_3$): δ 0.65 (s, 3H, CH_3), 0.85–2.00 (m, 38H, steroidal H), 2.42 (d, J = 12.2 Hz, 1H), 2.50 (s, 3H, CH_3), 2.99–3.01 (m, 1H, one of C(6)–H), 3.35 (m, 1H, one of C(6)–H)), 4.10 (m, 1H, one of C(11)–H), 4.38 (m, 1H, one of C(11)-H), 7.76 (s, 2H, aromatic H). ^{13}C NMR ($CDCl_3$): δ 11.9, 12.1, 18.7, 21.3, 22.6, 22.8, 23.8, 24.1, 28.0, 28.2, 30.4, 31.2, 31.5, 34.9, 35.8, 36.1, 39.5, 39.7, 39.8, 42.2, 43.8, 45.7, 52.6, 56.2, 56.3 (steroidal CH_3), 122.4, 130.9, 131.2, 135.7, 136.6, 143.1 ($Cl_3C_6H_2$), 159.5, 164.0 (C=N). HRMS (ESI): m/z calcd for the cation $C_{35}H_{51}Cl_3N_3^+$: 618.3143; found: 618.3173.

A fully completed Crystallographic Information File deposited with the CCDC is available (Deposition CCDC No. 754601).

Results and Discussion

The required starting material, (5α)-cholestan-3-one **1**, was easily prepared via a two-step procedure from cholesterol. Hydrogenation of the 5-ene moiety of cholesterol under Pd/C catalysis in tetrahydrofuran afforded 5α-dihydrocholesterol in 90% yield [27] which was oxidized with CrO_3 in acetic acid to provide **1** in 91% yield [28].

The synthetic route of the title compound **6** is illustrated in Scheme 1, which was commenced with the condensation of **1** with (2,4,6-trichlorophenyl)hydrazine in refluxing ethanol in the presence of catalytic amount of acetic acid to provide the corresponding hydrazone **2**. Upon treatment with 1.5 equivalents of *t*-BuOCl under external ice-water cooling, the hydrazone **2** was readily transformed to the α-chloroazo compounds **3** as a yellow to red oil. Since compound **3** is very prone to decomposition upon keeping, it should be used freshly as obtained for further step.

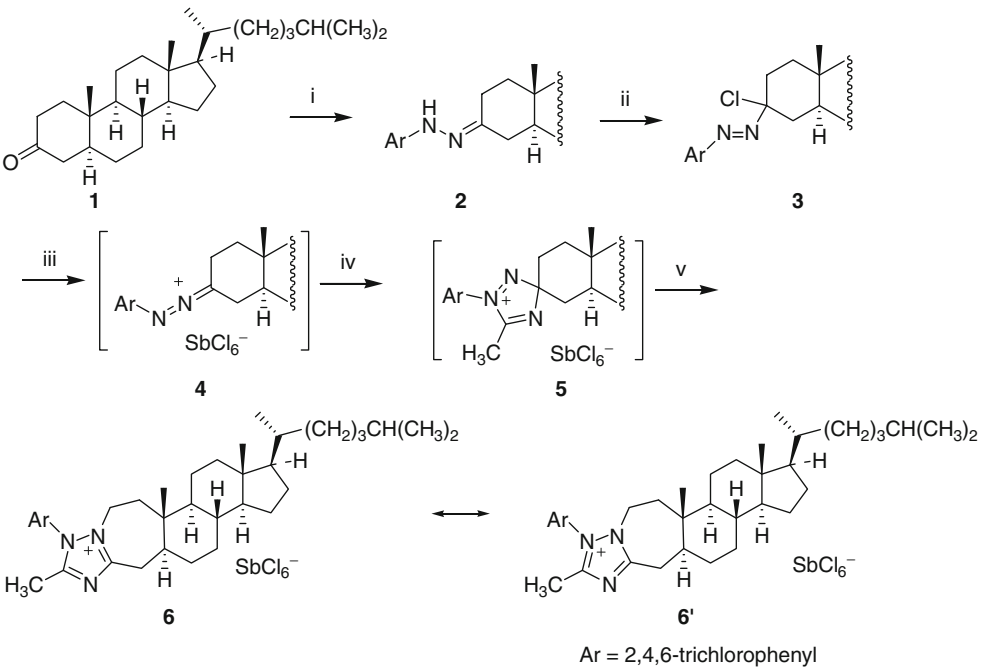
Next, a solution of 1.5 equivalent $SbCl_5$ in anhydrous CH_2Cl_2 was slowly dropped to a cold (−60 °C) solution of **3** and largely excessive amount of acetonitrile in anhydrous CH_2Cl_2. The mixture was stirred further at this temperature for about 1 h and then allowed to warm to 30 °C in a period of another hour. The mixture was allowed to stir at the same temperature for additional 1.5 h. Usual work-up afforded the [1,2,4]-triazolo fused 3-aza-A-homo-cholestane salt derivative **6** as white crystals in 90% yield.

The synthesis shares the same mechanistic scenario as reported for other triazolo fused bi- or tricyclic compounds [23–25]. As shown in detail in Scheme 1, $SbCl_5$-asssited departure of a chloride ion from **3** generated the tetracyclic 1-aza-2-azoniaallenium salt **4**, which belong to a class of highly reactive intermediates. In general, hetero-allenium ions like **4** functions well as a kind of positively charged 1,3-dipoles [29]. Thus, in the presence of acetonitrile, **4** is intercepted by polar [3^++2]-cycloadditon to the triple bond of acetonitrile to produce the 3-sipro-substituted 3*H*-1,2,4-triazolium salt **5**. Finally, on elevating the temperature to ambient temperature, ring enlargement via hetero-Wagner-Meerwein rearrangement of the primary cycloadduct **5** proceeds with insertion of the nitrogen atom into the carbon skeleton to furnish the isolated product **6**. Evidence supporting this selectivity was initially deduced from the observed strong downfield shift between 4.1 and 4.4 ppm for the two C(11)–methylene protons attached to the triazole ring.

Noteworthy is the exclusive migratory aptitude observed in the ring enlargement step which led to the isolation of **6** as sole product. The C(2) of the cholestane migrates in preference to the C(4), and exclusively to N(2) of the triazolium unit rather than N(4).

The data of IR, ^{1}H NMR, ^{13}C NMR, HRMS and elemental analysis for the product are in good agreement of the proposed structure of compound **6**. In preceding papers [23–25], we have revealed that the migratory aptitude of the substituents in the rearrangement **5** → **6** tends to parallel their ability to accommodate the respective carbocation. Based on this rule, one would expect that the final ring expansion should give the regioisomeric product **7** (see Fig. 1). Considering this controversy, the structural establishment required indisputable proofs. As such, the crystal of **6** was developed and subjected to X-ray diffraction analysis. Table 1 contains crystallographic data of compound **6**, and Table 2 lists the selected bond lengths and angles. Table 3 gives the selected torsional angles. The X-ray structure for **6** is shown in Fig. 2.

Compound **6** crystallized in the chiral space group P2(1). The five-membered triazole ring (C2–N3–N1–C1–N2) is



Scheme 1 Procedure of preparing the title compound **6**. *Reagents and conditions* (i) (2,4,6-Trichlorophenyl)hydrazine, AcOH/EtOH, reflux, 3 h; (ii) t-BuOCl/CH_2Cl_2, 0 °C, 30 min; (iii, iv) $SbCl_5$, CH_2Cl_2, −60 °C; MeCN/CH_2Cl_2, −60–30 °C, totally 2 h; (v) 30 °C, 1.5 h

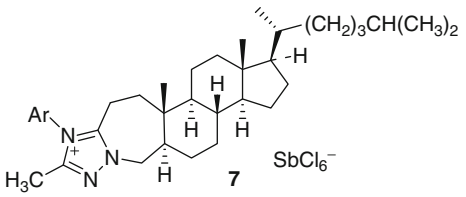


Fig. 1 Structure of a hypothetical isomeric product 7 from the reaction

Table 1 Crystal data and structure refinement for compound **6**

Empirical formula	$C_{35}H_{51}C_{19}N_3Sb$
Formula weight	954.59
CCDC deposit no.	754601
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 8.163(3) Å
	b = 11.214(4) Å
	c = 24.191(9) Å
	$\alpha = 90°$
	$\beta = 97.740(5)°$
	$\gamma = 90°$
Volume	2194.2(14) $Å^3$
Z	2
Density (calculated)	1.445 Mg m^{-3}
Absorption coefficient	1.205 mm^{-1}
F(000)	972
Crystal size	0.15 × 0.08 × 0.05 mm^3
θ range for data collection	1.70–26.01°
Index ranges	$-10 \le h \le 9$
	$-11 \le k \le 13$
	$-26 \le l \le 29$
Reflections collected	9990
Independent reflections	6689 [$R_{int} = 0.0538$]
Reflections observed (>2σ)	3185
Data completeness	0.991
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9422 and 0.8400
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	6689/1/439
Goodness-of-fit on F^2	0.820
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0514$, w$R_2 = 0.1254$
R indices (all data)	$R_1 = 0.1126$, w$R_2 = 0.1435$
Absolute structure parameter	−0.01(3)
Largest diff. peak and hole	0.579 and −0.446 e $Å^{-3}$

essentially planar (Rms deviation of fitted atoms = 0.0156). The ring contains a significantly long N(1)–N(3) distance of 1.378(11) Å, which represents a N–N single bond.

Table 2 Selected bond lengths (Å) and angles (°) of compound **6**

Bond lengths			
N1–C1	1.343(13)	N1–N3	1.378(11)
N2–C2	1.321(13)	N3–C2	1.328(12)
N1–C19	1.443(13)	N2–C1	1.328(13)
N3–C18	1.506(13)	C2–C3	1.462(14)
C3–C4	1.583(15)	C4–C16	1.600(15)
C16–C17	1.510(13)	C17–C18	1.456(13)
C18–N3	1.506(13)	C1–C25	1.440(15)
Bond angles			
C1–N1–N3	104.8(8)	C1–N1–C19	132.6(10)
N3–N1–C19	121.9(8)	C2–N2–C1	105.8(9)
C2–N3–N1	107.1(9)	C2)–N(3)–C18	130.8(10)
N1–N3–C18	122.1(8)	N2–C1–N1	111.3(11)
N2–C1–C25	125.2(10)	N1–C1–C25	123.3(10)
N2–C2–N3	110.9(9)	N2–C2–C3	124.6(10)
N3–C2–C3	124.5(12)	N3–C18–C17	112.4(8)

Table 3 Selected torsional angles (°) for compound **6**

C18–N3–C2–C3	1.25(1.69)	C16–C17–C18–N3	−69.83(1.42)
N3–C2–C3–C4	−55.33(1.41)	C2–N3–C18–C17	50.76(1.48)
C2–C3–C4–C16	74.02(1.25)	C1–N1–N3–C18	176.73(0.92)
C2–N3–C18–C17	50.76(1.48)	C1–N2–C2–C3	−177.82(1.04)
C3–C4–C16–C17	−60.53(1.17)	C1–N1–C19–C24	95.68(1.39)
C4–C16–C17–C18	62.35(1.33)	N3–N1–C19–C20	90.85(1.20)

However, it is slightly shorter than the N–N single bond value of 1.401 Å reported by Allen [30]. In a [1, 3, 4]-thiadiazole system a N–N distance of 1.373(3) Å has been found by Song [31] which is quite close to our value. In addition, Schantl has reported a stable five-membered azomethine imine in which a much shorter N–N distance of 1.303(2) Å was disclosed [32]. On the other hand, the other four bond lengths of N1–C1, N2–C2, N3–C2 and N2–C1 are nearly equal as the value ranges between 1.321(13) and 1.343(13) Å, which refer to a partial double bond, and are almost identical to those found in related delocalized system such as 1.338 Å in pyridine [33]. All above data suggest that there is a delocalized system in this five-membered ring, in which the positive charge is expected to reside mainly on the N(1) and N(3) atoms. In line with this assumption, two main resonance hybrids **6** and **6′** may be drawn (Scheme 1).

Due to hindered rotation about the N1–C19 bond, the trichlorophenyl ring at N1 is nearly perpendicular to the triazole ring. The dihedral angle between these two planes is found to be 87.26° (0.31°). This view was reinforced by the dihedral angles of 95.68(1.39)° for C1–N1–C19–C24 as

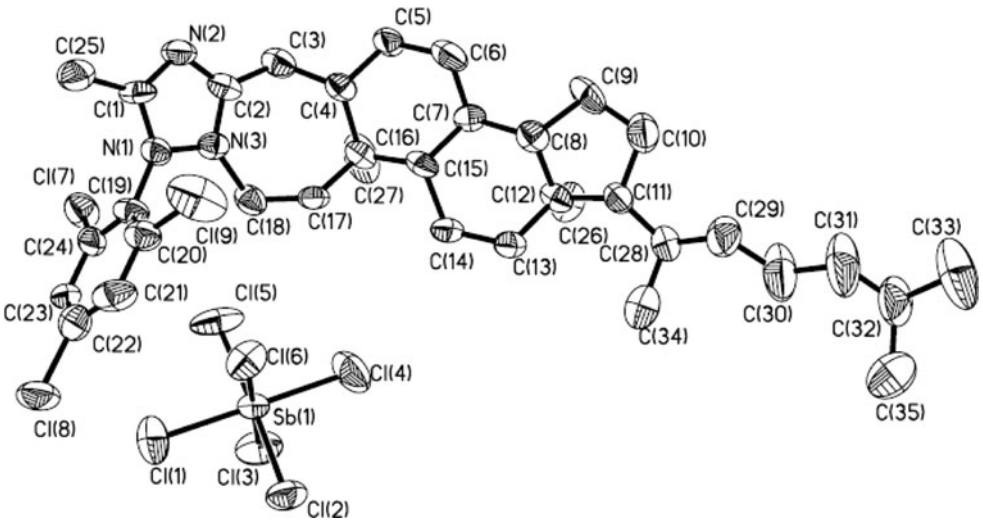


Fig. 2 Molecular structure of compound **6** showing the atomic labeling. Atoms are given by thermal ellipsoids at 50% probability. H atoms are omitted for clarity

well as 90.85(1.20)° for N3–N1–C19–C20. Besides, the rather long N1–C19 bond distance [1.443(13) Å] is indicative of a C(sp^2)–N single bond. Therefore, we conclude that no conjugation occurs between the two rings.

The seven-membered azepine ring is not planar, but adopts a chair-like conformation. This may be described in terms of the seven torsion angles inside the ring (Table 3). It can also be seen from the torsion angles of C1–N1–N3–C18 [176.73(0.92)°] and C1–N2–C2–C3 [−177.82(1.04)°] that C18 and C3 atoms are situated almost in the plan of the triazole ring. Aside from the normal C(sp^3)–C(sp^3) single bonds found for C16–C17 and C17–C18, the other two C(sp^3)–C(sp^3) bond lengths in this ring vary from 1.59(2) to 1.61(3) Å which are apparently longer than one would expect.[1]

In summary, we report in this paper the synthesis of a literature unprecedented [1,2,4]-triazolo-annulated 3-aza-A-homocholestane derivative **6** by cycloaddition of the cationic tetracyclic azocarbenium ion **4** with acetonitrile accompanied by a consecutive regio-selective ring expansion. The structure of this pentacyclic compound was determined by the analysis of spectroscopic data along with an X-ray structural diffraction analysis.

Supplementary Material

CCDC-754601 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK [fax: ++44(1223)336033].

[1] For comparison of the metric parameters with a 1*H*-1,2,4-triazolo[3,2-*d*][1,5]-benzoxaepinum salt investigated previously by us [34].

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References

1. Garratt PJ (1996) In: Katritzky AR, Rees CW, Scriven EFV (eds) Comprehensive HeterocyclicChemistry II, vol 4. Pergamon Press, Oxford, p 127
2. Turnbull K (1998) Prog Heterocycl Chem 10:153
3. Al-Masoudi IA, Al-Souda YA, Al-Salihi NJ, Al-Masoudi NA (2006) Khim Geterotsikl Soedin 11:1605
4. Terrell CL (1999) Mayo Clin Proc 74:78
5. Koltin Y, Hitchcock CA (1997) Curr Opin Chem Biol 1:176
6. Staben ST, Blaquiere N (2010) Angew Chem Int Ed Engl 49:325
7. Girgis AS, Barsoum FF (2009) Eur J Med Chem 44:1972
8. Cho H, Murakami K, Nakanishi H, Fujisawa AK, Isoshima H, Niwa M, Hayakawa K, Hase Y, Uchida I, Watanabe H, Wakitani K, Aisaka K (2004) J Med Chem 47:101
9. Broggini G, Garanti L, Molteni G, Zecchi G (1995) Synthesis 1483
10. Al-Soud YA, Qalalweh MNA, Al-Sa'doni HH, Al-Masoudi NA (2005) Heteroatom Chem 16:28
11. Kwon T, Heiman ASE, Oriaku T, Yoon KH, Lee J (1995) J Med Chem 38:1048
12. Elmegeed GA, Wardakhan WW, Younis M, Louca NA (2004) Arch Pharm Pharm Med Chem 337:140
13. Abdelhamid AO, Abdelhalim MM, Elmegeed GA (2007) J Heterocyclic Chem 44:7
14. Burbiel J, Bracher F (2003) Steroids 68:587
15. Elmegeed GA, Wardakhan WW, Baiuomy AR (2005) Pharmazie 60:328
16. Ahmad MS, Alam Z (1988) Indian J Chem Sect B: Org Chem Include Med Chem 27B:1001
17. Mushfiq M, Iqbal N (1986) J Chem Res-S 254
18. Elmegeed GA, Wardakhan WW, Younis M, Louca NA (2004) Arch Pharm 337:140
19. Desai P, Schildknegt K, Agrios KA, Mossman C, Milligan GL, Aube J (2000) J Am Chem Soc 122:7226
20. Ahmad MS, Alam Z (1988) Indian J Chem Sect B: Org Chem Include Med Chem 27B:336
21. Craig JC, Naik AR (1962) J Am Chem Soc 84:3410
22. Doorenbos NJ, Wu MT (1961) J Org Chem 26:2548

23. Meng QQ, Bai HX, Wang QR, Tao FG (2007) Synthesis 33
24. Wang QR, Liu XJ, Li F, Ding ZB, Tao FG (2002) Synth Commun 32:1327
25. Wang QR, Li Z, Yang HY, Li F, Ding ZB, Tao FG (2003) Synthesis 1231
26. Sheldrick GM (1997) SHELXL-97, Program for Crystal Structure Refinement; University of Göttingen, Germany
27. Hasan M, Rashid N, Khan KM, Snatzke G, Duddeck H, Voelter W (1995) Liebigs Ann 889
28. Brown FJ, Djerassi C (1980) J Am Chem Soc 102:807
29. Wang QR, Jochims JC, Kohlbrandt S, Dalenburg L, Al-Talib M, Hamed IAE (1992) Synthesis 710
30. Allen FH, Kennard O, Watson DG, Brammer L, Orpen AG, Taylor R (1987) J Chem Soc Perkin Trans II:S1
31. Song XJ, Tan XH, Wang YG (2008) J Chem Crystallogr 38:478
32. Schantl JG, Rettenbacher AS, Wurst K (1998) Angew Chem Int Ed Engl 37:2229
33. Dewar MJS, Thiel W (1977) J Am Chem Soc 99:4907
34. Liu XJ, Liu Y, Ding ZB, Wang QR, Zhang CZ (2000) J Heterocyclic Chem 37:287