LIST OF PUBLICATIONS
1) Rearrangement of Ethers: A New Route to Tolterodine.
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2) N,N-dimethylamino acrylate derivatives-Facile inexpensive synthesis of Rufinamide-an antiepileptic & Allopurinol-a drug for gout.
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3) Di and Trimerization of Acrylic reagent.
Veera Reddy Arava; Sashibhushan Malreddy; Srineevasulu Reddy Thummala. 
*Der pharma Chemica*, 2011, 3(2): 491-495.

4) Acid catalyzed Ether rearrangement total Synthesis of isomimosifoliol and dihydromimosifoliol.
Veera Reddy Arava; Sashibhushan Malreddy; Srineevasulu Reddy Thummala. 
*Synthetic communications* (In press).

5) Facile Acid Catalyzed Rearrangement of Ether to diarylmethanes.
Veera Reddy Arava; Sreenivasula Reddy Bandatmakuru; Sashibhushan Malreddy; Narayanaswamy Golla, Sreenivasula Reddy Thummala. 
*Der pharma Chemica*, (In press).
Rearrangement of Ethers: A New Route to Tolterodine

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Several different approaches have been reported for the asymmetric synthesis of tolterodine, utilizing asymmetric hydrogenation, conjugate addition of aryl boronic acids, Corey–Bakshi–Shibata (CBS) reduction, and copper hydride reduction as key steps.

The original synthesis and the modified approaches, which used the resolution methodology for the preparation of chiral tolterodine, went through the acid-catalyzed condensation of p-cresol to cinnamic acid. Although these modifications achieved good yields of rac-tolterodine, there is scope for more efficient methods using industrially feasible reagents.

RESULTS AND DISCUSSION

Tolterodine has a structural element with two different substituted phenyl rings attached to a carbon atom. We encountered this type of structural moiety in an ether to phenol rearrangement as shown in Scheme 1.

The retrosynthetic analysis of tolterodine leads to the intermediate ether 2 and diol 3 as shown in Scheme 2.

The diol 3 and compound 4 were prepared as per the De Castro procedure. The compound 4 obtained by the procedure was usually ~80% pure by high-performance liquid chromatography (HPLC). This was purified by salt (HCl) formation and rebasification to get >92% purity. The pure compound 4 was etherified with 4-fluoro toluene to get compound 2. The etherification is studied under different basic conditions to get optimum yields. The results are tabulated in Table 1.

Compound 2 was subjected to rearrangement conditions to yield rac-tolterodine in good yields. The rearrangement is studied under different conditions to get optimum yields. The results are tabulated in Table 2.

Our study also proved that the method described by De Castro for preparing the tolterodine from 4 with p-cresol may be passing through the intermediate 2. The rac-tolterodine 1 was resolved to prepare the drug using L-tartaric acid as a resolving agent.

In conclusion, we have developed a new route for tolterodine 1, without using the protection–deprotection strategy and with industrially feasible reagents.

Scheme 1. Rearrangement of ether to phenol.
completely removed. The organic layer was dried over anhydrous sodium sulfate and concentrated to get yellow oil of crude 4 (wt 30.0 g, yield 92%, HPLC purity 85.0%).

**Purification of 3-(Diisopropylamino)-1-phenylpropan-1-ol (4)**

The yellow oil (4) was dissolved in ethyl acetate (300 ml), and hydrogen chloride gas was bubbled through the solution until a white precipitate (sticky nature) was formed (pH 2–3). The ethyl acetate layer separated from the sticky mass, and then the mass was dissolved in water (100 ml) and washed with ethyl acetate (2 × 50 ml). The aqueous layer pH is adjusted to basic (pH 9–10) with 30% aqueous ammonia solution. The solution was extracted with dichloromethane (200 ml), and the aqueous layer was separated and re-extracted with dichloromethane (2 × 50 ml). The combined organic layers were then washed with water (2 × 100 ml) and dried over anhydrous sodium sulfate. The solution was concentrated at 30–35 °C to get pale yellow oil (wt 25.0 g, yield 90%, HPLC purity 92–93%).

IR (neat) (cm$^{-1}$): 3191, 3061, 3027, 2966, 2871, 2839, 1946, 1877, 1807, 1603, 1463, 1453, 1390, 1367, 1339, 1200, 1167, 1056, 984, 751, 699. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$= 1.05 (6 H, d, $J$= 6.54 Hz), 1.17 (6H, d, $J$= 6.71 Hz), 1.70 (1H, m), 1.9 (1H, m), 2.81 (2H, m), 3.20 (2H, m), 4.9 (1H, dd, $J_1$= 9.83, $J_2$= 2.03 Hz), 7.31 (5H, m). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$= 18.53, 21.49, 35.21, 43.89, 47.21, 47.33, 75.83, 125.50, 125.66, 126.98, 128.0, 128.16, 145.21. MW for C$_{15}$H$_{25}$NO [M + H]: Calcd.: 236.37, observed: 236.40

**Preparation of Diisopropyl-(3-phenyl-3-p-toluyloxy-propyl)-amine(2)**

To a stirred solution of dimethyl sulfoxide (456 ml), 12.0 g (0.05 mol) of 3-(diisopropylamino)-1-phenylpropan-1-ol (4) and 16.8 g (0.255 mol) of potassium hydroxide (85% assay) were added and heated at 100–105 °C for 90 min. The resulting slurry was allowed to cool to 80–85 °C, and 16.85 g (0.153 mol) of 4-fluoro toluene were added in 20 min. The reaction mixture was heated to reflux (140–145 °C) for 4 h and allowed to cool to ~90 °C; 70 ml of water and 70 ml of toluene were then added. The reaction mixture was stirred for 20 min, and then layers were separated. The aqueous layer was extracted again with 3 × 20 ml of toluene. The combined organic layers were washed with 3 × 20 ml of water and dried over anhydrous sodium sulfate. The solution was concentrated at 50–60 °C to get a brown oil (wt 15.0 g, yield 90%, HPLC purity 92–93%).

**Purification of Diisopropyl-(3-phenyl-3-p-toluyloxy-propyl)-amine(2)**

The obtained brown oil was dissolved in ethylacetate (100 ml), and 5.3 g of 85% orthophosphoric acid were added dropwise at rt (25–30 °C). After the addition was complete, the reaction mixture was stirred for 30 min and then cooled to 10–15 °C and stirred for 1 h. The slurry was then filtered, and the solids were washed with 20 ml of cold ethylacetate (10–15 °C). The solid was stirred in a mixture of 50 ml dichloromethane and 50 ml of water at 25–30 °C, and 15 ml of 30% aqueous ammonium hydroxide solution were added. The reaction mixture were stirred for 10 min at 25–30 °C, and the layers were separated. The organic layer was washed
0.022 mol) was added to the solution at 10–15 °C. The reaction mixture was stirred for 20 min at 20–25 °C (completion of the reaction was monitored by TLC). The reaction mixture was quenched in ice water (50 ml) and was basified to pH 9–10 with aqueous ammonium hydroxide. The reaction mixture was stirred for 30 min. The layers were separated, and the aqueous layer was extracted with dichloromethane (2 × 10 ml). The combined organic layers were collected, washed with water (2 × 50 ml), and dried over anhydrous sodium sulfate. The solution was concentrated at 30–35 °C to get pale yellow oil (wt 5.0 g, yield 65%, HPLC purity 60–65%).

The crude base was dissolved in 10 ml of n-hexane at about 50 °C. The clear solution was cooled to −5 to −10 °C for 3 h and the precipitated solids were filtered and dried to get pure racemic tolterodine base (wt 3.0 g, yield 60%, purity by HPLC 98.80%, Mp 72.3–73.5 °C).

IR (KBr) (cm⁻¹): 3058, 3023, 2974, 2936, 2831, 1699, 1607, 1509, 1491, 1365, 1263, 1223, 1163, 1136, 810, 740, 698. ¹H NMR (400 MHz, CDCl₃): δ = 1.10 (6H, d, J = 6.35 Hz), 1.15 (6H, d, J = 6.56 Hz), 2.09 (1H, m), 2.12 (3H, s), 2.37 (2H, m), 2.74 (2H, m), 3.25 (2H, m), 4.49 (1H, dd, J₁ = 10.96, J₂ = 3.90 Hz), 6.56 (1H, s), 6.84 (2H, m), 7.24 (1H, m), 7.33 (4H, d, J = 4.30 Hz), 10.1 (1H, br). ¹³C NMR (100 MHz, CDCl₃): δ = 19.46, 19.88, 20.69, 33.21, 39.27, 42.04, 47.87, 118.05, 126.04, 127.65, 128.19, 128.43, 128.56, 129.25, 132.3, 144.69, 153.12. MW for C₁₅H₂₃NO [M + H]: calcd.: 326.50, observed: 326.40.

REFERENCES
N, N-Dimethylamino acrylate derivatives - Facile inexpensive synthesis of Rufinamide-an antiepileptic & Allopurinol-a drug for gout

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ABSTRACT

A new protocol for the facile synthesis of Rufinamide and Allopurinol medicaments is developed by the utilization of N,N-dimethylamino acrylate derivatives.

Keywords: N,N-dimethylamino acrylate derivatives, Rufinamide, Allopurinol, Medicaments.

INTRODUCTION

Rufinamide is a triazole derivative that is an anticonvulsant medication used in combination with other medication and therapy to treat Lennox-Gastaut Syndrome and various other forms of epilepsy [1]. Among the various antiepileptic drugs (AEDs), Rufinamide is the one recently approved by USFDA for effective controlling of seizures. It is presumed to involve stabilization of the sodium channel inactive state, effectively keeping these ion channels closed.

Allopurinol is a structural isomer of hypoxanthine (a naturally occurring purine in the body) and is an enzyme inhibitor of xanthine oxidase [2]. It is used to treat chronic gout ("the king of diseases and the disease of kings" or "rich man’s disease") [3]. Gout is a medical condition usually characterized by recurrent attacks of acute inflammatory arthritis – a red, tender, hot, swollen joint. It may also present as tophi, kidney stones, or urate nephropathy, which is caused by elevated levels of uric acid in the blood which crystallize and are deposited in joints, tendons and surrounding tissues.
General Procedure for the synthesis of Allopurinol (2)
a) Synthesis of 3-Amino-4-carbethoxy pyrazole sulfate salt (8)

Ethyl-2-cyano-3-(dimethylamino)acrylate 7 (102.0 gm, 0.606 M) was dissolved in methanol (408.0 mL) at room temperature and added hydrazine hydrate [(38.0 gm, 1.25 M) 45.0 mL of 85% aqueous solution] drop wise at RT under nitrogen atmosphere. Stirred for 10 hrs at RT (The completion of the reaction was monitored by TLC). Evaporated methanol completely under vacuum at 45°C and added ethyl acetate (955.0 mL) at 20-25°C and stirred for 10 min to get clear solution. Washed with water (100.0 mL X 2) and sat. brine solution (100.0 mL) and then distilled out half of the solvent and given carbon treatment (10.0 gm) to the remaining solution. Added cone. Sulfuric acid (59.0 gm 1.0 M) drop wise with external cooling (0 - 5°C). Stirred for 1 hr and collected the solids through filtration and washed with ethyl acetate (50.0 mL X 2). Off-White powder; Yield: 84 %; HPLC purity: >99 %; mp: 176 - 180 °C; FT-IR (cm⁻¹): 3431 (-NH₂), 3312 (-NH), 1715 (C=O), 1639, 1566, 1335, 1211, 1079, 887, 597; ¹HNMR (ppm, DMSO): δ 11.78 (broad, s, 1H, -NH), 8 7.39 (s, 1H, -CH), 5 5.94 (s, 2H, -NH₂), 5 4.13 (q, 2H, J = 6.9 Hz, -CH₂), δ 1.22 (t, 3H, -CH₃); ¹³CNMR (DMSO/TMS) δ, 164.01, 156.57, 151.58, 139.77, 131.82, 93.78, 58.83, 14.82.

b) Synthesis of 1H-pyrazolo[3,4-d]pyrimidin-4-nol (2)

3-Amino-4-carbethoxy pyrazole sulfate salt 8 (126.0 gm, 0.497M) and 504.0 mL formamide were heated to 165 - 170°C under N₂ atmosphere and stirred for 14 to 16 hrs (Completion of the reaction was monitored by TLC). After completion of the starting material, cooled the slurry to RT and further to 0 - 5°C. Stirred for 1 hr and filtered the material. The obtained material (60.0 gm) was dissolved in 5% aqueous NaOH solution (540.0 mL) at RT and treated with activated carbon (6.0 gm). The aqueous layer pH adjusted to 3.5 to 4.0 with 2N HCl solution (370.0 mL) and stirred for 30 min at RT. Collected the solids through filtration and washed with DM Water (100.0 mL X 3) and finally with acetone (50.0 mL X 3). Off-White powder; Yield: 81 %; FT-IR (cm⁻¹): 3166 (NH), 3081, 3043, 2992, 2938, 2877, 1975, 1699 (C=O), 1586, 1478, 1389, 1366, 1239, 1228, 1159, 1085, 955, 913, 884, 813, 781, 707, 604 and 540; ¹HNMR (ppm, DMSO): δ 12.70 - 12.42 (broad, s, 2H, -NH & -OH), δ 8.10 (s, 1H, -CH), δ 7.90 (s, 1H, -CH); ¹³CNMR (DMSO/TMS) δ, 158.16, 155.0, 147.88, 134, 105.89; ESI-MS (m/z %): 137.1 (M+1, 100%).

RESULTS AND DISCUSSION

In continuation of our earlier work [5], now we wish to report our studies on the application of N, N-dimethylamino acrylate derivatives in the optimized preparation of Rufinamide and Allopurinol medicaments. The construction of heterocycles is an important aspect in synthetic organic chemistry. The process should be simple and should not contain tedious work-up for scale-up in industry as well as academics. As already mentioned the dimethylamino acrylate derivatives can be easily prepared from abundantly available inexpensive raw-materials i.e. DMF and DMS. These acrylate derivatives can be effectively used for the construction of many heterocycles bearing triazoles, pyrazoles, pyrazolo pyrimidines, oxazoles, isoxazoles, thiazoles etc. which are the building blocks for many biologically active molecules.

Rufinamide is an anti epileptic drug possessing triazole ring. Several synthetic routes have been reported earlier [4, 6, 7, and 8]. All the routes were mainly concentrated on the construction of triazole ring only by the cycloaddition of dipolarophile with the azide starting material, prepared
carried out with 1:1 mole ratio of azide 4 and acrylate 5 followed by ammonolysis. But here the yield obtained is only 48%. So, to improve the yield slight excess of acrylate (2.5:1) is taken for the cycloaddition reaction.

Dimethylamino acrylate derivatives have the same oxidation state as alkynes and can serve as alkyne synthons. Cycloaddition of these acrylates with alkyl azide results in 1,2,3-triazoline intermediate and with hydrazine hydrate results in pyrazoline intermediate which lose dimethylamine to aromatize the ring. The regiochemistry of the cycloadditions is controlled by the leaving group i.e. dimethylamine which is lost during the reaction [10].

Earlier syntheses of Allopurinol reported from ethoxy-methylene-cyanoacetic acid ethyl ester 12 [11] (Scheme 5), pyrazole-3,4-dicarboxylic acid 14 [12] (Scheme 6), cyanoace-tamide 21 [13] (Scheme 7), 4,6-dichloro-5-formylpyrimidine 25 [14] (Scheme 8).

We have synthesized 2, starting from ethyl-2-cyano-3-(dimethylamino) acrylate 7 in two step processes. First treating 7 with 85% hydrazine hydrate in methanol as solvent medium at room temperature followed by sulfate salt preparation of the formed amino pyrazole ring. Then further cyclisation is carried out with formamide at 165-170°C afforded light gray color solid which on
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Di and Trimerization of Acrylic reagents

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ABSTRACT

Trimerization of methyl-3-(dimethylamino) acrylate leading to 1,3,5-bezene tricarboxylate methyl ester and dimerization of 3-dimethylamino acrylonitrile leading to amino methylenated glutaconic acid dinitrile catalyzed by different acids in 1,2-dimethoxy ethane solvent is reported.

Keywords: 3-(dimethylamino) acrylate reagents, dimerization, trimerization.

INTRODUCTION

Dimerization of 3-(dimethylamino) acrylonitrile 1 was reported by Scotti and Frazza [1] during 1964 to give aminomethylenated glutaconic acid dinitrile 2. Helmut Kraus from Bayer reported [2] better yields (90%) in making 2 and used this intermediate to prepare 2-amino-5-aminomethyl pyridine derivative 3 [3] which is an important intermediate in the preparation of insecticides of the nitromethylene class and 6-amino-nicotononitriles 4 [4] are intermediates for synthesizing pharmaceutical and agrochemical active compounds.

Scheme 1: Dimerization of 1 to 2 and its pyridine derivatives

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MATERIALS AND METHODS

$^1$H & $^{13}$C NMR spectra are recorded using a Bruker 400 Spectrometer (400 & 100 MHz respectively) with TMS as internal standard. Mass spectra are recorded on a Perkin-Elmer mass spectrometer operating at 70 eV. IR spectra are recorded on Perkin Elmer Spectrophotometer as KBr pellets or neat. Analytical TLC is conducted on E-Merck 60F254 aluminum-packed silica gel plates (0.2mm). Developed plates are visualized using UV light or Iodine chamber. HPLC spectra are recorded on shimadzu 2010.

General procedure for the synthesis of 1,3,5-benzene tricarboxylate methyl ester (7)
To a solution of methyl-3-(dimethylamino) acrylate 5 (20.0gms, 0.155 M) in 1,2-dimethoxy ethane (40ml), sulphuric acid (15.19gms, 0.155 M) was added at 20-25°C. The reaction mixture was stirred for 24 hours at rt. (The completion of the reaction was monitored by TLC). After completion of the staning material, the reaction mass was quenched into ice water (100ml) and product 5 was extracted with ethylacetate (100ml X 2). The combined organic layers were washed with water (20ml), and the organic layer was dried over anhydrous sodium sulphate. Concentration of the solvent under reduced pressure at 50°C to gave crude product (10.0gms). Purification of crude compound on column chromatography furnished white powder of 1,3,5-benzene tricarboxylate methyl ester 7 (7.8gms). Yield 60%; mp: 142.3-144.6°C; GC purity: 99.79%; FT-IR (cm$^{-1}$): 1732 (C=O), 1255; $^1$H NMR (ppm, CDCl$_3$): δ 8.86 (s, 3H), 3.98 (s, 9H); $^{13}$C NMR (ppm, CDCl$_3$): 165.33, 134.51, 131.09, 52.55; ESI-MS (m/z %): 253.1(M+1).

General procedure for the synthesis of N,N-dimethylamino methylene-glutaconic acid dinitrile (2)
To a solution of 3-dimethylamino acrylonitrile 1 (2.0gms, 0.0208M) in 1,2-dimethoxy ethane (6ml), orthophosphoric acid (2.03gms, 0.0208M) was added at rt. The reaction mixture was stirred for 3 hours at rt. (Completion of the reaction was monitored by TLC). After completion of staning material, the reaction mixture was quenched into ice water (10ml) and stirred for 30min at 10°C. The precipitated solid was collected through filtration and recrystallised from 10% methanol in toluene to get pale orange colour solid 2 (0.90gms). Yield: 60%; mp: 119.2-120.2°C; GC purity: 99.0%; FT-IR (cm$^{-1}$): 2205 (CN), 1638, 1591, 1402, 968. $^1$H NMR (ppm, DMSO): δ 7.44 (s, 1H), 7.18 (d, 2H, J=15.69Hz), 4.97 (d, 1H, J=15.67Hz), 3.23 (d, 6H, J=27.22Hz); $^{13}$C NMR (ppm, CDCl$_3$): 156.97, 151.26, 120.57, 117.64, 82.24, 75.07, 46.98, 38.29; ESI-MS (m/z %): 148.1(M+1).

General procedure for the synthesis of N,N-dimethylamino methylene-glutaconic acid dinitrile (2) in Acetic acid
To a stirred and cold (20°C) solution of glacial acetic acid (200ml), 3-dimethylamino acrylonitrile 1 (19.2gms, 0.2M) was added and stirred at rt (25-28°C) for 17hours. Acetic acid was evaporated under vacuum at 50°C, and the residue was stirred with water (130ml). The obtained solid product was filtered under suction and washed with water, the material 2 was dried at 50°C to get 12.9gms (80%) of pale orange solid.

RESULTS AND DISCUSSION

For our ongoing research programme we are interested in making compound 6 (aminomethylenated glutaconic acid dimethylate) from methyl-3-(dimethylamino) acrylate 5.
We tried to synthesize compound 6 by Krass method as shown in (Scheme 2). To our surprise we got a different product, which by $^1$H-NMR has only two peaks at $\delta$ 8.86 (3H of phenyl) and $\delta$ 3.98 (9H of 3 ester methyls). It became obvious by the $^1$H-NMR spectra that the product obtained is not a dimer but a trimer 7. The product is conformed by other spectral methods and to the authentic sample.

Dimerization of 5 was tried in various catalytic acid conditions in 1,2-dimethoxy ethane as solvent medium (Table-1) to isolate 6, but all our efforts lead to trimerization product 7 only.

**Table 1: Trimerization of acrylate ester 5 to give 7.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Temp/Time</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Sulphuric acid</td>
<td>1,2-dimethoxyethane</td>
<td>25°C/24hours</td>
<td>60</td>
</tr>
<tr>
<td>02</td>
<td>Orthophosphoric acid</td>
<td>1,2-dimethoxyethane</td>
<td>80°C/6hours</td>
<td>45</td>
</tr>
<tr>
<td>03</td>
<td>Boron trifluoride etherate</td>
<td>1,2-dimethoxyethane</td>
<td>25°C/18hours</td>
<td>32</td>
</tr>
<tr>
<td>04</td>
<td>Aluminium chloride</td>
<td>1,2-dimethoxyethane</td>
<td>25°C/6hours</td>
<td>32</td>
</tr>
<tr>
<td>05</td>
<td>Silicotrifluoride</td>
<td>1,2-dimethoxyethane</td>
<td>60°C/2hours</td>
<td>40</td>
</tr>
<tr>
<td>07</td>
<td>Para toluenesulfonic acid</td>
<td>1,2-dimethoxyethane</td>
<td>80°C/10hours</td>
<td>30</td>
</tr>
<tr>
<td>08</td>
<td>Titaniumtetrachloride</td>
<td>1,2-dimethoxyethane</td>
<td>25°C/12hours</td>
<td>40</td>
</tr>
<tr>
<td>09</td>
<td>Glacial acetic acid</td>
<td>1,2-dimethoxyethane</td>
<td>25°C/17hours</td>
<td>47</td>
</tr>
</tbody>
</table>
With these results in hand, we tried the trimerization of \(1\) in different acid catalysts and 1,2-dimethoxy ethane as solvent medium (table 2) to get tricyano benzene, but all our efforts are in vain. We also have ended with the dimerization of \(1\) to \(2\) only.

### Table 2: Dimerization of \(1\) instead of trimerization in acid and DME solvent

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Time/ temp</th>
<th>solvent</th>
<th>%yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>-</td>
<td>25°C/17hours</td>
<td>Glacial acetic acid</td>
<td>80</td>
</tr>
<tr>
<td>02</td>
<td>Orthophosphoric acid</td>
<td>25°C/3hours</td>
<td>1,2-dimethoxyethane</td>
<td>60</td>
</tr>
<tr>
<td>03</td>
<td>Perchloric acid</td>
<td>25°C/4hours</td>
<td>1,2-dimethoxyethane</td>
<td>26</td>
</tr>
<tr>
<td>04</td>
<td>Aluminium chloride</td>
<td>25°C/12hours</td>
<td>1,2-dimethoxyethane</td>
<td>35</td>
</tr>
<tr>
<td>05</td>
<td>Silicon tetrachloride</td>
<td>80°C/2hours</td>
<td>1,2-dimethoxyethane</td>
<td>40</td>
</tr>
<tr>
<td>06</td>
<td>Boron trifluoride etherate</td>
<td>25°C/13hours</td>
<td>1,2-dimethoxyethane</td>
<td>30</td>
</tr>
<tr>
<td>07</td>
<td>Conc. HCl</td>
<td>25°C/3hours</td>
<td>1,2-dimethoxyethane</td>
<td>35</td>
</tr>
</tbody>
</table>

The results obtained by us are in accordance with the results of Kochetkov [5] reaction with \(\beta\)-aminovinylmethyl ketones to 1,3,5-triacetyl benzene [6]. The question remains unanswered why 3-dimethylamino acrylonitrile stopped at dimerization where as the ester and ketone derivatives lead to trimerization without the dimerization product.

**CONCLUSION**

Methyl-3-(dimethylamino) acrylate \(5\) undergoes trimerization directly without the dimerization product, where as 3-dimethylamino acrylonitrile \(1\) undergoes only dimerization instead of trimerization in 1,2-dimethoxy ethane solvent and various acid catalysts.

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**REFERENCES**

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Date: 18/07/2011
Title: Facile Acid Catalyzed Rearrangement Of Ethers to Diarylmethanes

Dear Dr Veerareddy, Arava

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