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Synthesis and reactivity of amino-substituted BEDT-TTF donors as building blocks for bifunctional materials

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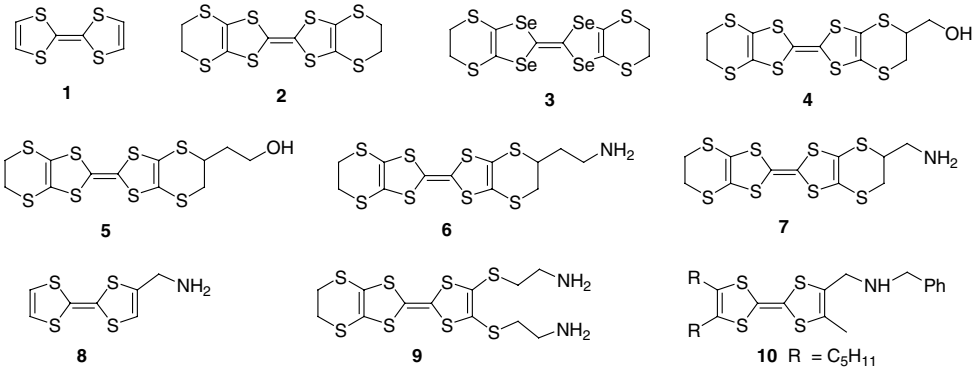
Abstract—The first two amino-substituted BEDT-TTF derivatives, aminomethyl-ET (AMET) and aminoethyl-ET (AEET), have been prepared; the critical step in both cases was a hetero Diels–Alder reaction with 1,3-dithiole-2,4,5-trithione. AEET shows expected reactivity towards electrophiles whereas AMET will not react with aryl acid chlorides or sulfonyl chlorides, but amides of AMET can be produced by DCC coupling and mixed anhydride methods.

1. Introduction

Tetrathiafulvalene, TTF, **1** and bis(ethylenedithio)tetrathiafulvalene, BEDT-TTF or ET, **2** are readily oxidisable organosulfur donors that have played major roles in the field of organic conductors over the last 15 years.[1] Particular highlights with ET are formation of superconducting radical cation salts[2] including a paramagnetic superconductor,[3] and a hybrid layered salt with $[CrMn(oxalate)_3]^-$ with independent electrical conductivity and ferromagnetic behaviour.[4] Recently, it was reported that the electrical properties of certain salts of the ET analogue BETS **3** with FeX_4^- (X = Cl, Br) can be controlled by an external magnetic field.[5] We are interested in preparing further such 'bifunctional materials' but with a covalent attachment between the organosulfur system and the molecular component, which brings additional physical properties such as magnetic behaviour, or a second conduction pathway. TTF is easily converted to its mono- or poly-lithio analogues that allow it to be functionalised readily. However, for the synthesis of simple ET derivatives the central double bond should be formed last.

Thus, we have prepared racemic hydroxymethyl- and hydroxyethyl-ET **4** and **5**,[6,7] and the former in its enantiopure form too,[8] and have shown that the hydroxyl group in **4** and **5** can be used to link to metal



Keywords: Organosulfur donors; BEDT-TTF; Organic conductors; Hetero Diels–Alder reaction.
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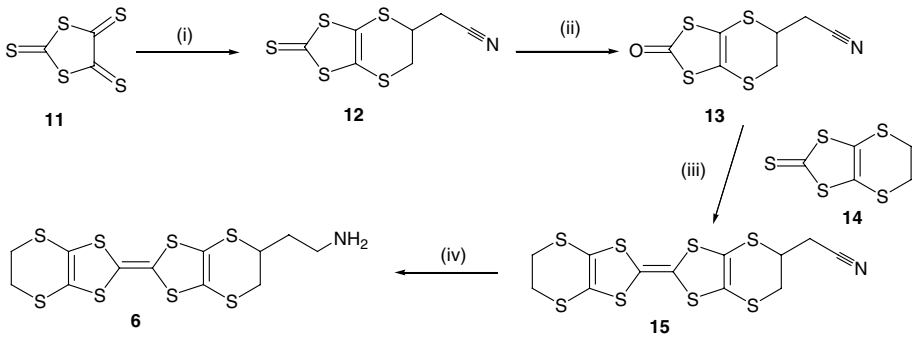


Scheme 1. Reagents and conditions: (i) allyl cyanide, toluene, reflux; (ii) $Hg(OAc)_2$, HOAc, $CHCl_3$ 20 °C; (iii) $P(OEt)_3$ 90 °C; (iv) $LiAlH_4$, THF, 20 °C.

binding groups either by ester formation or by tosylation and substitution.[7] Here we report the synthesis of the first two amino-substituted ET derivatives AEET **6** and AMET **7** and initial investigations into their reactivities for the preparation of amides, sulfonamides and heterocycles. Fabre and co-workers have prepared the rather unstable aminomethyl-TTF, **8**,[9] as well as secondary and tertiary amine derivatives,[9,10] and has installed amino groups into **9** by functional group interconversions from the diol.[11] Bryce and co-workers have used the benzylaminomethyl TTF **10** to prepare a covalently linked donor–acceptor system.[12]

2. Synthesis of AEET, 6

The trithione **11**, prepared in two steps from carbon disulfide,[13] reacted with allyl cyanide in refluxing toluene to furnish the cyanomethyl thione **12**[†] in 57% yield. This was converted smoothly by the standard procedure using mercuric acetate to the corresponding oxo derivative **13** and then cross-coupled with an excess of thione **14** in triethyl phosphite to give the cyanomethyl-ET **15** in an overall yield of 21% from **12**. The reduction of the nitrile to aminoethyl-ET, AEET, **6**[‡] was carried out using $LiAlH_4$ in THF in high yield (90%) and the product is stable to column chromatography and to exposure in the air (Scheme 1). The alternative reduction of the nitrile **15** using borane dimethyl sulfide was unsuccessful.

3. Synthesis of AMET, 7

It is known that self-couplings of thione or oxo compounds of type **16** that contain electron withdrawing substituents directly attached to the outer rings are not successful, for example, **16** X = CN, Y = H[14] and X = Y = CO_2Me,[15] often preferring Arbusov reactions with triethyl phosphite. This precluded the use of acrylamide or acrylonitrile in the synthesis of AMET. Furthermore, the reaction of trithione **11** with allylamine did not give the expected Diels–Alder product, but formed *N*,*N*′-diallylthiourea as the only product. However, prior Boc protection of the amino group avoided this problem; the trithione **11** reacted with *N*-Boc-allylamine in refluxing toluene to give thione **17**[§] in a yield of 67%. Conversion to the oxo compound **18** proceeded in a yield of 95% and cross-coupling with excess thione **14** in triethyl phosphite gave *N*-Boc-aminomethyl-ET **19** in a yield of 28%. Removal of the protecting group was accomplished by reaction with neat TFA at room temperature, which furnished the trifluoroacetate salt of AMET **20** in a quantitative yield after recrystallisation from THF/DCM. The free base **7**[¶] could be prepared from **20** in quantitative yield by deprotonation with aqueous sodium hydroxide in THF, extraction and recrystallised from THF/ether (Scheme 2).

4. Reactivity of AEET and AMET

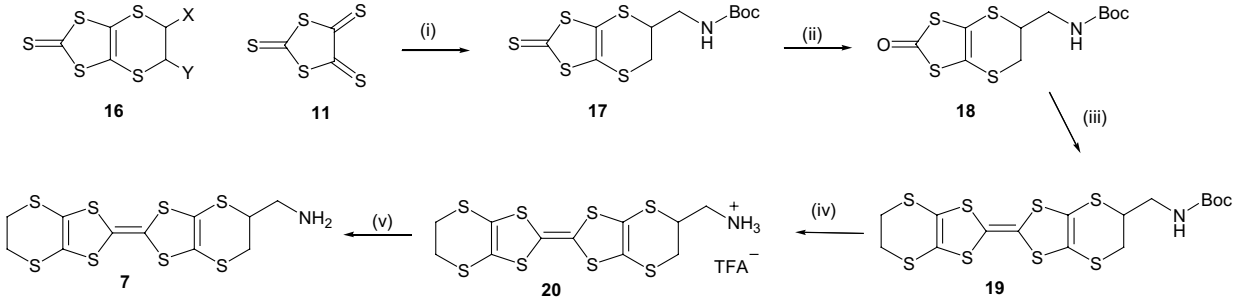
AMET **7** reacted with 2,5-dimethoxytetrahydrofuran in acetic acid and pyridine to furnish pyrrole **24** in a 57%

[†] δ_H ($CDCl_3$): 4.00 (m, 1H, 5-*H*), 3.50 (dd, 1H, $J = 2.9$, 13.9 Hz, 6-H_α), 3.55 (dd, 1H, $J = 5.2$, 13.9 Hz, 6-H_β), 2.98 (m, 2H, CH_2CN); δ_C ($CDCl_3$): 206.9 (*C*=S), 121.3, 120.8 (3a-, 7a-C), 115.8 (*C*≡*N*), 37.8 (5-*C*), 33.1 (6-*C*), 23.6 (CH_2CN); ν_{max} (KBr disk): 2947, 2905, 2241, 1418, 1407, 1324, 1282, 1227, 1061, 1010, 911, 884, 849, 782, 719, 667, 515, 459 cm^{-1}; *m*/*z* (APCI$^+$): 264 ([M]$^+$, 100%); HRMS: (EI) found [M]$^+$ 262.9020, $C_7H_5NS_5$ requires 262.9021.

[‡] δ_H (DMSO-d_6): 3.69 (m, 1H, 5-*H*), 3.23 (s, 4H, 5′-, 6′-*H*), 3.24 (m, 2H, CH_2NH_2), 2.67 (dd, 1H, $J = 7.2$, 13.1 Hz, 6-H_α), 2.72 (dd, 1H, $J = 6.7$, 13.1 Hz, 6-H_β) 1.84 (m, 2H, CH_2CH_2O); δ_C (DMSO-d_6): 114.4, 112.9, 112.2 (sp^2-*C*), 45.2 (5-*C*), 41.2 (CH_2NH_2), 38.8 (6-*C*), 36.9 (CH_2CH_2O), 30.1 (5′-, 6′-*C*); ν_{max} 3362, 2914, 2853, 2355, 1648, 1560, 1404, 1384, 1280, 880, 766 cm^{-1}; *m*/*z* (EI): 428 ([M+H]$^+$, 100%); HRMS: (EI) found [M+H]$^+$ 426.8812, $C_{12}H_{13}NS_8$ requires 426.8814.

[§] δ_H ($CDCl_3$): 4.96 (s, 1H, N*H*), 3.88 (m, 1H, 5-*H*), 3.43 (m, 2H, CH_2NH), 3.32 (dd, 1H, $J = 2.8$, 13.6 Hz, 6-H_α), 3.17 (dd, 1H, $J = 5.9$, 13.6 Hz, 6-H_β); 1.39 (s, 9H, $C(CH_3)_3$); δ_C ($CDCl_3$): 210.2 (*C*=S), 155.8 (*C*=O), 121.8, 122.5 (3a-, 7a-*C*), 80.6 ($C(CH_3)_3$), 44.1 (CH_2NH), 42.7 (5-*C*), 31.9 (6-*C*), 28.3 ($C(CH_3)_3$); ν_{max} (KBr disk): 3374, 2977, 2930, 1686, 1517, 1493, 1363, 1280, 1256, 1177, 1067, 951 cm^{-1}; *m*/*z* (EI): 353 ([M]$^+$, 100%); HRMS: (ES) found [M+H]$^+$ 353.9772, $C_{11}H_{15}NO_2S_5$ requires 353.9779.

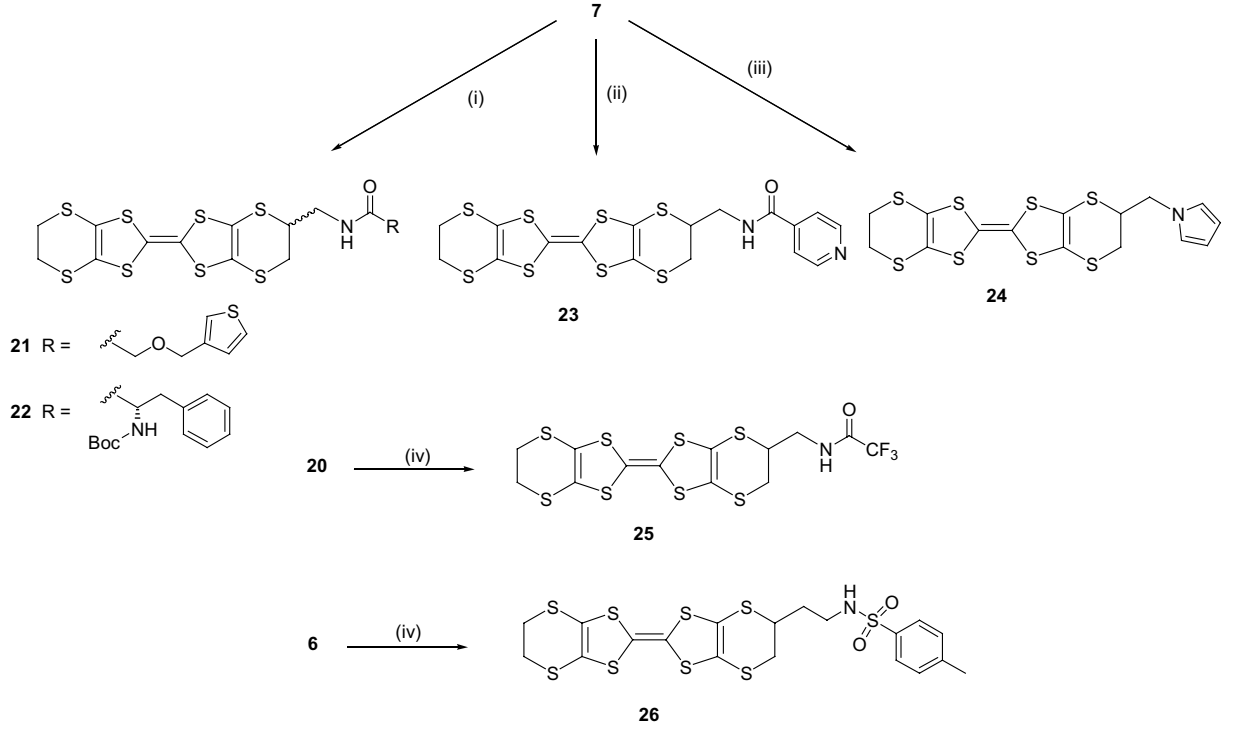
[¶] δ_H (DMSO-d_6): 3.65 (m, 1H, 5-*H*), 3.31 (s, 4H, 5′-, 6′-*H*), 3.26 (m, 2H, CH_2NH_2), 2.89 (dd, 1H, $J = 7.2$, 13.1 Hz, 6-H_α), 2.73 (dd, 1H, $J = 6.7$, 13.1 Hz, 6-H_β); δ_C (DMSO-d_6): 114.4, 112.9, 112.2 110.6, 110.2 (sp^2-*C*), 45.6 (5-*C*), 40.1 (CH_2NH_2), 38.9 (6-*C*), 29.6 (5′-, 6′-*C*); ν_{max}: 3364, 2918, 2861, 2357, 1649, 1562, 1410, 1404, 1382, 1282, 876, 641, 550 cm^{-1}; *m*/*z* (EI): 413 ([M+H]$^+$, 5%), 76 (100%); HRMS: (EI) found [M+H]$^+$ 413.8727, $C_{11}H_{11}NS_8$ requires 413.8730.



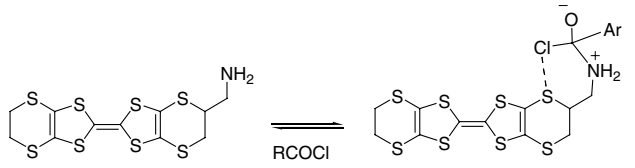
Scheme 2. Reagents and conditions: (i) *N*-Boc-allylamine, toluene, reflux; (ii) $Hg(OAc)_2$, HOAc, $CHCl_3$, 20 °C; (iii) $P(OEt)_3$, **14**, 90 °C; (iv) TFA, 20 °C; (v) THF, NaOH(aq), 20 °C.

yield, thus introducing a heterocycle on the side chain. AMET also underwent DCC coupling reactions in DCM using 1-hydroxybenzotriazole as catalyst. For example, it reacted with (thiophen-3-ylmethoxy)-acetic acid and (L)-*N*-Boc-phenylalanine to give amides **21** and **22**, respectively, the former containing a potentially polymerisable group. NMR indicated that **22** was a 50:50 mixture of the two possible diastereomers. Surprisingly, the reactions of both AMET and its trifluoroacetate salt **20** with various acid chlorides (benzoyl chloride, isonicotinoyl chloride and picolinoyl chloride) in pyridine or in THF/triethylamine mixtures did not yield the expected amides even with heating. Interestingly, although AMET failed also to form a sulfonamide with tosyl chloride in pyridine, its TFA salt **20** under similar conditions gave the trifluoroacetyl amide **25** (78%).This presumably occurred via a mixed anhydride between the tosyl chloride and trifluoroacetate. Following this lead, AMET was reacted with isonicotinic acid, tosyl chloride and pyridine at room temperature to give the isonicotinyl amide **23** in good yield (80%). In contrast, initial investigations into the reactivity of AEET show that it reacts readily with tosyl chloride in pyridine to furnish the expected sulfonamide **26** in good yield (89%) (Scheme 3).

We propose that the observed unreactivity of AMET towards acid chlorides and sulfonyl chlorides may be due to a S–Cl interaction in the initially formed tetrahedral intermediate, which makes loss of chloride much more difficult (Scheme 4). It is known that organic sulfides form short contacts with nucleophilic species in the plane of the sulfide group,[16] and the Cambridge Structural Database contains a number of examples of contacts with chloride or a bonded chlorine atom with S–Cl separations of ca. 3.3 Å, for example, in the radical



Scheme 3. Reagents and conditions: (i) RCOOH, DCC, DCM, 1-hydroxybenzotriazole, 20 °C; (ii) TsCl, isonicotinic acid, 20 °C; (iii) 2,5-dimethoxytetrahydrofuran, py, HOAc, reflux; (iv) TsCl, py, 20 °C.



Scheme 4.

cation salt $(ET)_3Cl_2(H_2O)_2$[17] and in ET salts with chlorinated rhenium clusters.[18] An S–O$^-$ interaction cannot be ruled out, though it would be expected to inhibit the formation of **21**–**24** too. S–O interactions have been proposed in related conjugated systems.[19] The unreactivity of AMET towards acyl chlorides is notable since the hydroxymethyl equivalent HMET, **4**, reacts with benzoyl chloride to furnish the expected benzoate, and the benzylaminomethyl-TTF **10** was reacted with acid chlorides to furnish amides.[12]

The reported chemistry opens up a route for incorporation of the ET grouping into molecules with potential bifunctional properties by covalent linking to the amino groups of AMET and AEET.

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