Pergamon

Tetrahedron Letters, Vol. 35, No. 41, pp. 7589-7592, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01631-3

Knoevenagel-like Condensations with Highly Stabilized Active Methylene Compounds

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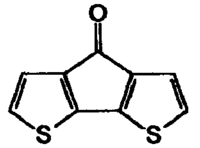
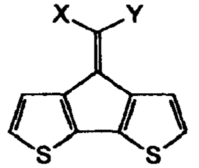
Abstract: Bis (phenylsulfonyl) methane, nonafluorobutylsulfonylacetonitrile or heptadecafluorooctylsulfonyl acetonitrile could be condensed with the strained ketone cyclopenta [2,1-b; 4,3-b'] dithiophen-4-one (1) to afford the corresponding α, β unsaturated sulfones using a combination of a Grignard reagent of the methylene compound, $TiCl_4$-activation of the ketone and N-methylmorpholine as base for the final deprotonation-elimination step.

During the course of our studies on the design and synthesis of lowered energy gap (E_{gap}) polymers[1] we prepared fused bithiophene monomers (2) possessing electron withdrawing groups X and Y *via* Knoevenagel condensation chemistry between the fused ketone 1 and the appropriately disubstituted methylene compound, XCH_2Y. One derivative (X,Y = CN) afforded a polymer with $E_{gap} \leq 0.8$ eV, which is one of the lowest values reported. We wished to extend this series to incorporate the even stronger electron-withdrawing $-SO_2R$ group but were initially discouraged by the report of Hanack[2] *et al* who found that the anions of methylene compounds containing this group were so stable that they did not readily react with carbonyls including aliphatic aldehydes or alicyclic and aromatic ketones.



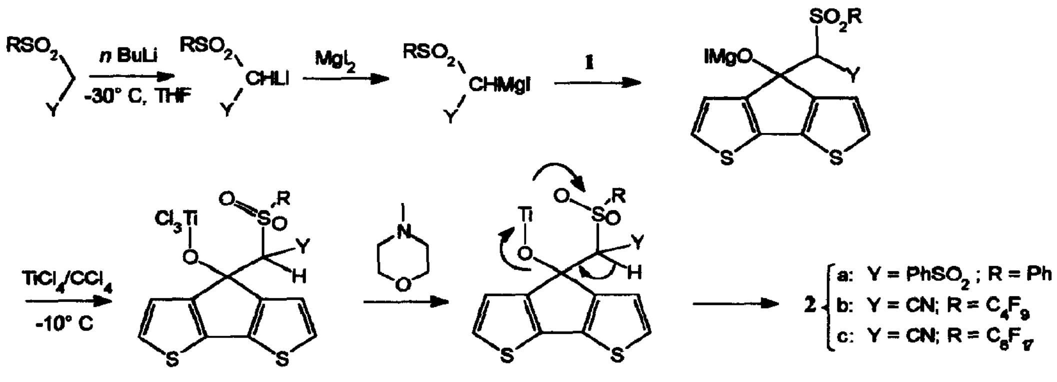
1



2

The Knoevenagel reaction can be effected by many reagents such as KF-alumina,[3] phase transfer catalysis,[4] methylene bis(magnesium iodide),[5] $TiCl_4$/pyridine,[6] $TiCl_4$/N-methylmorpholine,[7] ammonium acetate, benzylamine and glacial acetic acid,[8] piperidine-ethanol[9] and piperidinium acetate-benzene,[10] etc. The majority work well with aldehydes and moderately well for ketones, but often fail with hindered or less active ketones as was the case with **1**. We were able, however, to obtain monomers **2a** (X, Y = SO_2Ph), **2b** (X = -CN, Y = $-SO_2C_4F_9$) and **2c** (X = -CN, Y = $-SO_2C_8F_{17}$) by using a *combination* of these methods, outlined in Scheme 1. Here the active methylene was deprotonated with NaH and subsequently converted to the Grignard reagent by treatment with MgI_2. This anion was then added to a solution of 1 and the adduct was stabilized as its Ti chelate. The final deprotonation/elimination was effected by N-methylmorpholine. Using this procedure we could obtain the three monomers **2a-c** in 34, 57 and 52% yields, respectively. In all cases unreacted **1** could be recovered *via* column chromatography affording material balances in excess of 90%. Although the yields are moderate, they are acceptable given our inability to obtain these derivatives by any of the other methods tried. These three monomers could be electropolymerized to produce polymers with E_{gap}'s of ≈ 0.7 eV which are lower than the corresponding dicyano derivative[1c] and will be the subject of a future report.[11] The generality of this method has not yet been tested be we are particularly interested in applying it to condensations between 1 and bis(perfluoroalkylsulfonyl) methanes since these derivatives are expected[11] to afford even lower E_{gap} materials.

Scheme 1



EXPERIMENTAL

General. Nonafluorobutanesulfonyl acetonitrile and heptadecafluorooctanesulfonyl acetonitrile were prepared according to the method described by Hanack.[2] Cyclopenta [2,1-b; 4,3-b'] dithiophen-4-one was prepared according to procedures described by Gronowitz,[12] Jordens,[13] and Rodriguez[1] with some modifications. All the other chemicals were obtained from Aldrich Chemical Co. and were used without further purification unless otherwise noted. NMR spectra were taken on JEOL FX-200 and/or JEOL 270 MHz instruments using $CDCl_3$ and TMS as an internal standard. Infrared spectra were taken on a Mattson Galaxy 2025 FT-IR instrument. The UV/Vis/NIR spectra were obtained on a Perkin-Elmer Lambda 9 instrument and the spectra processed using Spectra-Calc software (Galactic Ind. Corp.). Elemental analysis were done at Oneida Research Service, Inc., NY. Uncorrected melting points were taken on an Electrothermal 9100 capillary melting/boiling point apparatus. All the reactions were conducted under dry conditions under a nitrogen atmosphere. THF was dried over sodium and freshly distilled prior to the reactions. n-Butyllithium was titrated as described by Juaristi.[14]

Synthesis of monomers: 2a. A 100 mL 3 necked round bottom flask, fitted with magnetic stirring, reflux condenser, N_2 inlet and a dry-ice/isopropanol bath was charged with 593 mg (2 mmol) of bis(phenylsulfonyl) methane and the reaction flask was evacuated and flushed with N_2 several times. THF (17 mL) was added to dissolve the methylene compound and the reaction mixture was cooled to -40° C. Next 1.3mL of n-BuLi (1.6M in hexane) were added dropwise to form the anion as a white suspension. The reaction mixture was allowed to reach room temperature and stirred for 40 min. after which 15.3 mL (2.2 mmol) of a 0.1438M solution of MgI_2 in benzene/ether were added dropwise to form the Grignard reagent which was stirred 30 min at room temperature. Fused ketone **1** (385 mg, 2 mmol) dissolved in dry THF was added dropwise to the reaction mixture which was then refluxed for 5 Hs. The reaction mixture was cooled to -10° C and 1.5 mL of $TiCl_4$ were added dropwise followed by stirring for 3 Hs to form the titanium complex. The reaction was cooled to -10° C and 1.5 mL of N-methyl morpholine were added dropwise followed by stirring for 8 Hs at room temperature. Brine (75 mL) was added to hydrolyze the reaction mixture, the layers were separated and the aqueous layer was extracted with 3 x 50 mL of ether. The ethereal layers were joined and washed with 5 x 50 mL brine, 50 mL 5% w/v aqueous $NaHCO_3$ and 50 mL water to neutral pH. The organic layer was dried over anhyd. Na_2SO_4 and solvent evaporated to dryness. The crude product was purified by column chromatography using silica gel and eluted with a mixture of hexane/ dichloromethane to afford 323 mg (34.3 % yield) of pure compound **2a** as a blue solid and 238 mg (61.8%) of recovered unreacted **1**. Compound **2a** had a m.p. = 255.7-256.6°C and exhibited a single blue spot on TLC. IR (KBr pellet, cm^{-1}): 3146, 3105, 2924, 2852, 1518, 1448, 1385, 1332, 1221, 1149, 1082, 736, 680. ^{1}H NMR, δ (ppm): 6.86 and 6.88 (d, J=4.69 Hz, 2H of thiophene rings), 7.53-7.38 (m, 6H *meta* and *para* of phenyl rings), 7.84 and 7.81 (d, J=7.81 Hz, 4H *ortho* of phenyl rings), 7.95 and 7.92 (d, 2H of thiophene rings); UV/Vis ($CHCl_3$): λ_{max} = 590 nm; Elemental analysis: found (calculated): %C =56.12 (56.15); %H = 3.03 (3.00) as $C_{22}H_{14}O_4S_4$. Compound **2b**, prepared in a similar manner from nonafluorobutanesulfonyl acetonitrile and **1**, was obtained as green plates after crystallization from ligroine in 52.0 % yield with m.p. = 142.5-143.3° C. IR (KBr pellet, cm^{-1}): 3101, 2220 (CN), 1548, 1386, 1352, 1238, 1175, 1136 (SO_2), 1030-806 (CF); ^{1}H NMR, δ(ppm): 6.99 and 6.97 (d, J=5.49 Hz, 1H of thiophene rings), 7.10 and 7.08 (d, J= 5.49 Hz, 1 H of thiophene rings), 7.57-7.50 (2d, J=4.88 Hz, 2H of thiophene rings); UV/Vis ($CHCl_3$): λ_{max} = 650 nm; Elemental analysis: found (calculated): %C=36.30 (36.22), %H=0.83 (0.81), %N=2.85 (2.82) as $C_{15}H_4F_9NO_2S_3$. Likewise compound **2c** could be prepared from **1** and heptadecafluorooctylsulfonyl acetonitrile as green plates in 57% yield with recovery of unreacted **1** (37%). Monomer **2c** had a m.p. = 160.3-161.6° C, and displayed a single spot in TLC silica strip in 100% CH_2Cl_2 with Rf = 0.568. IR (KBr pellet, cm^{-1}): 3101, 2962, 2924, 2852, 2220 (CN), 1549, 1387, 1352, 1238-1136 (SO_2) 1030-696 (CF); ^{1}H NMR, δ (ppm) : 6.99 & 6.97 (d, J = 5.49 Hz, 1H), 7.10 & 7.08 (d, J = 5.49, 1H), 7.57-7.50 (2d, J = 4.88, 5.49, 2H); UV/Vis ($CHCl_3$): λ_{max} = 642 nm; Elemental analysis: found (calculated) : %C = 32.77 (32.72), %H = 0.61 (0.58), %N = 2.0.4 (2.01) as $C_{19}H_8F_{17}NO_2S_3$.

ACKNOWLEDGMENT

Acknowledgment is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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(*Received in USA* 22 *June* 1994; *revised* 18 *August* 1994; *accepted* 23 *August* 1994)